Regio- and Stereoselective Synthesis of Thiazoline Derivatives via the Thioketene-Induced Ring Expansion of Aziridines

Qiuyue Wu and Jiaxi Xu*
State Key Laboratory of Chemical Resource Engineering, Department of Organic Chemistry, College of Chemistry, Beijing University of Chemical Technology, Beijing 100029, China.
jxxu@mail.buct.edu.cn

Supporting information

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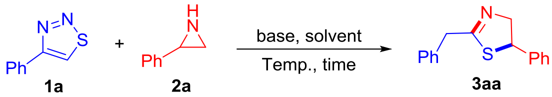
General Information

Melting points were measured on a Yanaco MP-500 melting point apparatus and are uncorrected. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer in $CDCl_3$. Chemical shifts are reported in ppm and referenced to tetramethylsilane (TMS) or residual solvent peaks as internal standards (tetramethylsilane 0 ppm for ^{1}H and $CDCl_3$ 77.00 ppm for ^{13}C). The high-resolution mass spectra were obtained under ESI ionization using an Agilent LC/MSD TOF mass spectrometer. Specific rotations were measured on an Anton Paar MCP500 polarimeter. Column chromatography was carried out on silica gel (200−300 mesh) with a mixture of petroleum ether (PE, 60 °C−90 °C) and ethyl acetate (EA) as the eluent. All reactions were monitored by thin-layer chromatography (TLC) where practical, using silica gel GF254 fluorescent treated silica gel plates, which were visualized under UV light (254 nm). The enantiomeric excesses were determined by chiral HPLC analysis using an Agilent 1260 LC instrument with Daicel Chiralpak AS-H and Daicel Chiralpak AS-H column with a mixture of isopropyl alcohol and hexane as eluents.Commercial-grade reagents and solvents were used as received without further purification unless otherwise noted, anhydrous solvents were purified with the standard processes.

Detailed optimization of the reaction conditions

Initially, 4-phenyl-1,2,3-thiadiazole (1a) as the precursor of phenylthioketene and 2-phenylaziridine (**2a**) were selected as the model substrates to optimize the reaction conditions (Table 1). Initially, the reaction was conducted in acetonitrile in a microwave reactor in the presence of different inorganic and organic bases. All tested inorganic bases K_2CO_3, Cs_2CO_3, and K_3PO_4 and organic base DMAP promoted the reaction and gave the product 2-benzyl-5-phenylthiazoline (**3aa**) in 53%, 38%, 46%, and 52% yields, respectively (Entries 1–3 and 6). However, pyridine and DIEPA are inefficient (Entries 5 and 7). The structure of **3aa** was identified by comparison of its spectral data with the reported ones.[11] Different solvents were tested. Although toluene, chlorobenzene, 1,2-dichloroethane, and THF are inert due to poor solubility of K_2CO_3 in them (not shown), polar solvents DMSO and DMF are more efficient (Entries 9 and 11). Elevating temperature did not improve the yield (Entries 8 and 10). The bases were evaluated again in the best solvent DMF, showing that K_2CO_3 is the best choice (Entries 11–14). Increasing amounts of aziridine **2a** and base K_2CO_3 did not improved the yield (Entries 15–20). Finally, the optimal reaction conditions were determined as thiadiazole (0.1 mmol), aziridine (0.1 mmol) and base K_2CO_3 (0.1 mmol) in DMF (0.5 mL) at 130 °C for 5 min under microwave irradiation (Table 1, entry 11).

Table S1. Optimization of the reaction conditions[a]



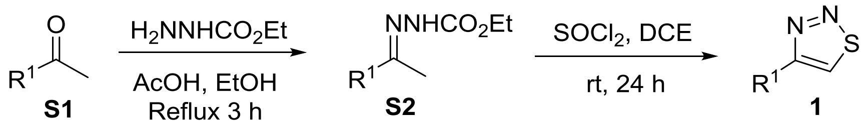
Entry	**2a** mmol	Base/ mmol	Solvent	Temp./ °C	Time Min.	Yield%
1	0.1	K_2CO_3/0.1	MeCN	130	5	53
2	0.1	Cs_2CO_3/0.1	MeCN	130	5	38
3	0.1	K_3PO_4/0.1	MeCN	130	5	46
4	0.1	DBU/0.1	MeCN	130	5	41
5	0.1	Py/0.1	MeCN	130	5	0
6	0.1	DMAP/0.1	MeCN	130	5	52
7	0.1	DIPEA/0.1	MeCN	130	5	trace
8	0.1	K_2CO_3/0.1	MeCN	160	5	53
9	0.1	K_2CO_3/0.1	DMSO	130	5	58
10	0.1	K_2CO_3/0.1	DMSO	140	180[b]	35
11	0.1	K_2CO_3/0.1	DMF	130	5	68
12	0.1	Cs_2CO_3/0.1	DMF	130	5	50
13	0.1	K_3PO_4/0.1	DMF	130	5	48
14	0.1	DBU/0.1	DMF	130	5	44
15	0.2	K_2CO_3/0.1	DMF	130	5	63
16	0.2	K_2CO_3/0.2	DMF	130	5	63
17	0.2	K_2CO_3/0.3	DMF	130	5	62
18	0.3	K_2CO_3/0.1	DMF	130	5	61
19	0.3	K_2CO_3/0.2	DMF	130	5	53
20	0.3	K_2CO_3/0.3	DMF	130	5	57

[a]Reactions were conducted on a 0.1 mmol scale of **1a** in the presence of base in anhydrous solvent (0.5 mL) in a microwave reactor. All yields are the NMR yields. [b]Heated in an oil bath.

General procedure for synthesis of 4-substituted 1,2,3-thiadiazoles 1

4-Substituted 1,2,3-thiadiazoles were synthesized according to reported procedures.[1] Ketone **S1** (10 mmol) and ethyl hydrazinecarboxylate **S2** (1.3 g, 12.5 mmol) were added into a round bottom flask with a magneton followed by addition of ethanol (7 mL) as solvent and acetic acid (0.13 mL, 0.176 g, 3 mmol) as a catalyst. The flask was then connected to a condenser pipe and kept refluxing in an oil bath for 3 hours. After the reaction was finished, the solvent was removed under reduced pressure. The residue in the flask containing ethyl hydrazinecarboxylate **S2** was dissolved in 14 mL of pre-dried dichloroethane, into which was added $SOCl_2$ (3.3 mL, 5.4 g, 45 mmol) dropwise. After stirring at room temperature for 24 hours, excess $SOCl_2$ was firstly removed by rotary evaporator. The solution was neutralized with saturated sodium bicarbonate aqueous solution till no gas generated. The solution in the flask was then extracted with dichloromethane (10 mL x 3). The organic layers were combined and dried over Na_2SO_4. After removal of solvent, the residue was purified by silica gel column chromography (PE/EA = 5:1, *v*/*v*) to give 1,2,3-thiadiazole **1**.

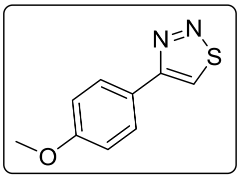
[1] (a) Hurd, C. D.; Mori, R. I. *J. Am. Chem. Soc.* **1955**, *77*, 5359; (b) Kobori, T.; Fujita, M.; Hiyama, T.; Kondo, K. *Heterocycles* **1993**, *36*, 4.



Scheme S1. Synthesis of 1,2,3-thiadiazoles **1**

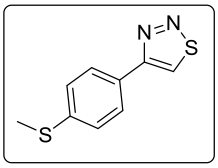
Synthesis of 1,2,3-thiadiazoles **1a**,**1b**, **1c**, **1d**, **1i**, **1j**, **1k**, **1l**, **1m** ,**1o**,**1s**, **1t** and **1u** was reported in the previous work of our group.[2]

4-(4-Methoxyphenyl)-1,2,3-thiadiazole (1e) [CAS:18212-22-1]



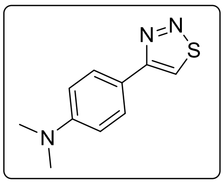
Colorless crystals, 1.71g, 61% yield, R_f = 0.30 (PE/EtOAc = 5:1, v/v), m.p. 83 – 85 °C (Lit.[3] 88 – 89 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (s, 1H), 8.01 – 7.95 (m, 2H), 7.06 – 7.00 (m, 2H), 3.88 (s, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 162.7, 160.5, 128.7, 128.4, 123.6, 114.5, 55.4.

4-(4-(Methylthio)phenyl)-1,2,3-thiadiazole (1f) [CAS: 2104659-06-3]



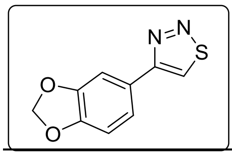
Pale yellow crystals, 896 mg, 43% yield, R_f = 0.35 (PE/EtOAc = 5:1, *v/v*), m.p. 112 – 113 °C (Lit.[4] 135 – 137 °C). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.59 (s, 1H), 8.02 – 7.93 (m, 2H), 7.41 – 7.33 (m, 2H), 2.54 (s, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 162.5, 140.5, 129.3, 127.7, 127.4, 126.6, 15.4.

***N*,*N*-Dimethyl-4-(1,2,3-thiadiazol-4-yl)aniline (1g) [CAS: 2387106-66-1]**



Pale yellow crystals, 1.70g, 83% yield, R_f = 0.2 (PE/EtOAc = 5:1, *v/v*), m.p. 99 – 101 °C (Lit.[5] 115 – 117 °C). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.40 (s, 1H), 7.98 – 7.83 (m, 2H), 6.86 – 6.71 (m, 2H), 3.03 (s, 6H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 163.5, 151.0, 128.3, 126.7, 118.8, 112.3, 40.3.

4-(Benzo[*d*][1,3]dioxol-5-yl)-1,2,3-thiadiazole (1h) [CAS: 313251-27-3]

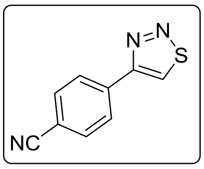


White crystals, 673 mg, 33% yield, R_f = 0.45 (PE/EtOAc = 5:1, *v/v*), m.p. 110 – 115 °C (Lit.[6] 124 – 126 °C). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.50 (s, 1H), 7.56 – 7.51 (m, 2H), 6.95

[2] (a) He, W.; Zhuang, J. P.; Yang, Z. H.; Xu, J. X. *Org. Biomol. Chem.* **2017**, *15*, 5541; (b) He, W.; Zhuang, J. P.; Du, H. G.; Yang, Z. H.; Xu, J. X. *Org. Biomol. Chem.* **2017**, *15*, 9424.
[3] Butler, R. N.; O'Donoghue, D. A. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1223.
[4] Ishikawa, T.; Kimura, M.; Kumoi, T.; Iida, H. *ACS Catalysis* **2017**, *7*, 4986.
[5] Lu, Y.; Sun, Y.; Abdukader, A.; Liu, C. *Synlett* **2021**, *32*, 1044.
[6] Chen, J.; Jiang, Y.; Yu, J.-T.; Cheng, J. *J. Org. Chem.* **2016**, *81*, 271.

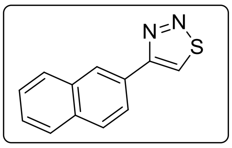
– 6.90 (m, 1H), 6.04 (s, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 162.6, 148.6, 148.4, 128.8, 124.9, 121.5, 108.9, 107.8, 101.5.

4-(1,2,3-Thiadiazol-4-yl)benzonitrile (1n) [CAS: 82894-99-3]



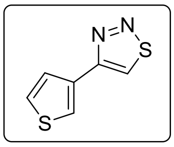
Yellow crystals, 1.15 g, 61% yield, R_f = 0.20 (PE/EtOAc = 5:1, *v/v*), m.p. 121 – 123 °C (Lit.[7] 109 – 110 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.81 (s, 1H), 8.22 – 8.15 (m, 2H), 7.84 – 7.77 (m, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 160.8, 134.8, 133.0, 132.1, 127.8, 118.3, 112.9.

4-(Naphthalen-2-yl)-1,2,3-thiadiazole (1p) [CAS: 77414-52-9]



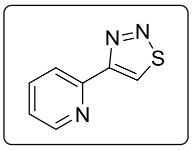
Pale pink crystals, 2.10 g, 99% yield, R_f = 0.50 (PE/EtOAc = 5:1, *v/v*), m.p. 199 – 200 °C (Lit.[8] 202 – 203 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (s, 1H), 8.64 – 8.58 (m, 1H), 8.11 (dd, J = 8.5, 1.8 Hz, 1H), 8.01 – 7.86 (m, 3H), 7.60 – 7.51 (m, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 133.7, 133.5, 130.1, 129.0, 128.5, 128.1, 127.8, 126.9, 126.8, 124.7.

4-(Thiophen-3-yl)-1,2,3-thiadiazole (1q) [CAS: 176037-41-5]



Pale pink crystals, 1.43 g, 85% yield, R_f = 0.20 (PE/EtOAc = 5:1, *v/v*), m.p. 55 – 56 °C (Lit.[9] 67 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (s, 1H), 7.98 (dd, J = 3.0, 1.3 Hz, 1H), 7.62 (dd, J = 5.1, 1.3 Hz, 1H), 7.45 (dd, J = 5.0, 3.0 Hz, 1H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 158.4, 132.1, 129.2, 126.9, 126.4, 124.1.

4-(Pyridin-2-yl)-1,2,3-thiadiazole (1r) [CAS: 176037-42-6]



Pale yellow crystals, 552 mg, 34% yield, R_f = 0.15 (DCM/MeOH = 100:1, *v/v*), m.p. 176 – 177 °C (Lit.[10] 163 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.23 (d, J = 4.4 Hz, 1H), 8.74 – 8.63 (m, 1H), 8.47 (dt, J = 7.9, 1.1 Hz, 1H), 7.87 (td, J = 7.7, 1.8 Hz, 1H), 7.39 – 7.30 (m, 1H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 163.3, 149.8, 149.7, 137.3, 133.9, 123.9, 122.4.

General procedure for synthesis of *N*-unsubstituted aziridines 2

Synthesis of *N*-unprotected aziridines **2a**, (*S*)-**2a**, **2b**, **2c**, **2d**, **2e**, **2f**, **2g**, **2h**, (*S*)-**2h**, **2i**, (*S*)-**2i**, **2j**, (*S*)-**2j**, and **2m** was reported in the previous work of our group.[11] *N*-Unprotected aziridines **2k** and **2l** were prepared from the

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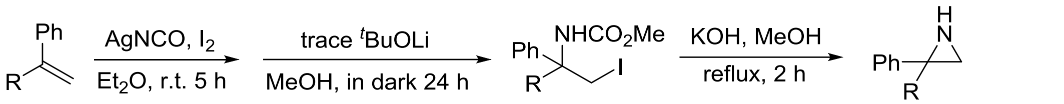
[7] Lu, Y.; Sun, Y.; Abdukader, A.; Liu, C. *Synlett* **2021**, *32*, 1044.
[8] Li, W.; Zhang, J.; He, J.; Xu, L.; Vaccaro, L.; Liu, P.; Gu, Y. *Frontiers in Chemistry* **2020**, *8*.
[9] Clausen, R. P.; Becher, J. *Tetrahedron* **1996**, *52*, 3171.
[10] Hayat, F.; Salahuddin, A.; Zargan, J.; Azam, A. *Eur. J. Med. Chem.* **2010**, *45*, 6127.
[11] (a) Chen, X.; Lin, C.; Du, H.; Xu, J. *Adv. Synth. Catal.* **2019**, *361*, 1647; (b) Chen, X.; Huang, Z.; Xu, J. *Adv. Synth. Catal.* **2021**, *363*, 3098.

corresponding epoxides through the ring-opening with NaN_3 and the Blum aziridination. *N*-Unprotected aziridines **2n** and **2o** were synthesized according to the reported procedures.[12]



S3: R= Me
S4: R= Ph

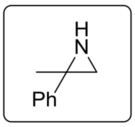
S5: R= Me
S6: R= Ph

2n: R= Me, 53% yield in two steps
2o: R= Ph, 74% yield in two steps

Scheme S2. Synthesis of 2,2-disubstituted aziridines **2n**,**o**

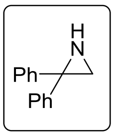
In a round bottom flask, AgNCO (969 mg, 6.5 mmol) and I_2 (1.27 g, 5.0 mmol) were dissolved in 10 mL of Et_2O. After stirring at room temperature for 30 min, the flask was then moved into an ice bath followed by adding 5 mmol of alkenes **S3** or **S4** slowly. When the solution turned into pale colour, inoganic salts were removed by filtration. 10 mL of anhydrous methanol and 1 drop of a diluted solution of ^tBuOLi (prepared by dissolving 160 mg of ^tBuOLi in 1 mL of MeOH) were added in the solution. The solution was then kept stirring under dark at room temperature for 24 hours. After removal of most solvent by rotary evaporator, the resulting solution was extracted with Et_2O (10 mL x 3). The combined organic phase was washed with iced water and dried over sodium sulfate. After removal of solvent, the residue containing iodo isocyanate **S5** or **S6** was dissolved in methanolic KOH (prepared by dissolving 37 g of KOH in 400 mL of MeOH) and kept refluxing in an oil bath for 2 hours. The solution was concentrated followed by extraction with Et_2O (10 mL x 3). The organic layer was combined, washed with water, and then dried over Na_2SO_4. After removal of solvent, the residue was purified by silica gel column chromography alkalized with triethylamine (DCM/MeOH = 50:1, *v*/*v*) to give *N*-unprotected aziridines **2n** and **2o**.

2-Methyl-2-phenylaziridine (2n) [CAS: 22596-57-2]



Pale yellowish oil, 352 mg, 53 % yield, R_f = 0.45 (DCM/MeOH = 50:1, *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.26 (m, 4H), 7.26 – 7.18 (m, 1H), 2.02 – 1.85 (m, 2H), 1.60 (s, 3H), 0.63 (brs, 1H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ143.5, 128.2, 126.6, 126.0, 36.7, 34.9, 25.0.

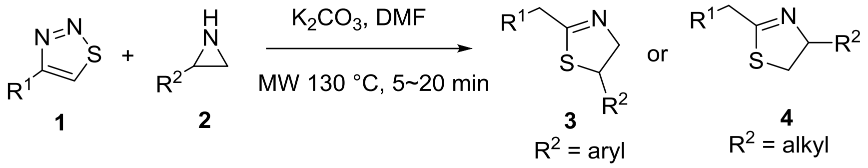
2,2-Diphenylaziridine (2o) [CAS: 25564-63-0]



Pale yellowish oil, 720 mg, 74 % yield, R_f = 0.20 (DCM/MeOH = 50:1, *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.20 (m, 10H), 2.37 (s, 2H), 0.96 (brs, 1H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 142.6, 128.3, 127.7, 127.1, 43.9, 35.4.

[12] (a) Hassner, A.; Heathcock, C. *J. Org. Chem.* **1965**, *30*, 1748; (b) Hassner, A.; Lorber, M. E.; Heathcock, C. H. *J. Org. Chem.* **1967**, *32*, 540.

General procedure for synthesis of 2-substitutted thiazolines 3 and 4



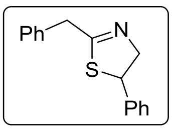
Scheme S3. Synthesis of thiazolines **3** and **4**.

Thiadiazole **1** (0.2 mmol), *N*-unprotected aziridine **2** (0.4 mmol), K_2CO_3 (28 mg, 0.2 mmol), and 1 mL of super dry DMF [or thiadiazole **1** (0.3 mmol), *N*-unprotected aziridine **2** (0.4 mmol), K_2CO_3 (42 mg, 0.3 mmol), and 1.5 mL of super dry DMF] were added into a 10 mL pre-dried microwave tube with a magneton. The tube was then heated by microwave reactor at 130 °C for 5 – 30 minutes. After the reaction finished, the suspension was added water (10 mL) and extracted with ethyl acetate (5 mL × 3). The organic layer was combined and dried over Na_2SO_4. After removal of solvent the residuewas purified with silica gel column chromography with a mixture of petroleum ether (PE) (60–90 °C) and ethyl acetate (EA) (20:1 to 5:1, *v*/*v*) as eluent to give product **3** and **4**.

Gram scale synthesis of (*S*)-4ah:

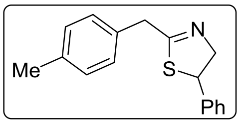
Thiadiazole **1a** (1.62 g, 10 mmol), *N*-unprotected aziridine (*S*)-**2h** (2.66 g, 20 mmol), K_2CO_3 (1.38 g, 10 mmol) and 20 mL of super dry DMF were added into a 35 mL pre-dried microwave tube with a magneton. The tube was then heated by a microwave reactor at 130 °C for 20 minutes. After the work-up procedure, (*S*)-**4ah** was obtained with 1.65 g, 62% yield.

2-Benzyl-4-phenyl-4,5-dihydrothiazole (3aa)



Reaction conditions: **1a** (0.3 mmol) and **2a** (0.4 mmol) for 10 min. Pale yellowish oil, 47 mg, 62% yield, R_f = 0.3 (PE/EA = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.18 (m, 10H), 4.91 (dd, J = 9.0, 5.8 Hz, 1H), 4.55 (ddt, J = 15.7, 9.1, 1.6 Hz, 1H), 4.36 (ddt, J = 15.7, 5.9, 1.4 Hz, 1H), 3.87 (t, J = 1.6 Hz, 2H). ^{13}C NMR{^{1}H (101 MHz, $CDCl_3$) δ 169.7, 142.0, 135.9, 129.1, 128.7, 128.6, 127.6, 127.1, 126.9, 72.8, 55.2, 40.8. HRMS (ESI-TOF) *m/z* [M+H]$^+$ calcd. for $C_{16}H_{16}NS^+$ 254.0998, found 254.1008.

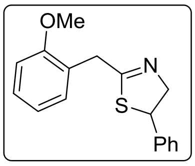
2-(4-Methylbenzyl)-5-phenyl-4,5-dihydrothiazole (3ba)



Reaction conditions: **1b** (0.2 mmol) and **2a** (0.4 mmol) for 30 min. Yellowish oil, 39 mg, 73% yield, R_f = 0.30 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.18 (m, 6H), 7.13 (d, J = 7.8 Hz, 2H), 4.90 (dd, J = 9.0, 5.8 Hz, 1H), 4.54 (ddt, J = 15.6, 9.0, 1.6 Hz, 1H), 4.35 (ddt, J = 15.7, 5.8, 1.4 Hz, 1H), 3.85 (d, J = 16.0 Hz, 1H), 3.81(d, J = 16.0 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 170.1, 142.0, 136.7, 132.8, 129.6, 129.3, 129.2, 128.9, 128.7, 127.6, 126.9, 72.7, 55.1, 40.4, 21.1. HRMS (ESI-TOF) *m/z*

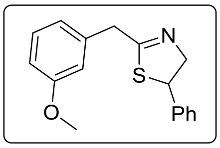
$[M+H]^+$ calcd. for $C_{17}H_{18}NS^+$ 268.1154, found 268.1151.

2-(2-Methoxybenzyl)-5-phenyl-4,5-dihydrothiazole (3ca)



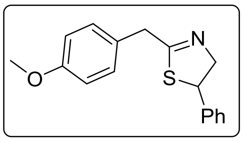
Reaction conditions: **1c** (0.2 mmol) and **2a** (0.4 mmol) for 15 min. Pale Yellowish oil, 43 mg, 76% yield, R_f = 0.15 (PE/EtOAc = 5:1, *v/v*). ^1H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.19 (m, 7H), 6.96 – 6.84 (m, 2H), 4.87 (dd, J = 9.0, 5.5 Hz, 1H), 4.54 (ddt, J = 15.6, 9.0, 1.7 Hz, 1H), 4.36 (ddt, J = 15.6, 5.5, 1.4 Hz, 1H), 3.91 – 3.89 (m, 2H), 3.84 (s, 3H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): δ 170.1, 157.4, 142.5, 130.6, 128.7, 128.6, 127.5, 127.0, 124.7, 120.5, 110.5, 72.7, 55.3, 54.8, 35.1. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{18}NOS^+$ 284.1104, found 284.1095.

2-(3-Methoxybenzyl)-5-phenyl-4,5-dihydrothiazole (3da)



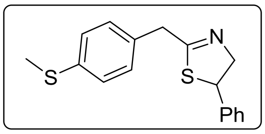
Reaction conditions: **1d** (0.2 mmol) and **2a** (0.4 mmol) for 30 min. Pale yellowish oil, 28 mg, 50% yield, R_f = 0.30 (PE/EtOAc = 5:1, *v/v*). ^1H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.24 (m, 3H), 7.24 – 7.19 (m, 3H), 6.94 – 6.78 (m, 3H), 4.93 (dd, J = 9.0, 5.7 Hz, 1H), 4.56 (ddt, J = 15.7, 9.0, 1.5 Hz, 1H), 4.37 (ddt, J = 15.6, 5.7, 1.3 Hz, 1H), 3.85 (s, 2H), 3.79 (s, 3H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): δ 169.7, 159.7, 142.0, 137.4, 129.6, 128.7, 127.6, 126.9, 121.5, 114.6, 112.7, 72.7, 55.2, 55.2, 40.9. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{18}NOS^+$ 284.1104, found 284.1096.

2-(4-Methoxybenzyl)-5-phenyl-4,5-dihydrothiazole (3ea)



Reaction conditions: **1e** (0.2 mmol) and **2a** (0.4 mmol) for 15 min. Pale yellowish oil, 40 mg, 71% yield, R_f = 0.15 (PE/EtOAc = 5:1, *v/v*). ^1H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.18 (m, 7H), 6.89 – 6.83 (m, 2H), 4.91 (dd, J = 9.0, 5.7 Hz, 1H), 4.55 (ddt, J = 15.6, 9.0, 1.6 Hz, 1H), 4.36 (ddt, J = 15.7, 5.8, 1.4 Hz, 1H), 3.81 (s, 2H), 3.78 (s, 3H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): δ 170.3, 158.7, 142.0, 130.1, 128.7, 128.0, 127.6, 126.9, 114.0, 72.8, 55.2, 55.1, 39.9. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{18}NOS^+$ 284.1104, found 284.1100.

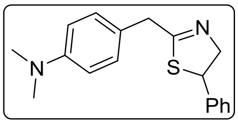
2-(4-(Methylthio)benzyl)-5-phenyl-4,5-dihydrothiazole (3fa)



Reaction conditions: **1f** (0.2 mmol) and **2a** (0.4 mmol) for 15 min. Brown oil, 43 mg, 72 % yield, R_f = 0.20 (PE/EtOAc = 5:1, *v/v*). ^1H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.16 (m, 9H), 4.93 (dd, J = 9.0, 5.8 Hz, 1H), 4.56 (ddt, J = 15.7, 9.0, 1.6 Hz, 1H), 4.36 (ddt, J = 15.7, 5.8, 1.3 Hz, 1H), 3.85 (dt, J = 15.6, 1.6 Hz, 1H), 3.71 (dt, J = 15.6, 1.6 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): δ 169.6, 141.9, 137.2, 132.7, 129.6, 128.7, 127.6, 126.9, 126.8, 72.8, 55.2, 40.2, 15.8. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{18}NS_2^+$ 300.0875, found

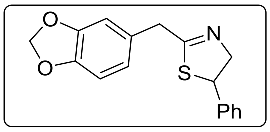
300.0877.

(*N,N*-Dimethyl-4-((5-phenyl-4,5-dihydrothiazol-2-yl)methyl)aniline (3ga)



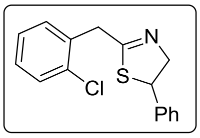
Reaction conditions: **1g** (0.2 mmol) and **2a** (0.4 mmol) for 15 min. Brown oil, 40 mg, 67% yield, R_f = 0.15 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.30 – 7.19 (m, 5H), 7.19 – 7.14 (m, 2H), 6.73 – 6.66 (m, 2H), 4.89 (dd, *J* = 9.0, 5.8 Hz, 1H), 4.55 (ddt, *J* = 15.6, 9.0, 1.5 Hz, 1H), 4.35 (ddt, *J* = 15.6, 5.8, 1.3 Hz, 1H), 3.81 (d, *J* = 16.0 Hz, 1H), 3.76 (d, *J* = 16.0 Hz, 1H), 2.92 (s, 6H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 171.0, 149.7, 142.1, 129.8, 128.7, 127.5, 127.0, 123.6, 112.7, 72.8, 55.0, 40.6, 39.9. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{18}H_{21}N_2S^+$ 297.1420, found 297.1419.

2-(Benzo[*d*][1,3]dioxol-5-ylmethyl)-5-phenyl-4,5-dihydrothiazole (3ha)



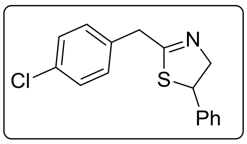
Reaction conditions: **1h** (0.2 mmol) and **2a** (0.4 mmol) for 15 min. Yellowish oil, 33 mg, 56% yield, R_f = 0.30 (PE/EtOAc = 5:1, *v/v*).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.20 (m, 5H), 6.80 – 6.76 (m, 3H), 5.93 (s, 2H), 4.92 (dd, *J* = 9.0, 5.8 Hz, 1H), 4.56 (ddt, *J* = 15.7, 9.1, 1.6 Hz, 1H), 4.36 (ddt, *J* = 15.7, 5.9, 1.4 Hz, 1H), 3.80 (dt, *J* = 16.0, 1.6 Hz, 1H), 3.76 (dt, *J* = 16.0, 1.6 Hz, 1H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 170.0, 147.7, 146.7, 141.9, 129.5, 128.7, 127.6, 126.9, 122.2, 109.5, 108.3, 101.0, 72.7, 55.2, 40.4. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{16}NO_2S^+$ 298.0896, found 298.0887.

2-(2-Chlorobenzyl)-5-phenyl-4,5-dihydrothiazole (3ia)



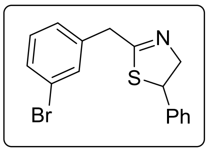
Reaction conditions: **1i** (0.2 mmol) and **2a** (0.4 mmol) for 5 min. Brown oil, 48 mg, 84% yield, R_f = 0.30 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.41 – 7.34 (m, 2H), 7.32 – 7.17 (m, 7H), 4.56 (ddt, *J* = 15.7, 9.1, 1.9 Hz, 1H), 4.38 (ddt, *J* = 15.7, 5.7, 1.6 Hz, 1H), 4.03 (dt, *J* = 16.0, 1.7 Hz, 1H), 3.99 (dt, *J* = 16.0, 1.7 Hz, 1H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 168.5, 142.0, 134.5, 134.2, 131.2, 129.6, 128.7, 128.7, 127.6, 127.0, 126.9, 72.8, 55.2, 38.3. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{16}H_{15}ClNS^+$ 288.0608, found 288.0604.

2-(4-Chlorobenzyl)-5-phenyl-4,5-dihydrothiazole (3ja)



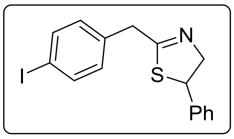
Reaction conditions: **1j** (0.2 mmol) and **2a** (0.4 mmol) for 15 min. Yellowish oil, 38 mg, 66% yield, R_f = 0.40 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.40 – 7.13 (m, 9H), 4.94 (dd, *J* = 9.0, 5.7 Hz, 1H), 4.55 (ddt, *J* = 15.7, 9.1, 1.6 Hz, 1H), 4.36 (ddt, *J* = 15.7, 5.7, 1.3 Hz, 1H), 3.83 (t, *J* = 1.5 Hz, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 169.1, 141.8, 134.4, 133.1, 130.4, 128.7, 127.7, 126.9, 72.7, 55.3, 40.0. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{16}H_{15}ClNS^+$ 288.0608, found 288.0605.

2-(3-Bromobenzyl)-5-phenyl-4,5-dihydrothiazole (3ka)



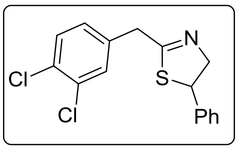
Reaction conditions: **1k** (0.2 mmol) and **2a** (0.4 mmol) for 5 min. Yellowish oil, 46 mg, 69% yield, R_f = 0.30 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (t, *J* = 1.9 Hz, 1H), 7.40 (dt, *J* = 7.7, 1.7 Hz, 1H), 7.33 – 7.16 (m, 7H), 4.95 (dd, *J* = 9.0, 5.7 Hz, 1H), 4.57 (ddt, *J* = 15.7, 9.0, 1.6 Hz, 1H), 4.38 (ddt, *J* = 15.7, 5.7, 1.4 Hz, 1H), 3.84 (t, *J* = 1.5 Hz, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 168.4, 141.7, 136.1, 131.3, 131.3, 131.0, 130.5, 128.8, 128.5, 127.8, 126.9, 72.7, 55.5, 39.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{16}H_{15}BrNS^+$ 332.0103, found 332.0098.

2-(4-Iodobenzyl)-5-phenyl-4,5-dihydrothiazole (3la)



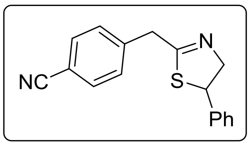
Reaction conditions: **1l** (0.2 mmol) and **2a** (0.4 mmol) for 5 min. Yellowish oil, 48 mg, 63% yield, R_f = 0.3 (PE/EA = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 – 7.61 (m, 2H), 7.32 – 7.18 (m, 5H), 7.09 – 7.02 (m, 2H), 4.93 (dd, *J* = 9.0, 5.8 Hz, 1H), 4.55 (ddt, *J* = 15.7, 9.0, 1.7 Hz, 1H), 4.36 (ddt, *J* = 15.6, 5.8, 1.5 Hz, 1H), 3.80 (s, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 168.9, 141.7, 137.6, 135.5, 131.1, 128.7, 127.7, 126.9, 92.7, 72.7, 55.3, 40.2. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{16}H_{15}INS^+$ 379.9964, found 379.9969.

2-(3,4-Dichlorobenzyl)-5-phenyl-4,5-dihydrothiazole (3ma)



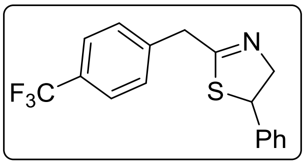
Reaction conditions: **1m** (0.2 mmol) and **2a** (0.4 mmol) for 5 min. Yellowish oil, 39 mg, 61% yield, R_f = 0.30 (PE/EtOAc = 5:1, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.37 (m, 2H), 7.33 – 7.20 (m, 5H), 7.15 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.96 (dd, *J* = 9.0, 5.7 Hz, 1H), 4.56 (ddt, *J* = 15.8, 9.0, 1.6 Hz, 1H), 4.38 (ddt, *J* = 15.8, 5.7, 1.4 Hz, 1H), 3.81 (t, *J* = 1.5 Hz, 2H). ^{13}C NMR{1H} (101 MHz, $CDCl_3$): δ 168.4, 141.7, 136.1, 131.1, 130.5, 128.9, 128.8, 128.5, 127.8, 127.0, 126.9, 72.7, 55.5, 39.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{16}H_{14}Cl_2NS^+$ 322.0219, found 322.0211.

4-((5-Phenyl-4,5-dihydrothiazol-2-yl)methyl)benzonitrile (3na)



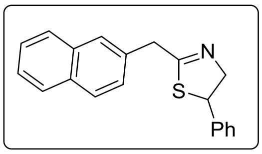
Reaction conditions: **1n** (0.2 mmol) and **2a** (0.4 mmol) for 15 min. Yellowish oil, 15 mg, 27% yield, R_f = 0.30 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 – 7.59 (m, 2H), 7.47 – 7.39 (m, 2H), 7.34 – 7.18 (m, 5H), 4.98 (dd, *J* = 9.1, 5.8 Hz, 1H), 4.57 (ddt, *J* = 15.8, 9.1, 1.6 Hz, 1H), 4.38 (ddt, *J* = 15.8, 5.8, 1.4 Hz, 1H), 3.92 (t, *J* = 1.5 Hz, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 167.9, 141.6, 141.4, 132.4, 129.9, 128.8, 128.4, 127.8, 126.9, 125.6, 118.7, 111.2, 72.8, 55.6, 40.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{15}N_2S^+$ 279.0950, found 279.0959.

5-Phenyl-2-(4-(trifluoromethyl)benzyl)-4,5-dihydrothiazole (3oa)



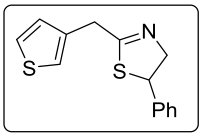
Reaction conditions: **1o** (0.2 mmol) and **2a** (0.4 mmol) for 5 min. Brown oil, 37 mg, 58% yield, R_f = 0.10 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.19 (m, 5H), 4.97 (dd, *J* = 9.0, 5.8 Hz, 1H), 4.57 (ddt, *J* = 15.7, 9.0, 1.6 Hz, 1H), 4.38 (ddt, *J* = 15.8, 5.9, 1.4 Hz, 1H), 3.92 (s, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 168.6, 141.7, 140.0, 129.5, 128.8, 127.8, 126.9, 125.60, 125.56, 72.8, 55.5, 40.4. ^{19}F NMR{^{1}H} (377 MHz, $CDCl_3$) δ -62.48. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{15}F_3NS^+$ 322.0872, found 322.0869.

2-(Naphthalen-2-ylmethyl)-5-phenyl-4,5-dihydrothiazole (3pa)



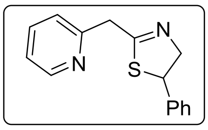
Reaction conditions: **1p** (0.2 mmol) and **2a** (0.4 mmol) for 15 min. Brown oil, 28 mg, 46% yield, R_f = 0.30 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.76 (m, 4H), 7.49 – 7.40 (m, 3H), 7.28 – 7.16 (m, 5H), 4.92 (dd, *J* = 9.0, 5.7 Hz, 1H), 4.57 (ddt, *J* = 15.7, 9.0, 1.6 Hz, 1H), 4.38 (ddt, *J* = 15.7, 5.8, 1.3 Hz, 1H), 4.03 (s, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 169.7, 141.9, 133.5, 133.4, 132.5, 128.7, 128.3, 127.8, 127.7, 127.6, 127.6, 127.2, 126.9, 126.1, 125.8, 72.8, 55.3, 41.0. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{20}H_{18}NS^+$ 304.1154, found 304.1149.

5-Phenyl-2-(thiophen-3-ylmethyl)-4,5-dihydrothiazole (3qa)



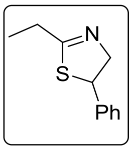
Reaction conditions: **1q** (0.2 mmol) and **2a** (0.4 mmol) for 15 min. Brown oil, 50 mg, 97% yield, R_f = 0.20 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.20 (m, 6H), 7.16 (dq, *J* = 3.0, 1.0 Hz, 1H), 7.05 (dd, *J* = 4.9, 1.3 Hz, 1H), 4.94 (dd, *J* = 9.0, 5.7 Hz, 1H), 4.57 (ddt, *J* = 15.7, 9.1, 1.6 Hz, 1H), 4.37 (ddt, *J* = 15.7, 5.7, 1.4 Hz, 1H), 3.90 (t, *J* = 1.8 Hz, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 169.2, 142.0, 135.7, 128.7, 128.3, 127.6, 126.9, 125.9, 122.8, 72.8, 55.2, 35.3. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{14}H_{14}NS_2^+$ 260.0562, found 260.0566.

4-Phenyl-2-(pyridin-2-ylmethyl)-4,5-dihydrothiazole (3ra)



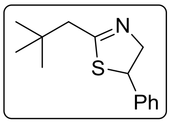
Reaction conditions: **1r** (0.2 mmol) and **2a** (0.4 mmol) for 15 min. Yellowish oil, 17 mg, 33% yield, R_f = 0.05 (PE/EtOAc = 5:1, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 – 8.54 (m, 1H), 7.66 (td, *J* = 7.7, 1.9 Hz, 1H), 7.37 – 7.30 (m, 1H), 7.30 – 7.17 (m, 6H), 4.97 (dd, *J* = 9.1, 5.8 Hz, 1H), 4.59 (ddt, *J* = 15.7, 9.1, 1.6 Hz, 1H), 4.38 (ddt, *J* = 15.7, 5.8, 1.4 Hz, 1H), 4.09 (t, *J* = 1.6 Hz, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 168.1, 156.1, 149.6, 141.9, 136.7, 128.7, 127.6, 127.0, 123.5, 122.1, 72.8, 55.4, 43.4. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd. for $C_{15}H_{15}N_2S^+$ 277.0770, found 277.0760.

2-Ethyl-5-phenyl-4,5-dihydrothiazole (3sa)



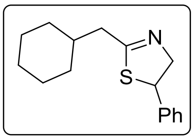
Reaction conditions: **1s** (0.2 mmol) and **2a** (0.4 mmol) for 5 min. Pale yellowish oil, 19 mg, 50% yield, R_f = 0.45 (PE/EA = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.22 (m, 5H), 4.94 (dd, *J* = 9.0, 5.6 Hz, 1H), 4.54 (ddt, *J* = 15.5, 9.0, 1.8 Hz, 1H), 4.35 (ddt, *J* = 15.6, 5.6, 1.5 Hz, 1H), 2.58 (qt, *J* = 7.5, 1.6 Hz, 2H), 1.26 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 172.0, 142.3, 128.7, 127.6, 126.9, 72.8, 54.8, 27.7, 11.8. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{11}H_{14}NS^+$ 192.0841, found 192.0849.

2-Neopentyl-5-phenyl-4,5-dihydrothiazole (3ta)



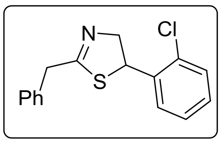
Reaction conditions: **1t** (0.2 mmol) and **2a** (0.4 mmol) for 5 min. Colourless oil, 10 mg, 21% yield, R_f = 0.3 (PE/EA = 5/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.21 (m, 5H), 4.94 (dd, *J* = 9.1, 5.7 Hz, 1H), 4.56 (ddt, *J* = 15.7, 9.1, 1.2 Hz, 1H), 4.39 (ddt, *J* = 15.6, 5.7, 1.0 Hz, 1H), 2.50 (d, *J* = 14.4 Hz, 1H), 2.46 (d, *J* = 14.4 Hz, 1H), 1.07 (s, 9H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 168.5, 142.4, 128.8, 127.6, 127.0, 72.7, 55.3, 47.7, 31.4, 29.9. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{14}H_{20}NS^+$ 234.1311, found 234.1319.

2-(Cyclohexylmethyl)-5-phenyl-4,5-dihydrothiazole (3ua)



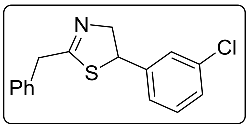
Reaction conditions: **1u** (0.3 mmol) and **2a** (0.4 mmol) for 30 min. Pale yellowish oil, 45 mg, 58% yield, R_f = 0.55 (PE/EA = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.21 (m, 5H), 4.94 (dd, *J* = 9.1, 5.7 Hz, 1H), 4.54 (ddt, *J* = 15.6, 9.1, 1.5 Hz, 1H), 4.35 (ddt, *J* = 15.6, 5.8, 1.3 Hz, 1H), 2.44 (dt, *J* = 6.8, 1.5 Hz, 2H), 1.86 – 1.61 (m, 6H), 1.36 – 1.09 (m, 3H), 1.07 – 0.93 (m, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 170.1, 142.3, 128.7, 127.6, 127.0, 72.7, 54.8, 42.0, 36.7, 33.1, 26.2, 26.0. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{16}H_{22}NS^+$ 260.1467, found 260.1473.

2-Benzyl-5-(2-chlorophenyl)-4,5-dihydrothiazole (3ab)



Reaction conditions: **1a** (0.2 mmol) and **2b** (0.4 mmol) for 15 min. Yellowish oil, 40 mg, 70% yield, R_f = 0.45 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.38 – 7.25 (m, 7H), 7.21 – 7.14 (m, 2H), 5.37 (dd, *J* = 8.9, 4.2 Hz, 1H), 4.55 (ddt, *J* = 15.8, 8.9, 1.7 Hz, 1H), 4.40 (ddt, *J* = 15.8, 4.2, 1.3 Hz, 1H), 3.88 (t, *J* = 1.4 Hz, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 169.7, 139.5, 135.8, 132.6, 129.5, 129.1, 128.7, 128.7, 127.9, 127.4, 127.2, 70.9, 51.0, 40.8. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{16}H_{15}ClNS^+$ 288.0608, found 288.0606.

2-Benzyl-5-(3-chlorophenyl)-4,5-dihydrothiazole (3ac)

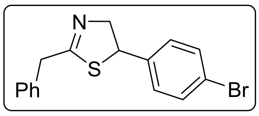


Reaction conditions: **1a** (0.2 mmol) and **2c** (0.4 mmol) for 10 min. Yellowish oil, 14 mg, 24% yield, R_f = 0.40 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.16 (m, 8H), 7.11 – 7.06 (m, 1H), 4.86 (dd, *J* = 9.0, 5.2 Hz, 1H), 4.56 (ddt, *J* = 15.7, 9.0, 1.6 Hz, 1H), 4.35 (ddt, *J* = 15.7, 5.2, 1.3 Hz, 1H), 3.89 (s, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 169.7, 144.2, 135.8, 134.7, 130.0, 129.1, 128.7, 127.8, 127.2, 127.1, 125.1, 72.7, 54.5, 40.8. HRMS (ESI-TOF) *m/z* [M+H]$^+$ calcd. for $C_{14}H_{15}ClNS^+$ 288.0608, found 288.0605.

2-Benzyl-5-(4-chlorophenyl)-4,5-dihydrothiazole (3ad)

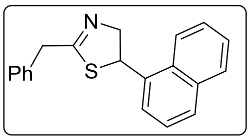
Reaction conditions: **1a** (0.2 mmol) and **2d** (0.4 mmol) for 15 min. Yellowish oil, 36 mg, 63% yield, R_f = 0.35 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.21 (m, 7H), 7.16 – 7.10 (m, 2H), 4.88 (dd, *J* = 9.0, 5.3 Hz, 1H), 4.55 (ddt, *J* = 15.7, 9.0, 1.6 Hz, 1H), 4.33 (ddt, *J* = 15.6, 5.2, 1.4 Hz, 1H), 3.87 (s, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 169.7, 140.7, 135.8, 133.4, 129.1, 128.9, 128.7, 128.3, 127.2, 72.7, 54.4, 40.8. HRMS (ESI-TOF) *m/z* [M+H]$^+$ calcd. for $C_{16}H_{15}ClNCS^+$ 288.0608, found 288.0604.

2-Benzyl-5-(4-bromophenyl)-4,5-dihydrothiazole (3ae)



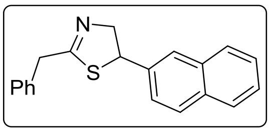
Reaction conditions: **1a** (0.2 mmol) and **2e** (0.4 mmol) for 10 min. Yellowish oil, 31 mg, 47% yield, R_f = 0.40 (PE/EA = 5/1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.34 (m, 2H), 7.34 – 7.23 (m, 5H), 7.11 – 7.03 (m, 2H), 4.85 (dd, *J* = 9.0, 5.3 Hz, 1H), 4.54 (ddt, *J* = 15.7, 9.0, 1.6 Hz, 1H), 4.32 (ddt, *J* = 15.7, 5.3, 1.3 Hz, 1H), 3.87 (t, *J* = 1.5 Hz, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 169.6, 141.2, 135.8, 131.8, 129.1, 128.7, 128.6, 127.2, 121.4, 72.7, 54.5, 40.8. HRMS (ESI-TOF) *m/z* [M+H]$^+$ calcd. for $C_{16}H_{15}BrNS^+$ 332.0103, found 332.0099.

2-Benzyl-5-(naphthalen-1-yl)-4,5-dihydrothiazole (3af)



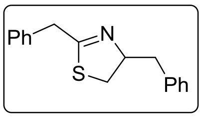
Reaction conditions: **1a** (0.2 mmol) and **2f** (0.4 mmol) for 15 min. Yellowish oil, 36 mg, 59% yield, R_f = 0.30 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 – 7.89 (m, 1H), 7.87 – 7.82 (m, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.53 – 7.46 (m, 3H), 7.42 – 7.23 (m, 6H), 5.70 (dd, *J* = 8.8, 5.1 Hz, 1H), 4.72 – 4.54 (m, 2H), 3.92 (dt, *J* = 17.2, 1.8 Hz, 1H), 3.88 (dt, *J* = 17.2, 1.8 Hz, 1H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 170.1, 136.9, 136.0, 133.9, 130.5, 129.06, 129.14, 128.7, 128.3, 127.2, 126.4, 125.8, 125.5, 124.1, 122.7, 70.7, 51.2, 41.0. HRMS (ESI-TOF) *m/z* [M+H]$^+$ calcd. for $C_{20}H_{18}NS^+$ 304.1154, found 304.1151.

2-Benzyl-5-(naphthalen-2-yl)-4,5-dihydrothiazole (3ag)



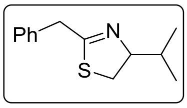
Reaction conditions: **1a** (0.2 mmol) and **2g** (0.4 mmol) for 15 min. Yellowish oil, 38 mg, 63% yield, R_f = 0.30 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.69 (m, 3H), 7.61 (d, *J* = 1.8 Hz, 1H), 7.48 – 7.39 (m, 2H), 7.37 – 7.23 (m, 6H), 5.08 (dd, *J* = 9.0, 5.5 Hz, 1H), 4.61 (ddt, *J* = 15.7, 9.0, 1.5 Hz, 1H), 4.46 (ddt, *J* = 15.7, 5.5, 1.3 Hz, 1H), 3.91 (t, *J* = 1.5 Hz, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 169.9, 139.2, 136.0, 133.1, 132.8, 129.1, 128.8, 128.7, 127.8, 127.6, 127.2, 126.3, 126.0, 125.6, 124.8, 72.6, 55.4, 40.8. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{20}H_{18}NS^+$ 304.1154, found 304.1149.

2,4-Dibenzyl-4,5-dihydrothiazole (4ah)



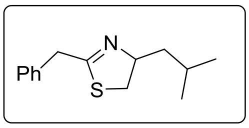
Reaction conditions: **1a** (0.2 mmol) and **2i** (0.4 mmol) for 10 min. Pale yellowish oil, 32 mg, 60 % yield, R_f = 0.40 (PE/EA = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.26 (m, 7H), 7.25 – 7.20 (m, 3H), 4.78 – 4.70 (m, 1H), 3.82 (s, 2H), 3.19 (dd, *J* = 14.0, 5.2 Hz, 1H), 3.17 (dd, *J* = 11.2, 8.4 Hz, 1H), 2.99 (dd, *J* = 11.2, 6.8 Hz, 1H), 2.74 (dd, *J* = 13.6, 9.1 Hz, 1H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 169.5, 138.3, 136.1, 129.2, 129.1, 128.6, 128.5, 127.1, 126.4, 78.1, 40.9, 40.1, 37.7. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{18}NS^+$ 268.1154, found 268.1161.

2-Benzyl-4-isopropyl-4,5-dihydrothiazole (4ai)



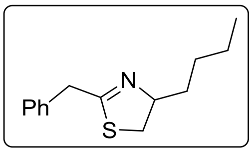
Reaction conditions: **1a** (0.2 mmol) and **2h** (0.4 mmol) for 5 min. Pale yellowish oil, 36 mg, 82% yield, R_f = 0.60 (PE/EA = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.21 (m, 5H), 4.28 (tdt, *J* = 9.0, 6.0, 1.4 Hz, 1H), 3.84 (dd, *J* = 16.0, 1.2 Hz, 1H), 3.79 (dd, *J* = 16.0, 1.6 Hz, 1H), 3.23 (dd, *J* = 10.9, 8.9 Hz, 1H), 2.99 (dd, *J* = 10.9, 9.1 Hz, 1H), 2.02 (dhept, *J* = 6.8, 6.8 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 168.4, 136.3, 129.0, 128.5, 127.0, 83.4, 40.9, 35.5, 32.8, 19.5, 18.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{13}H_{18}NS^+$ 220.1154, found 220.1161.

2-Benzyl-4-isobutyl-4,5-dihydrothiazole (4aj)



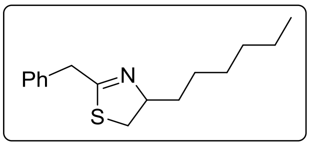
Reaction conditions: **1a** (0.2 mmol) and **2j** (0.4 mmol) at 125 °C for 15 min. Yellowish oil, 20 mg, 43 % yield, R_f = 0.30 (DCM/EtOAc = 200:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 – 7.07 (m, 5H), 4.57 – 4.42 (m, 1H), 3.81 (s, 2H), 3.33 (dd, *J* = 10.8, 8.3 Hz, 1H), 2.89 (dd, *J* = 10.8, 7.9 Hz, 1H), 1.87 – 1.65 (m, 2H), 1.46 – 1.33 (m, 1H), 0.98 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 168.3, 136.2, 129.0, 128.6, 127.0, 75.5, 44.2, 40.93, 39.0, 25.7, 22.9, 22.5. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{14}H_{20}NS^+$ 234.1311, found 234.1304.

2-Benzyl-4-buty-4,5-dihydrothiazole (4ak)



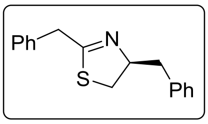
Reaction conditions: **1a** (0.2 mmol) and **2k** (0.4 mmol) at 125 °C for 15 min. Pale yellowish oil, 19 mg, 41 % yield, R_f = 0.30 (DCM/EtOAc = 200:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.37 – 7.21 (m, 5H), 4.50 – 4.35 (m, 1H), 3.81 (s, 2H), 3.33 (dd, *J* = 10.8, 8.8 Hz, 1H), 2.93 (dd, *J* = 10.8, 8.0 Hz, 1H), 1.89 – 1.75 (m, 1H), 1.63 – 1.52 (m, 1H), 1.49 – 1.30 (m, 4H), 0.92 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 168.4, 136.2, 129.1, 128.6, 127.1, 77.3, 40.9, 38.6, 34.8, 28.7, 22.7, 14.0. HRMS (ESI-TOF) *m/z* [M+H]$^+$ calcd. for $C_{14}H_{20}NS^+$ 234.1311, found 234.1307..

2-Benzyl-4-hexyl-4,5-dihydrothiazole (4al)



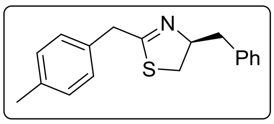
Reaction conditions: **1a** (0.2 mmol) and **2l** (0.4 mmol) at 125 °C for 15 min. Pale yellowish oil, 16 mg, 31 % yield, R_f = 0.40 (DCM/EtOAc = 200:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.52 – 7.03 (m, 5H), 4.51 – 4.35 (m, 1H), 3.81 (s, 2H), 3.33 (dd, *J* = 10.8, 8.5 Hz, 1H), 2.92 (dd, *J* = 10.8, 8.0 Hz, 1H), 1.88 – 1.74 (m, 1H), 1.70 – 1.50 (m, 1H), 1.49 – 1.37 (m, 2H), 1.37 – 1.25 (m, 6H), 0.89 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 168.4, 136.2, 129.1, 128.6, 127.0, 77.4, 40.9, 38.6, 35.1, 31.7, 29.3, 26.5, 22.6, 14.1. HRMS (ESI-TOF) *m/z* [M+H]$^+$ calcd. for $C_{16}H_{24}NS^+$ 262.1624, found 262.1616.

(*S*)-2,4-Dibenzyl-4,5-dihydrothiazole ((*S*)-4ah)



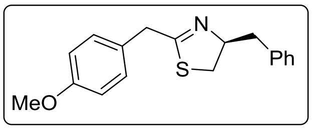
Reaction conditions: **1a** (0.2 mmol) and (*S*)-**2h** (0.4 mmol) for 5 min. Pale yellowish oil, 39 mg, 73% yield. R_f = 0.40 (PE/EA = 5:1, *v/v*). $[\alpha]_D^{25}$ -69.3° (c 0.40, CH_2Cl_2). Ee% > 99%, HPLC analysis: Daicel Chiralpak AD-H (*i*-PrOH/hexane = 0.9/99.1, *v/v*, 1.0 mL/min, 210 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.26 (m, 7H), 7.24 – 7.18 (m, 3H), 4.81 – 4.68 (m, 1H), 3.82 (s, 2H), 3.20 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.17 (dd, *J* = 10.8, 10.0 Hz, 1H), 2.99 (dd, *J* = 11.1, 6.8 Hz, 1H), 2.74 (dd, *J* = 13.6, 9.1 Hz, 1H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 169.5, 138.3, 136.1, 129.3, 129.1, 128.6, 128.5, 127.1, 126.4, 78.1, 40.9, 40.1, 37.7. HRMS (ESI-TOF) *m/z* [M+H]$^+$ calcd. for $C_{17}H_{18}NS^+$ 268.1154, found 268.1160.

(*S*)-4-Benzyl-2-(4-methylbenzyl)-4,5-dihydrothiazole ((*S*)-4bh)



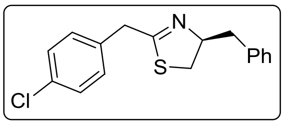
Reaction conditions: **1b** (0.2 mmol) and (*S*)-**2h** (0.4 mmol) for 10 min. Yellowish oil, 27 mg, 48% yield, R_f = 0.40 (PE/EtOAc = 5:1, *v/v*). $[\alpha]_D^{25}$ -57.0° (c 0.44, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.33 – 7.27 (m, 2H), 7.24 – 7.11 (m, 7H), 4.73 (tt, *J* = 9.2, 6.8 Hz, 1H), 3.80 (d, *J* = 15.2 Hz, 1H), 3.76 (d, *J* = 15.2 Hz, 1H), 3.19 (dd, *J* = 13.6, 5.2 Hz, 1H), 3.16 (dd, *J* = 10.8, 8.4 Hz, 1H), 2.99 (dd, *J* = 11.1, 6.8 Hz, 1H), 2.73 (dd, *J* = 13.6, 9.2 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 169.9, 138.4, 136.7, 133.0, 129.3, 129.3, 128.9, 128.5, 128.5, 128.4, 126.4, 78.1, 40.5, 40.2, 37.6, 21.1. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{18}H_{20}NS^+$ 282.1311, found 282.1320.

(*S*)-4-Benzyl-2-(4-methoxybenzyl)-4,5-dihydrothiazole ((*S*)-4eh)



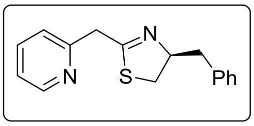
Reaction conditions: **1e** (0.2 mmol) and (*S*)-**2h** (0.4 mmol) for 15 min. Yellowish oil, 34 mg, 57% yield, R_f = 0.20 (PE/EtOAc = 5:1, *v/v*). $[\alpha]^{25}_{D}$ -54.4° (c 0.54, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.26 (m, 2H), 7.25 – 7.17 (m, 5H), 6.89 – 6.83 (m, 2H), 4.73 (tt, *J* = 9.2, 6.8 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 2H), 3.23 – 3.13 (m, 2H), 2.99 (dd, *J* = 11.1, 6.8 Hz, 1H), 2.73 (dd, *J* = 13.6, 9.2 Hz, 1H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): δ 170.2, 158.8, 138.4, 130.2, 129.3, 128.6, 128.2, 126.5, 114.1, 78.2, 55.3, 40.2, 40.1, 37.7. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{18}H_{20}NOS^+$ 298.1260, found 298.1269.

(*S*)-4-Benzyl-2-(4-chlorobenzyl)-4,5-dihydrothiazole ((*S*)-4jh)



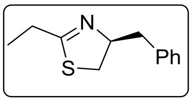
Reaction conditions: **1j** (0.2 mmol) and (*S*)-**2h** (0.4 mmol) for 10 min. Yellowish oil, 24 mg, 40% yield, R_f = 0.25 (PE/EtOAc = 5:1, *v/v*). $[\alpha]^{25}_{D}$ -72.6° (c 0.38, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.28 (m, 4H), 7.25 – 7.23 (m, 1H), 7.23 – 7.19 (m, 4H), 4.74 (tt, *J* = 9.0, 6.8 Hz, 1H), 3.78 (s, 2H), 3.24 – 3.14 (m, 2H), 3.01 (dd, *J* = 11.1, 6.8 Hz, 1H), 2.74 (dd, *J* = 13.6, 9.0 Hz, 1H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): δ 168.9, 138.2, 134.5, 130.4, 129.3, 128.7, 128.5, 126.5, 78.1, 40.1 (2C), 37.8. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{17}ClNS^+$ 302.0765, found 302.0772.

(*S*)-4-Benzyl-2-(pyridin-2-ylmethyl)-4,5-dihydrothiazole ((*S*)-4rh)



Reaction conditions: **1r** (0.2 mmol) and (*S*)-**2h** (0.4 mmol) for 30 min. Brown oil, 25 mg, 47% yield, R_f = 0.15 (DCM/MeOH = 20:1, *v/v*). $[\alpha]^{25}_{D}$ -36.8° (c 0.38, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.63 – 8.54 (m, 1H), 7.65 (dt, *J* = 1.9, 7.7 Hz, 1H), 7.36 – 7.27 (m, 3H), 7.25 – 7.16 (m, 4H), 4.76 (tt, *J* = 9.1, 6.8 Hz, 1H), 4.03 (s, 2H), 3.27 – 3.15 (m, 2H), 3.03 (dd, *J* = 11.1, 6.8 Hz, 1H), 2.75 (dd, *J* = 13.6, 9.1 Hz, 1H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): δ 168.0, 156.3, 149.6, 138.3, 136.6, 129.3, 128.5, 126.4, 123.4, 122.1, 78.0, 43.5, 40.1, 37.8. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{16}H_{17}N_2S^+$ 269.1107, found 269.1114.

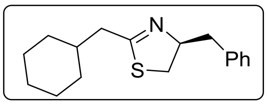
(*S*)-4-Benzyl-2-ethyl-4,5-dihydrothiazole ((*S*)-4sh)



Reaction conditions: **1s** (0.2 mmol) and (*S*)-**2h** (0.4 mmol) for 30 min. Pale yellowish oil, 13 mg, 32% yield, R_f = 0.25 (PE/EtOAc = 5:1, *v/v*). $[\alpha]^{25}_{D}$ -57.1° (c 0.34, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.28 (m, 2H), 7.26 – 7.20 (m, 3H), 4.74 – 4.66 (m, 1H), 3.26 – 3.13 (m, 2H), 3.01 (dd, *J* = 11.1, 6.8 Hz, 1H), 2.72 (dd, *J* = 13.6, 9.3 Hz, 1H), 2.53 (dq, *J* = 1.4, 7.6, Hz, 2H), 1.22 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR{^1H}

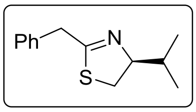
(101 MHz, $CDCl_3$): *δ* 171.9, 138.5, 129.3, 128.5, 126.4, 78.0, 40.3, 37.4, 27.9, 12.0. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{12}H_{16}NS^+$ 206.0998, found 206.1007.

(*S*)-4-Benzyl-2-(cyclohexylmethyl)-4,5-dihydrothiazole ((*S*)-4uh)



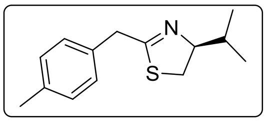
Reaction conditions: **1u** (0.2 mmol) and (*S*)-**2h** (0.4 mmol) for 30 min. Colorless oil, 31 mg, 57% yield, R_f = 0.50 (PE/EtOAc = 5:1, *v/v*). $[\alpha]_D^{25}$ -45.0° (c 0.54, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.32 – 7.28 (m, 2H), 7.26 – 7.20 (m, 3H), 4.74 – 4.67 (m, 1H), 3.23 – 3.13 (m, 2H), 3.01 (dd, *J* = 11.1, 6.6 Hz, 1H), 2.72 (dd, *J* = 13.6, 9.3 Hz, 1H), 2.39 (d, *J* = 7.0 Hz, 2H), 1.82 – 1.60 (m, 6H), 1.34 – 1.09 (m, 3H), 1.04 – 0.91 (m, 2H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): *δ* 169.9, 138.5, 129.3, 128.5, 126.4, 78.0, 42.0, 40.2, 37.3, 36.8, 33.0, 33.0, 26.2, 26.1. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{24}NS^+$ 274.1624, found 274.1632.

(*S*)-2-Benzyl-4-isopropyl-4,5-dihydrothiazole ((*S*)-4ai)



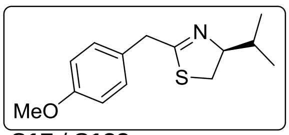
Reaction conditions: **1a** (0.2 mmol) and (*S*)-**2i** (0.2 mmol) for 5 min. Pale yellowish oil, 31 mg, 71% yield, R_f = 0.60 (PE/EA = 5:1, *v/v*). $[\alpha]_D^{25}$ -62.2° (c 0.36, CH_2Cl_2). Ee% > 99%, HPLC analysis: Daicel Chiralpak AS-H (*i*-PrOH/hexane = 0.3/99.7, *v/v*, 1.0 mL/min, 210 nm). ^1H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.22 (m, 5H), 4.29 (dtt, *J* = 6.0, 9.0, 1.5 Hz, 1H), 3.84 (d, *J* = 15.2 Hz, 1H, 3.80 (d, *J* = 16.0 Hz, 1H), 3.24 (dd, *J* = 10.9, 8.9 Hz, 1H), 2.99 (dd, *J* = 10.9, 9.1 Hz, 1H), 2.02 (dhept, *J* = 6.8, 6.8 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): δ 168.5, 136.3, 129.1, 128.5, 127.0, 83.4, 40.9, 35.5, 32.8, 19.5, 18.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{13}H_{18}NS^+$ 220.1154, found 220.1161.

(*S*)-4-Isopropyl-2-(4-methylbenzyl)-4,5-dihydrothiazole ((*S*)-4bi)



Reaction conditions: **1b** (0.2 mmol) and (*S*)-**2i** (0.4 mmol) for 15 min. Yellowish oil, 34 mg, 73% yield, R_f = 0.55 (PE/EtOAc = 5:1, *v/v*). $[\alpha]_D^{25}$ -59.9° (c 0.68, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.20 – 7.06 (m, 4H), 4.28 (dtt, *J* = 6.0, 9.0, 1.5 Hz, 1H), 3.80 (dd, *J* = 15.6, 1.2 Hz, 1H), 3.76 (dd, *J* = 15.6, 1.2 Hz, 1H), 3.22 (dd, *J* = 10.9, 8.9 Hz, 1H), 2.98 (dd, *J* = 10.9, 9.1 Hz, 1H), 2.32 (s, 3H), 2.02 (dhept, *J* = 6.6, 6.6 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): *δ* 168.8, 136.6, 133.2, 129.2, 128.9, 83.4, 40.5, 35.5, 32.8, 21.1, 19.5, 18.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{14}H_{20}NS^+$ 234.1311, found 234.1321.

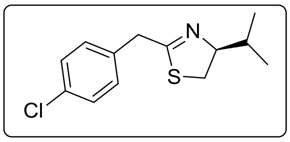
(*S*)-4-Isopropyl-2-(4-methoxybenzyl)-4,5-dihydrothiazole ((*S*)-4ei)



Reaction conditions: **1e** (0.2 mmol) and (*S*)-**2i** (0.4 mmol) for 15 min. Yellowish oil, 28 mg, 56% yield, R_f = 0.25

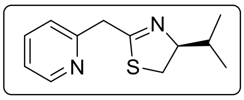
(PE/EtOAc = 5:1, *v/v*). $[\alpha]_D^{25}$ -45.9° (c 0.44, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.23 – 7.17 (m, 2H), 6.88 – 6.82 (m, 2H), 4.28 (dtt, *J* = 6.0, 9.0, 1.5 Hz, 1H), 3.79 (s, 3H), 3.76 – 3.75 (m, 2H), 3.23 (dd, *J* = 11.0, 9.0 Hz, 1H), 2.98 (dd, *J* = 11.0, 9.0 Hz, 1H), 2.02 (dhept, *J* = 6.6, 6.6 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 169.0, 158.6, 130.1, 128.4, 114.0, 83.4, 55.2, 40.0, 35.5, 32.9, 19.5, 18.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{14}H_{20}NOS^+$ 250.1260, found 250.1268.

(*S*)-2-(4-Chlorobenzyl)-4-isopropyl-4,5-dihydrothiazole ((*S*)-4ji)



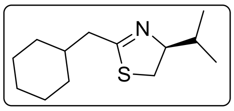
Reaction conditions: **1j** (0.2 mmol) and (*S*)-**2i** (0.4 mmol) for 15 min. Yellowish oil, 33 mg, 65% yield, R_f = 0.35 (PE/EtOAc = 5:1, *v/v*). $[\alpha]_D^{25}$ -56.6° (c 0.64, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.31 – 7.26 (m, 2H), 7.24 – 7.20 (m, 2H), 4.28 (dtt, *J* = 6.6, 9.0, 1.5 Hz, 1H), 3.80 (dd, *J* = 16.0, 1.2 Hz, 1H), 3.75 (dd, *J* = 16.0, 1.4 Hz, 1H), 3.25 (dd, *J* = 11.0, 9.0 Hz, 1H), 3.01 (dd, *J* = 11.0, 9.0 Hz, 1H), 2.08 – 1.95 (dhept, *J* = 6.6, 6.6 Hz, 1H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 167.8, 134.7, 132.9, 130.4, 128.7, 83.4, 40.1, 35.7, 32.9, 19.5, 18.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{13}H_{17}ClNS^+$ 254.0765, found 254.0775.

(*S*)-4-Isopropyl-2-(pyridin-2-ylmethyl)-4,5-dihydrothiazole ((*S*)-4ri)



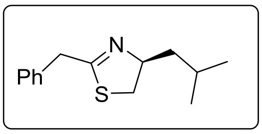
Reaction conditions: **1r** (0.2 mmol) and (*S*)-**2i** (0.4 mmol) for 30 min. Yellowish oil, 17 mg, 39% yield, R_f = 0.30 (DCM/MeOH = 20:1, *v/v*). $[\alpha]_D^{25}$ -41.8° (c 0.50, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.57 (d, *J* = 4.4 Hz, 1H), 7.64 (dt, *J* = 1.2, 7.6 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.18 (dd, *J* = 6.6, 5.3 Hz, 1H), 4.32 – 4.26 (m, 1H), 4.03 (s, 2H), 3.27 (dd, *J* = 10.8, 8.8 Hz, 1H), 3.03 (dd, *J* = 11.0, 9.0 Hz, 1H), 2.03 (dhept, *J* = 6.8, 6.8 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 166.7, 156.5, 149.5, 136.6, 123.4, 122.0, 83.4, 43.5, 35.7, 32.9, 19.6, 18.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{12}H_{17}N_2S^+$ 221.1107, found 221.1116.

(*S*)-2-(cyclohexylmethyl)-4-isopropyl-4,5-dihydrothiazole ((*S*)-4ui)



Reaction conditions: **1u** (0.2 mmol) and (*S*)-**2i** (0.4 mmol) for 30 min. Colorless oil, 29 mg, 64% yield, R_f = 0.70 (PE/EtOAc = 5:1, *v/v*). $[\alpha]_D^{25}$ -46.8° (c 0.44, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 4.29 – 4.22 (m, 1H), 3.23 (dd, *J* = 10.9, 8.9 Hz, 1H), 3.00 (dd, *J* = 10.9, 9.0 Hz, 1H), 2.43 – 2.30 (m, 2H), 2.08 – 1.95 (m, 1H), 1.80 – 1.59 (m, 6H), 1.32 – 1.07 (m, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.99 – 0.96 (m, 1H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.93 – 0.89 (m, 1H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): *δ* 168.7, 83.3, 42.0, 36.8, 35.0, 33.0, 32.9, 32.7, 26.3, 26.1, 19.5, 18.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{13}H_{24}NS^+$ 226.1624, found 226.1634.

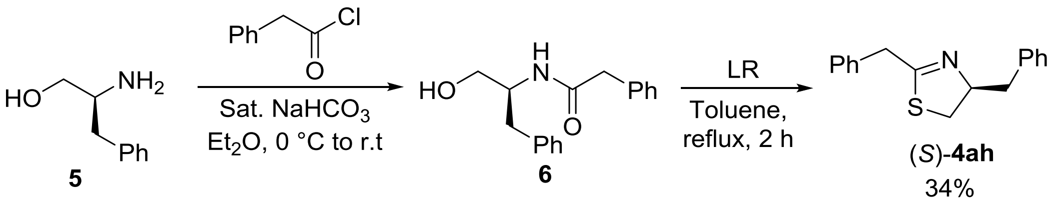
(*S*)-2-Benzyl-4-isobutyl-4,5-dihydrothiazole ((*S*)-4aj)



Reaction conditions: **1a** (0.2 mmol) and (*S*)-**2j** (0.4 mmol) at 125 °C for 30 min. Pale yellowish oil, 13 mg, 28% yield, R_f = 0.30 (DCM/EtOAc = 5:1, *v/v*). $[\alpha]_D^{25}$ -85.4° (c 1.10, CH_2Cl_2). Ee% > 99%, HPLC analysis: Daicel Chiralpak AD-H (*i*-PrOH/hexane = 1/99, *v/v*, 1.0 mL/min, 210 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.14 (m, 5H), 4.58 – 4.41 (m, 1H), 3.81 (s, 2H), 3.33 (dd, *J* = 10.8, 8.3 Hz, 1H), 2.89 (dd, *J* = 10.8, 7.9 Hz, 1H), 1.88 – 1.69 (m, 2H), 1.45 – 1.33 (m, 1H), 0.98 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 168.3, 136.2, 129.0, 128.6, 127.0, 75.5, 44.2, 41.0, 39.0, 25.7, 22.9, 22.5. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{14}H_{20}NS^+$ 234.1311, found 234.1304.

Mechanistic studies

(1) The product structure of 2,4-dialkylthiazolines from the reactions of 4-substituted 1,2,3-thiadiazoles **1** with 2-alkylaziridines **2** was confirmed by the parrel synthesis of thiazoline (*S*)**-4ah** from (*S*)-2-amino-3-phenylpropan-1-ol (**5**).

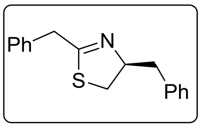


Scheme S4. Synthesis of thiazoline (S)-**4ah** from (*S*)-2-amino-3-phenylpropan-1-ol (**5**).

(a) (*S*)-2-Amino-3-phenylpropan-1-ol (**5**) (439 mg, 3.2 mmol) was dissolved in 6 mL of Et_2O in a round bottom flask in an ice bath. After addition of saturated sodium bicarbonate aqueous solution (3 mL), 2-phenylacetyl chloride (504 mg, 3.2 mmol) was added into the flask dropwise. The solution was then kept stirring at room temperature till the reaction finished. Then the solution was quenched with saturated ammonium chloride aqueous solution (20 mL) and extracted with DCM (5 mL × 3). The organic layer was combined, dried over sodium sulfate, and concentrated. The residue was then purified by recrystallization to give colorless crystals (*S*)-*N*-(1-hydroxy-3-phenylpropan-2-yl)-2-phenylacetamide (**6)** in 67% yield (575 mg).

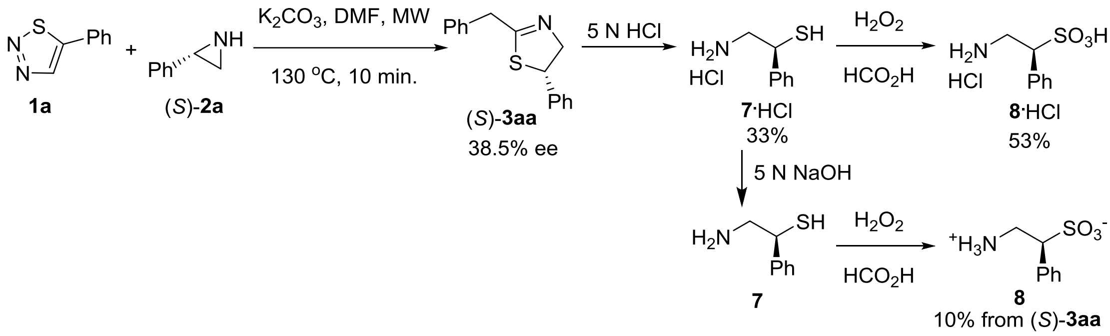
(b) (*S*)-*N*-(1-Hydroxy-3-phenylpropan-2-yl)-2-phenylacetamide (**6**) (269 mg, 1.0 mmol) and Lawson's reagent (404 mg, 1.0 mmol) were dissolved in 30 mL of toluene in a round bottom flask. The solution was kept refluxing under N_2 atmosphere in an oil bath for 2 hours. After the reaction was finished, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromography (PE/EA = 20:1, v/v) to give product (*S*)**-4ah**.

(*S*)-2,4-Dibenzyl-4,5-dihydrothiazole ((*S*)-4ah)



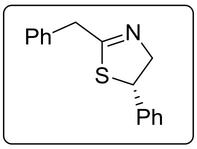
Pale yellowish oil, 92 mg, 34% yield, R_f = 0.45 (PE/EtOAc = 5:1, *v/v*). $[\alpha]_D^{25}$ -71.1° (c 0.56, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.17 (m, 10H), 4.78 – 4.70 (m, 1H), 3.84 (d, *J* = 15.2 Hz, 1H), 3.80 (d, *J* = 15.2 Hz, 1H), 3.24 – 3.13 (m, 2H), 3.00 (dd, *J* = 11.1, 6.8 Hz, 1H), 2.74 (dd, *J* = 13.6, 9.1 Hz, 1H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): δ 169.6, 138.3, 136.1, 129.3, 129.1, 128.6, 128.5, 127.1, 126.4, 78.0, 40.9, 40.1, 37.7. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{18}NS^+$ 268.1154, found 268.1159.

(2) The configuration of major enantiomer in product (*S*)-**3aa**, which was prepared from **1a** and (*S*)-**2a** according to the general procedure, was identified by the following derivatization transformation.



Scheme S5. Reaction of thiadiazole **1a** and (*S*)-2-phenylaziridine (*S*)-**2a** and further conversion of the product (*S*)-**3aa**.

(*S*)-2-Benzyl-4-phenyl-4,5-dihydrothiazole ((*S*)-3aa)



Reaction conditions: **1a** (2 mmol) and (*S*)-**2a** (4 mmol) for 15 min. Pale yellowish oil, 437 mg, 86% yield, R_f = 0.3 (PE/EA = 5:1, *v/v*). $[\alpha]_D^{25}$ -36.9° (c 1.02, CH_2Cl_2), ee% = 38.5%. HPLC analysis: Daicel Chiralpak AD-H (*i*-PrOH/hexane = 10/90, *v/v*, 1.0 mL/min, 210 nm). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 4H), 7.29 – 7.19 (m, 6H), 4.91 (dd, *J* = 9.0, 5.7 Hz, 1H), 4.55 (ddt, *J* = 15.7, 9.0, 1.6 Hz, 1H), 4.36 (ddt, *J* = 15.6, 5.7, 1.4 Hz, 1H), 3.87 (t, *J* = 1.5 Hz, 2H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$) δ 169.7, 141.9, 135.9, 129.1, 128.7, 128.6, 127.6, 127.1, 126.9, 72.8, 55.2, 40.8. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{15}H_{14}NS^+$ 254.0998, found 254.1004.

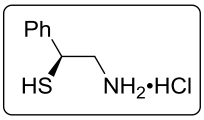
The hydrochlorides of compounds **7** and **8** were synthesized according to the reported procedures.[13] To a three-necked round bottom flask connected with a condenser tube were added (*S*)-**3aa** (253 mg, 1 mmol) and 5 mL of 5 N HCl aqueous oxygen-free solution and sealed with a N_2 ballon. The flask was then kept refluxing in an oil bath for 12 hours till the reaction finished. The suspension was washed with Et_2O (5 mL × 3). The aqueous phase was collected. After removal of water, 2-amino-1-phenylethane-1-thiol

[13] (a) Mercey, G.; Bregeon, D.; Gaumont, A.-C.; Levillain, J.; Gulea, M. *Tetrahedron Lett.* **2008**, *49*, 6553. (b) Xu, J. X.; Xu, S.; Zhang, Q. *Heteroat. Chem.* **2005**, *16*, 466.

hydrochloride (**7·HCl**) was obtained as colorless crystals.

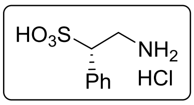
In a round bottom flask, 1 mL of 30% H_2O_2 was added dropwise to 5 mL of 98% formic acid in an ice–water bath. The solution was kept stirring for 1 hour. Then a solution of 2-amino-1-phenylethane-1-thiol hydrochloride (**7·HCl**) (23.7 mg, 0.12 mmol) in 1 mL of 98% formic acid was added into the flask. The mixture was kept stirring overnight. After removal of solvent and washing with CH_2Cl_2, the residue was recrystallized from methanol to give colorless crystals 1-phenyltaurine hydrochloride (**8·HCl**).

(*S*)-2-Amino-1-phenylethane-1-thiol hydrochloride (7·HCl)



Colorless crystals, 63 mg, 33 % yield, m.p. 157 – 160 °C (Lit.[14] 157 – 160 °C). $[\alpha]_D^{25}$ +25.4° (c 1.95, H_2O), 38.5%ee. ^1H NMR (400 MHz, D_2O): δ 7.55 – 7.39 (m, 5H), 4.29 (t, J = 7.9 Hz, 1H), 3.53 (qd, J = 13.1, 7.9 Hz, 2H). ^{13}C NMR{^1H} (101 MHz, D_2O): δ 139.5, 129.5, 128.7, 127.1, 46.1, 40.3.

(*S*)-2-Amino-1-phenylethane-1-sulfonic acid hydrochloride (8·HCl)



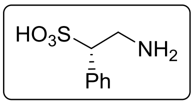
Colorless crystals, 15 mg, 53% yield, m.p.> 300°C. $[\alpha]_D^{25}$ +9.2° (c 0.60, H_2O), 38.5%ee. ^1H NMR{^1H} (400 MHz, D_2O) δ 7.49 (s, 4H), 4.38 (dd, J = 8.4, 6.8 Hz, 1H), 3.87 (dd, J = 13.3, 6.8 Hz, 1H), 3.66 (dd, J = 13.3, 8.4 Hz, 1H). ^{13}C NMR{^1H} (101 MHz, D_2O) δ 132.0, 129.3, 129.1, 62.8, 40.1.

The compound **8** was prepared according to the reported procedures.[13] To a three-necked round bottom flask connected with a condenser tube were added (*S*)-**3aa** (405 mg, 1.6 mmol) and 10 mL of 5 N HCl aqueous oxygen-free solution and sealed with a N_2 ballon. The flask was then kept refluxing in an oil bath for 12 hours till the reaction finished. The suspension was washed with Et_2O (5 mL × 3). The aqueous phase was collected and then neutralized with 5 N NaOH aqueous solution till pH 11~13. The alkalized aqueous phase was extracted with ethyl acetate (5 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude 2-amino-1-phenylethane-1-thiol (**7**) was dissolved in 3 mL of formic acid for the following oxidation without futher purification.

To a round bottom flask, 1.2 mL of 30% H_2O_2 was added dropwise to 12 mL of 98% formic acid in an ice–water bath. The solution was kept stirring for 1 hour. Then the solution prepared above was added dropwise into the flask. The mixture was kept stirring overnight till nearly colorless. The suspension was then washed with CH_3Cl (5 mL × 3). After removal of water, the residue was recrystallized in methanol to give colorless crystals 1-phenyltaurine (**8**), 31 mg, 10% yield.

(*S*)-2-Amino-1-phenylethane-1-sulfonic acid (8)

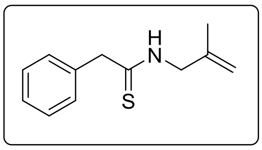
[14] Nishimura, H.; Takamatsu, H. *Yakugaku Zasshi* **1964**, *84*, 797.



Colorless crystals, 31 mg, 10% yield. m.p.> 300 °C. $[\alpha]_D^{25}$ +3.1° (c 0.62, H_2O), 38.5%ee. Lit.[15] $[\alpha]_D^{25}$ -5.5° for (*R*)-enantiomer (c 0.80, H_2O). ^1H NMR (400 MHz, D_2O): *δ* 7.54 – 7.39 (m, 5H), 4.37 (t, *J* = 7.6 Hz, 1H), 3.89 – 3.79 (m, 1H), 3.67 – 3.56 (m, 1H). ^{13}C NMR{^1H} (101 MHz, D_2O): *δ* 135.3, 132.0, 129.3, 129.1, 128.2, 127.1, 126.0, 62.8, 40.1.

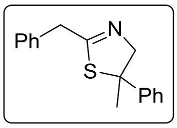
(3) Reactions of 4-phenyl-1,2,3-thiadiazole (**1a**) with different 2,2-disubstituted *N*-unprotected aziridines **2m**, **2n,** or **2o**.

***N*-(2-Methylallyl)-2-phenylethanethioamide (9am)**



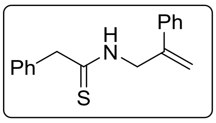
Reaction conditions: **1a** (0.2 mmol) and **2m** (0.4 mmol) for 15 min. Pale yellowish oil, 29 mg, 70% yield, R_f = 0.40 (PE/EtOAc = 5:1, *v/v*). ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.45 – 7.27 (m, 5H), 7.06 (brs, 1H), 4.82 (t, *J* = 1.4 Hz, 1H), 4.63 (t, *J* = 1.4 Hz, 1H), 4.24 (d, *J* = 5.7 Hz, 2H), 4.20 (s, 2H), 1.69 (s, 3H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): *δ* 202.2, 139.8, 134.6, 129.6, 129.3, 128.0, 111.6, 53.1, 51.1, 20.6. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{12}H_{16}NS^+$ 206.0998, found 206.1007.

2-Benzyl-5-methyl-5-phenyl-4,5-dihydrothiazole (3an)



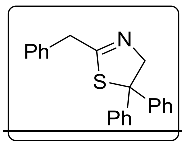
Reaction conditions: **1a** (0.2 mmol) and **2n** (0.4 mmol) for 10 min. Pale yellowish oil, 19 mg, 36% yield, R_f = 0.25 (PE/EtOAc = 5:1, *v/v*). ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.64 – 6.97 (m, 10H), 4.36 (dt, *J* = 15.3, 1.6 Hz, 1H), 4.29 (dt, *J* = 15.2, 1.2 Hz, 1H), 3.86 (dt, *J* = 16.0, 1.2 Hz, 1H), 3.82 (dt, *J* = 16.0, 1.2 Hz, 1H), 1.78 (s, 3H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): *δ* 170.2, 144.4, 136.0, 129.1, 128.6, 128.4, 127.1, 127.0, 126.1, 77.4, 65.6, 41.3, 30.1. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{18}NS^+$ 268.1154, found 268.1160.

2-Phenyl-*N*-(2-phenylallyl)ethanethioamide (9an)



Reaction conditions: **1a** (0.2 mmol) and **2n** (0.4 mmol) for 10 min. Pale yellowish oil, 8 mg, 15% yield, R_f = 0.35 (PE/EtOAc = 5:1, *v/v*). ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.34 – 7.21 (m, 8H), 7.11 – 7.02 (m, 2H), 6.93 (brs, 1H), 5.41 (d, *J* = 0.9 Hz, 1H), 5.13 – 5.08 (m, 1H), 4.71 – 4.64 (m, 2H), 4.09 (s, 2H). ^{13}C NMR{^1H} (101 MHz, $CDCl_3$): *δ* 201.9, 142.5, 137.7, 134.4, 129.4, 129.1, 128.6, 128.3, 127.7, 126.0, 115.0, 53.0, 49.9. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{18}NS^+$ 268.1154, found 268.1161.

2-Benzyl-5,5-diphenyl-4,5-dihydrothiazole (3ao)

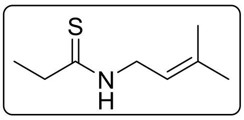


Reaction conditions: **1a** (0.2 mmol) and **2o** (0.4 mmol) for 10 min. Pale Yellowish oil, 31 mg, 47 % yield, R_f = 0.30 (PE/EtOAc

[15] Chen, N.; Jia, W. Y.; Xu, J. X. *Eur. J. Org. Chem*. **2009**, *(33)*, 5841–5846.

= 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 – 6.60 (m, 15H), 4.70 (s, 2H), 3.82 (s, 2H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 169.9, 144.9, 135.7, 129.1, 128.6, 128.3, 127.1, 127.12, 127.08, 75.6, 73.9, 41.2. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{22}H_{20}NS^+$ 330.1311, found 330.1319.

N-(3-Methylbut-2-en-1-yl)propanethioamide (9si)



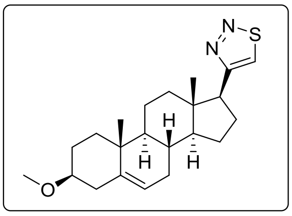
Reaction conditions: **1s** (0.2 mmol) and (*S*)-**2i** (0.4 mmol) for 30 min. Pale yellowish oil, 17 mg, 54% yield, R_f = 0.40 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.33 – 5.28 (m, 1H), 4.20 (t, *J* = 6.0 Hz, 2H), 2.66 (q, *J* = 7.5 Hz, 2H), 1.76 (d, *J* = 1.2 Hz, 3H), 1.70 (d, *J* = 1.6 Hz, 3H), 1.30 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 206.0, 139.0, 117.9, 44.4, 40.0, 25.7, 18.1, 13.5. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_8H_{16}NS^+$ 158.0998, found 158.1010.

Applications

Pregnenolone was methylated with methyl iodide according to the reported procedure,[16] in which the amount of CH_3I should only be carefully controlled slightly excess of pregnenolone. 4-((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-Methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-1,2,3-thiadiazole (**1v**) was synthesized according to the general procedure for synthesis of 1,2,3-thiadiazole **1** in 10 mmol scale as listed above.

The pregnenolone 3-methyl ether derivatives **3va**, **3vf**, **3vg** and (*S*)-**4vh** were synthesized according to the general procedure for synthesis of thiazolines **3** and **4**.

4-((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-Methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-1,2,3-thiadiazole (1v)



Colorless crystals, 1.0 g, 27% yield, R_f = 0.60 (PE/EtOAc = 5:1, *v/v*), m.p. 167 – 168 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (s, 1H), 3.40 – 3.38 (m, 1H), 3.36 (s, 3H), 3.44 – 3.39 (m, 1H), 2.37 – 2.03 (m, 4H), 1.98 – 1.82 (m, 4H), 1.70 – 1.27 (m, 10H), 1.14 – 1.02 (m, 2H), 1.01 (s, 3H), 0.51 (s, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 164.9, 141.1, 131.2, 121.3, 80.3, 77.2, 56.2, 55.6, 50.3, 50.3, 44.4, 38.7, 37.8, 37.2, 37.0, 32.3, 31.9, 28.0, 27.4, 24.7, 20.7, 19.4, 13.0. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{22}H_{33}N_2OS^+$ 373.2308, found 373.2305.

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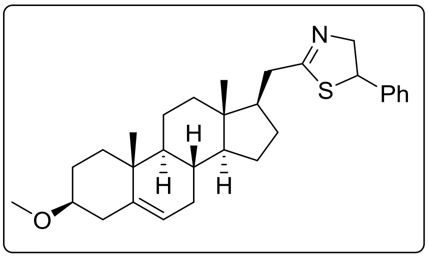
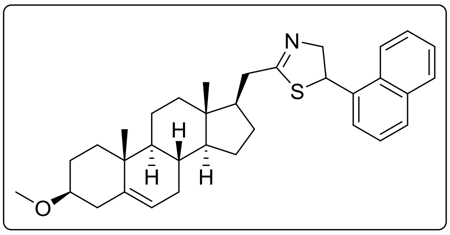
[16] Hirayama, Y.; Okuzumi, K.; Masubuti, H.; Uekusa, H.; Girault, J.-P.; Fujimoto, Y. *J. Org. Chem.* **2014**, *79*, 5471.

2-(((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-Methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)methyl)-5-phenyl-4,5-dihydrothiazole (3va)



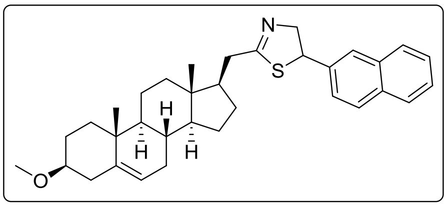
Reaction conditions: **1v** (0.3 mmol) and **2a** (0.4 mmol) for 30 min. Diastereomeric thiazolines **3va**. Pale yellowish oil, 78 mg, 56 % yield, R_f = 0.35 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.20 (m, 5H), 5.38 – 5.32 (m, 1H), 4.94 – 4.90 (m, 1H), 4.51 (dd, *J* = 15.6, 9.2 Hz, 1H), 4.33 (ddd *J* = 15.5, 5.5, 5.5 Hz, 1H), 3.34 (s, 3H), 3.10 – 3.02 (m, 1H), 2.68 – 2.62 (m, 1H), 2.43 – 2.35 (m, 2H), 2.20 – 2.12 (m, 1H), 2.02 – 1.84 (m, 4H), 1.82 – 1.74 (m, 2H), 1.70 – 1.65 (m, 1H), 1.60 – 1.36 (m, 6H), 1.26 – 1.12 (m, 2H), 1.10 – 1.03 (m, 2H),1.01 (s, 3H), 0.99 – 0.92 (m, 1H), 0.65 (s, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 170.93, 170.92, 142.42, 142.21, 140.8, 128.7, 128.48, 127.49, 126.87, 126.81, 121.3, 80.2, 72.6, 72.4, 55.54, 55.51, 55.47, 54.7, 54.6, 50.3, 48.8, 42.2, 38.6, 37.3, 37.1, 36.9, 35.2, 35.1, 31.8, 28.1, 28.0, 27.9, 24.6, 20.7, 19.3, 12.41, 12.38. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{30}H_{42}NOS^+$ 464.2982, found 464.2977.

2-(((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-Methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)methyl)-5-(naphthalen-1-yl)-4,5-dihydrothiazole (3vf)



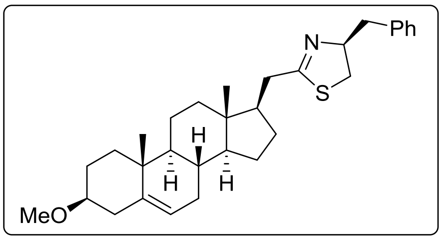
Reaction conditions: **1v** (0.1 mmol) and **2f** (0.2 mmol) for 15 min. Diastereomeric thiazolines **3vf**. Pale yellowish oil, 34 mg, 67 % yield. R_f = 0.40 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.2 Hz, 1H), 7.87 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.61 – 7.38 (m, 4H), 5.73 – 5.65 (m, 1H), 5.37 – 5.34 (m, 1H), 4.68 – 4.50 (m, 2H), 3.35 (d, *J* = 1.3 Hz, 3H), 3.10 – 3.01 (m, 1H), 2.73 – 2.60 (m, 1H), 2.47 – 2.35 (m, 2H), 2.22 – 2.10 (m, 1H), 2.05 – 1.83 (m, 4H), 1.82 – 1.73 (m, 2H), 1.70 – 1.62 (m, 1H), 1.62 – 1.32 (m, 6H), 1.22 – 1.04 (m, 3H), 1.00 (s, 3H), 0.99 – 0.80 (m, 2H), 0.65 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.45, 171.38, 140.9, 137.4, 137.2, 133.9, 130.57, 130.51, 129.1, 128.3, 126.4, 125.8, 125.5, 124.0, 123.9, 122.8, 121.4, 80.3, 77.2, 70.4, 70.3, 55.60, 55.57, 50.6, 50.5, 50.4, 49.0, 48.9, 42.3, 38.7, 37.4, 37.2, 37.0, 35.42, 35.35, 31.9, 28.1, 28.0, 27.9, 24.6, 20.8, 19.4, 12.5. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{34}H_{44}NOS^+$ 514.3138, found 514.3134.

2-(((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-Methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)methyl)-5-(naphthalen-2-yl)-4,5-dihydrothiazole (3vg)



Reaction conditions: **1v** (0.1 mmol) and **2g** (0.2 mmol) for 15 min. Diastereomeric thiazolines **3vg**. Pale yellowish oil, 32 mg, 62% yield, R_f = 0.30 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 – 7.75 (m, 3H), 7.69 (t, *J* = 2.4 Hz, 1H), 7.51 – 7.38 (m, 3H), 5.37 – 5.35 (m, 1H), 5.13 – 5.08 (m, 1H), 4.64 – 4.53 (m, 1H), 4.49 – 4.43 (m, 1H), 3.36 (s, 3H), 3.13 – 2.98 (m, 1H), 2.75 – 2.62 (m, 1H), 2.50 – 2.35 (m, 2H), 2.24 – 2.10 (m, 1H), 2.04 – 1.76 (m, 6H), 1.73 – 1.64 (m, 1H), 1.62 – 1.34 (m, 6H), 1.28 – 1.12 (m, 2H), 1.12 – 1.03 (m, 2H), 1.01 (s, 3H), 0.96 (ddt, *J* = 12.5, 7.5, 2.6 Hz, 1H), 0.67 (s, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 171.09, 171.04, 140.9, 132.8, 128.9, 127.8, 127.6, 126.4, 126.0, 125.6, 125.5, 124.9, 124.8, 121.4, 80.3, 77.2, 72.4, 72.3, 55.62, 55.60, 55.55, 55.0, 54.9, 50.4, 48.9, 42.3, 38.7, 37.40, 37.39, 37.2, 36.9, 35.3, 35.2, 31.91, 31.89, 28.2, 28.1, 28.0, 24.6, 20.8, 19.4, 12.47, 12.45. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{34}H_{44}NOS^+$ 514.3138, found 514.3135.

(4*S*)-4-Benzyl-2-(((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)methyl)-4,5-dihydrothiazole ((*S*)-4vh)

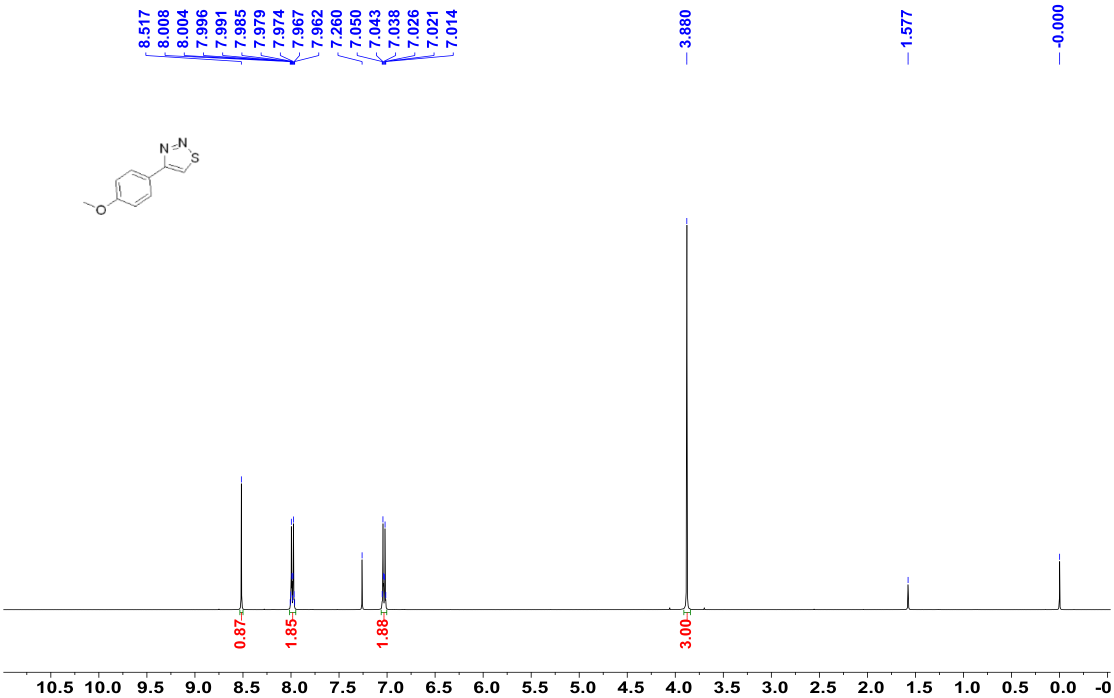


Reaction conditions: **1v** (0.2 mmol) and **2h** (0.4 mmol) for 20 min. $[\alpha]_D^{25}$ -105.8° (c 1.20, CH_2Cl_2). Colorless oil, 51 mg, 53% yield, R_f = 0.35 (PE/EtOAc = 5:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.16 (m, 5H), 5.36 – 5.34 (m, 2H), 4.71 – 4.64 (m, 1H), 3.35 (s, 3H), 3.20 – 3.13 (m, 1H), 3.10 – 2.96 (m, 2H), 2.72 – 2.58 (m, 2H), 2.43 – 2.30 (m, 2H), 2.19 – 2.12 (m, 1H), 2.05 – 1.83 (m, 4H), 1.79 – 1.61 (m, 3H), 1.59 – 1.55 (m, 2H), 1.50 – 1.30 (m, 4H), 1.27 – 1.03 (m, 4H), 1.01 (s, 3H), 0.95 (dd, *J* = 11.6, 4.7 Hz, 1H), 0.65 (s, 3H). ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$): δ 170.9, 140.9, 129.2, 128.5, 126.4, 121.4, 80.3, 77.9, 55.7, 55.6, 50.4, 48.8, 42.3, 40.0, 38.7, 37.4, 37.3, 37.2, 37.0, 35.4, 31.9, 28.1, 28.0, 24.6, 20.8, 19.4, 12.4. HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd. for $C_{31}H_{44}NOS^+$ 478.3138, found 478.3142.

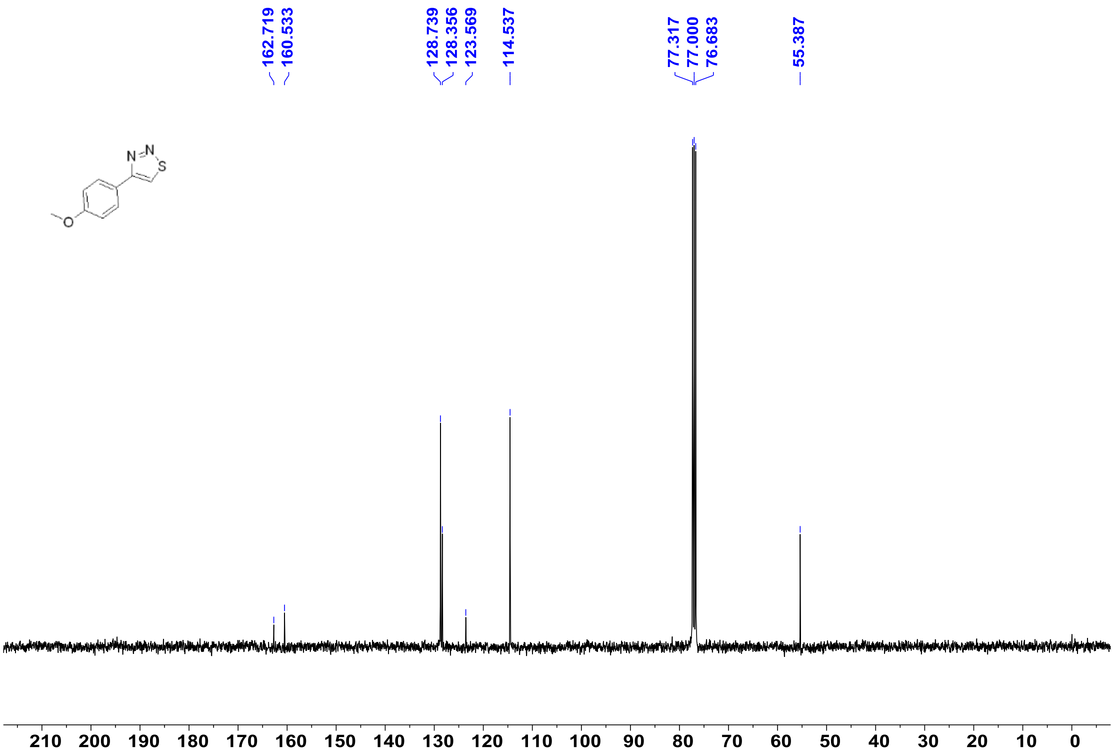
Copies of NMR spectra of synthesized 1,2,3-thiadiazoles 1

4-(4-Methoxyphenyl)-1,2,3-thiadiazole (1e)

[1]H MNR (400 MHz, $CDCl_3$)

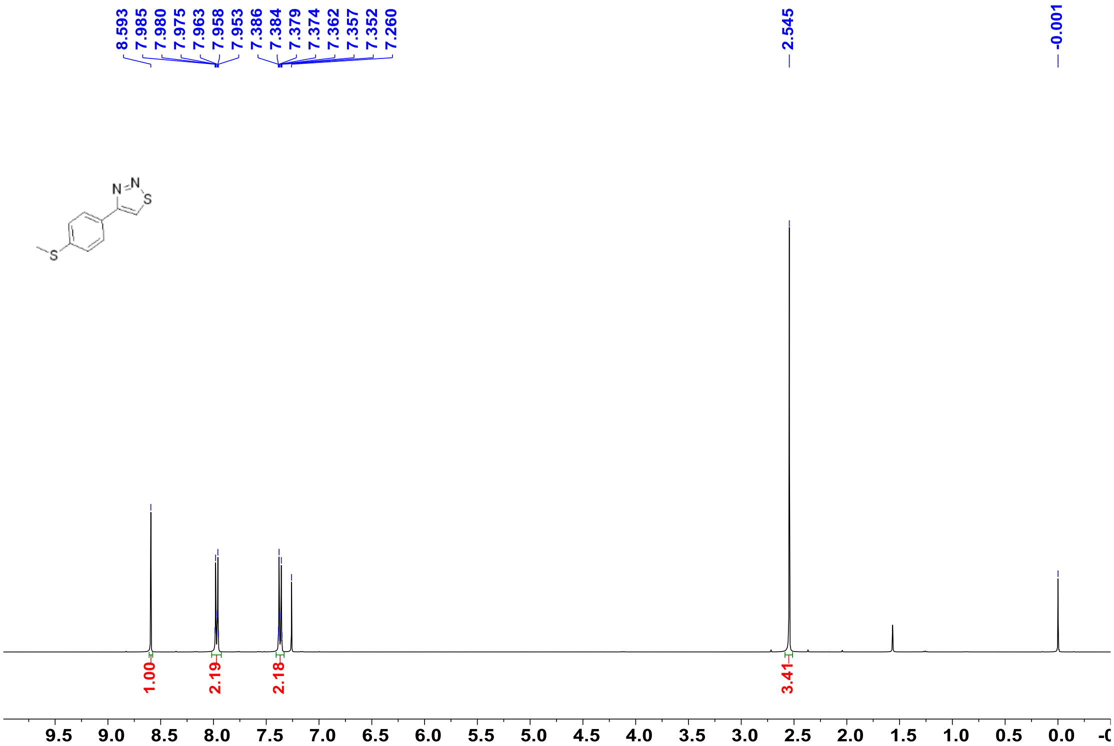


[13]C NMR{[1]H} (101 MHz, $CDCl_3$)

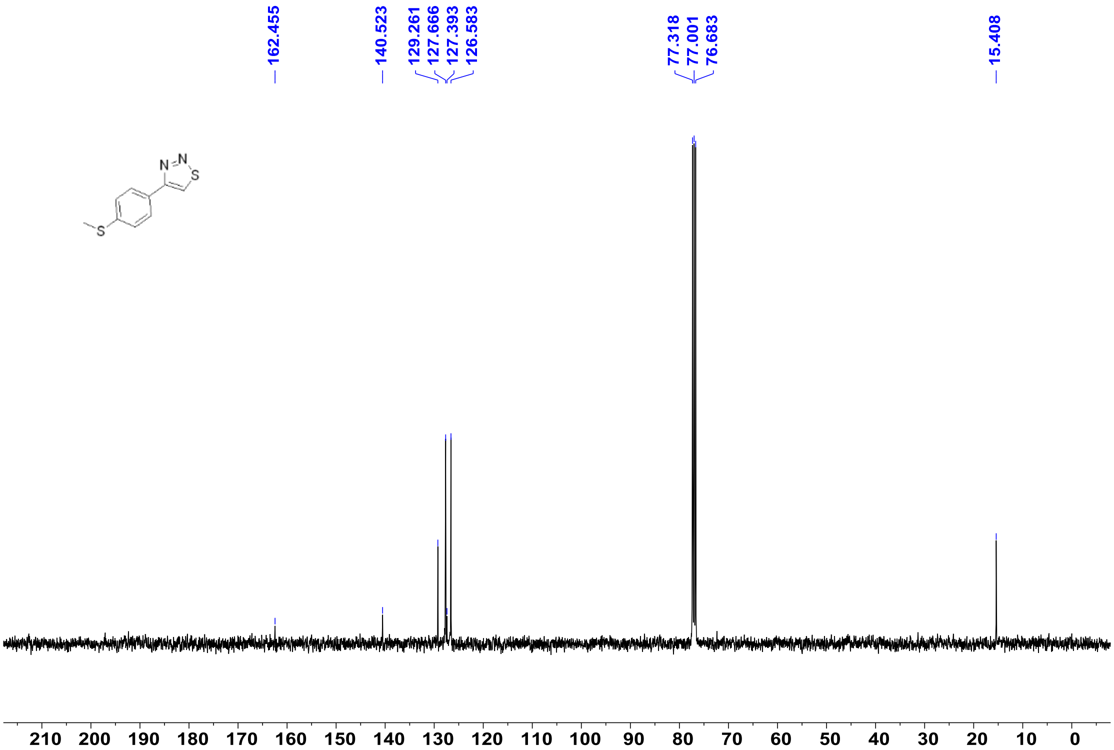


4-(4-(Methylthio)phenyl)-1,2,3-thiadiazole (1f)

[1]H MNR (400 MHz, $CDCl_3$)

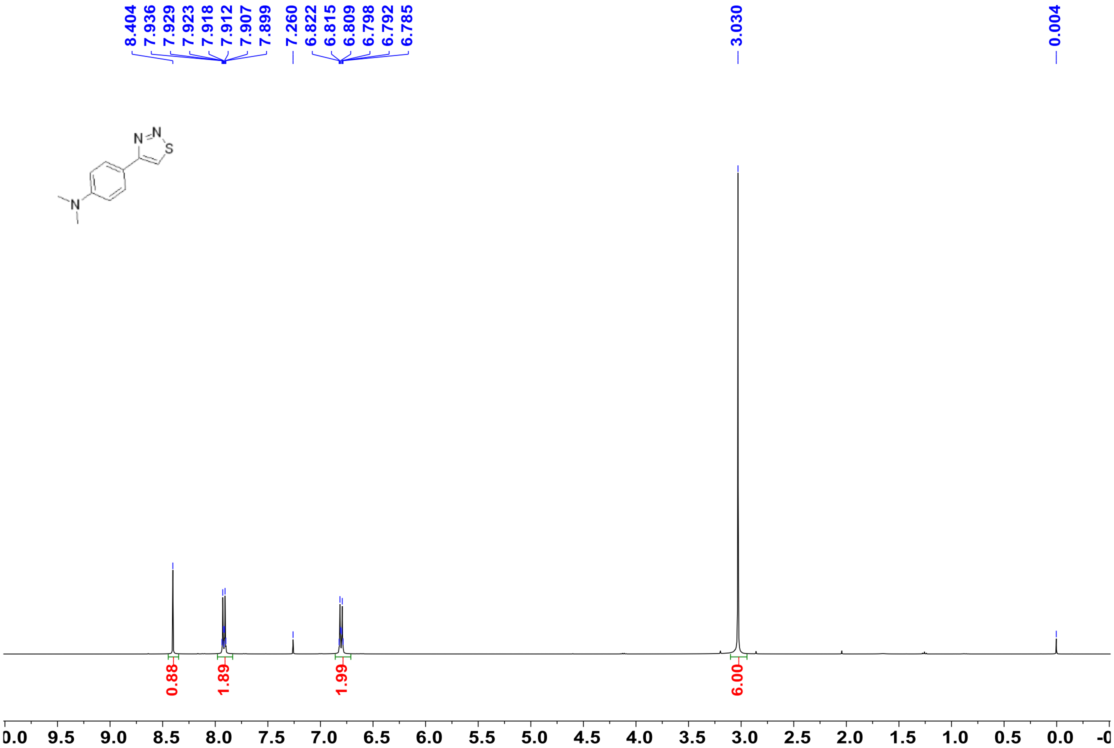


[13]C NMR{[1]H} (101 MHz, $CDCl_3$)

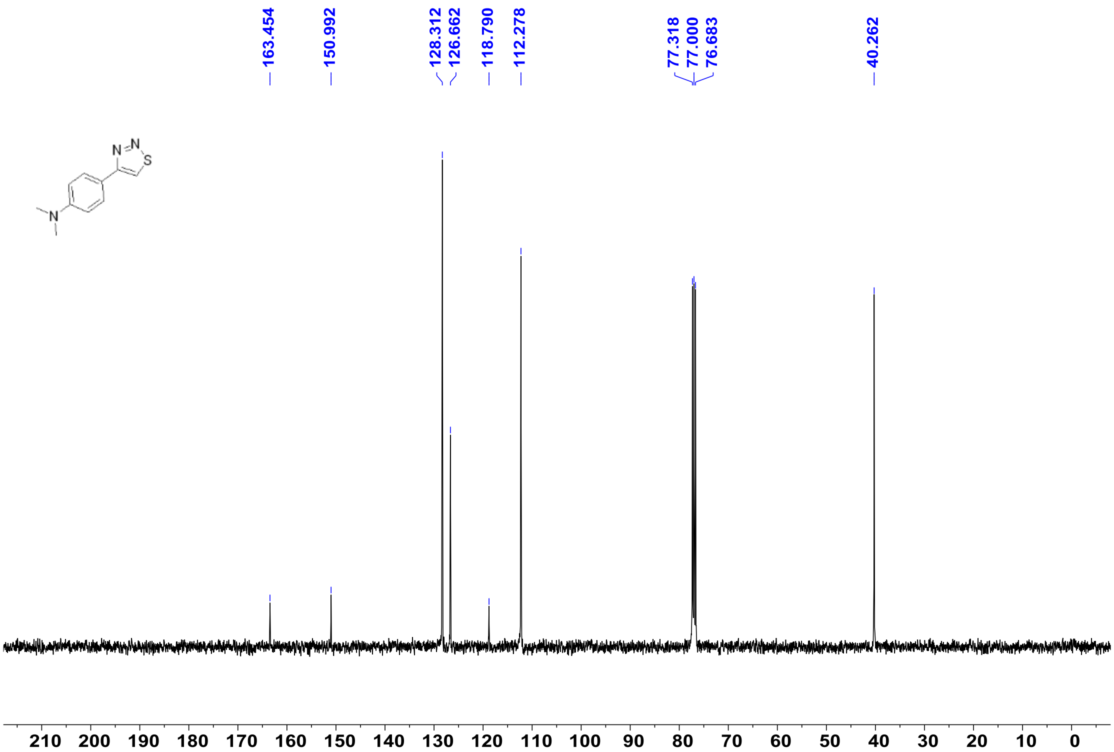


N,*N*-Dimethyl-4-(1,2,3-thiadiazol-4-yl)aniline (1g)

[1]H MNR (400 MHz, $CDCl_3$)

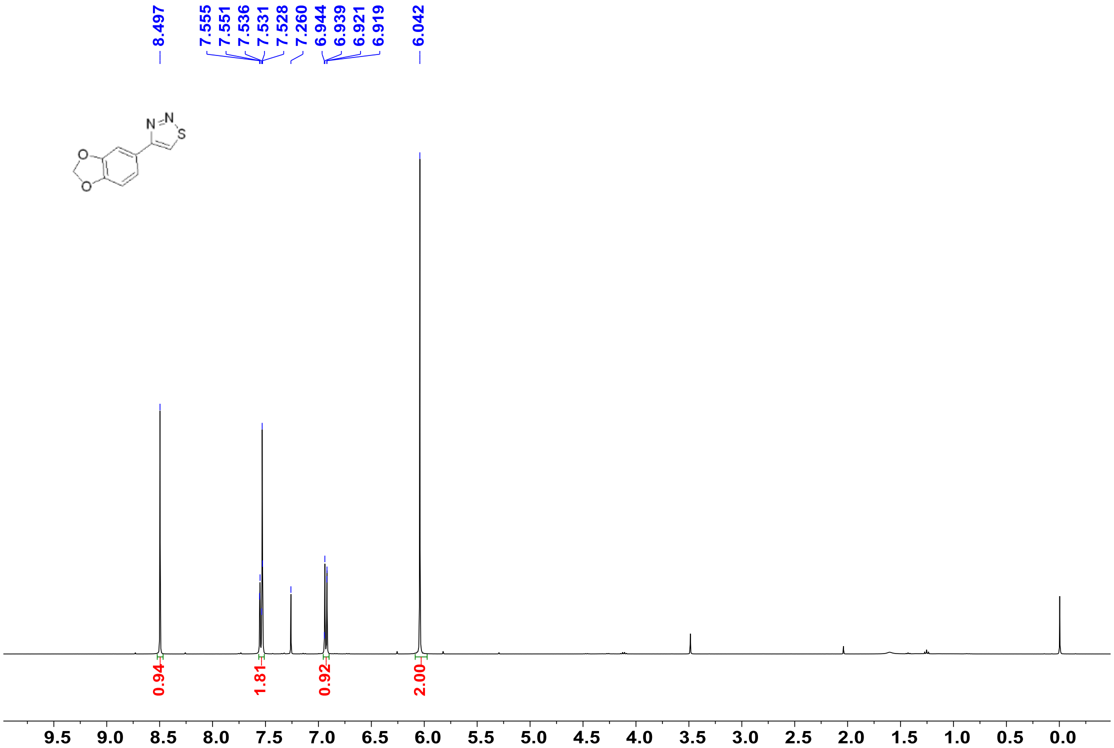


[13]C NMR{[1]H} (101 MHz, $CDCl_3$)

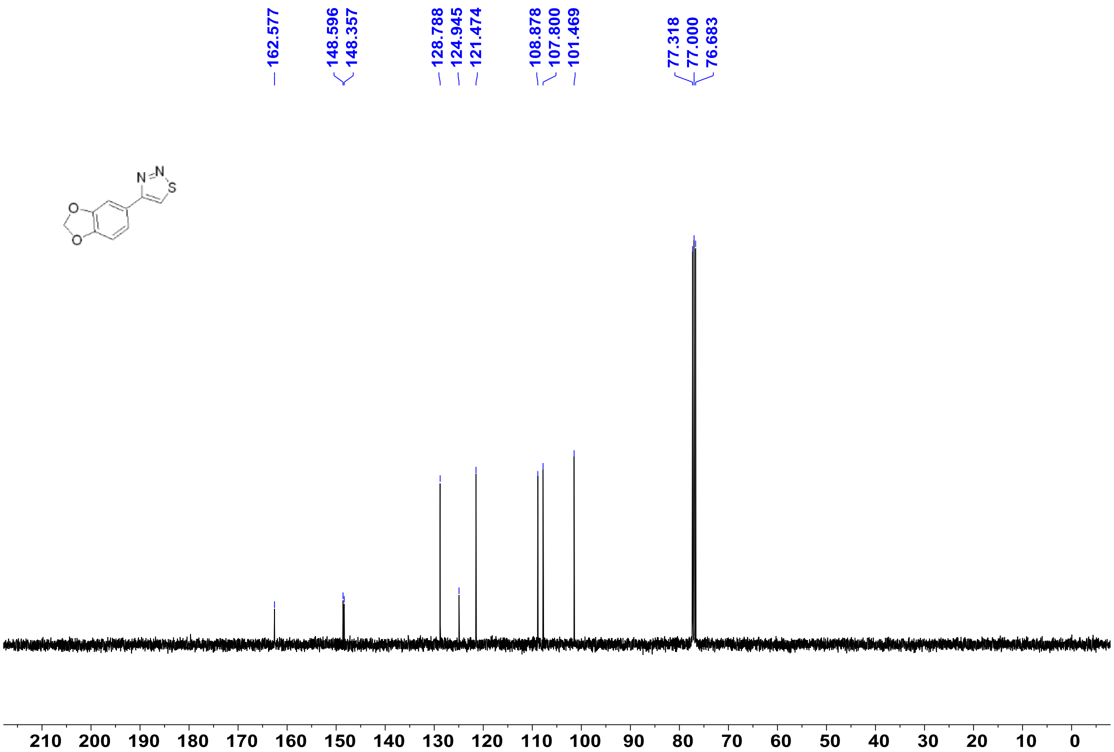


4-(Benzo[*d*][1,3]dioxol-5-yl)-1,2,3-thiadiazole (1h)

^{1}H MNR (400 MHz, $CDCl_3$)

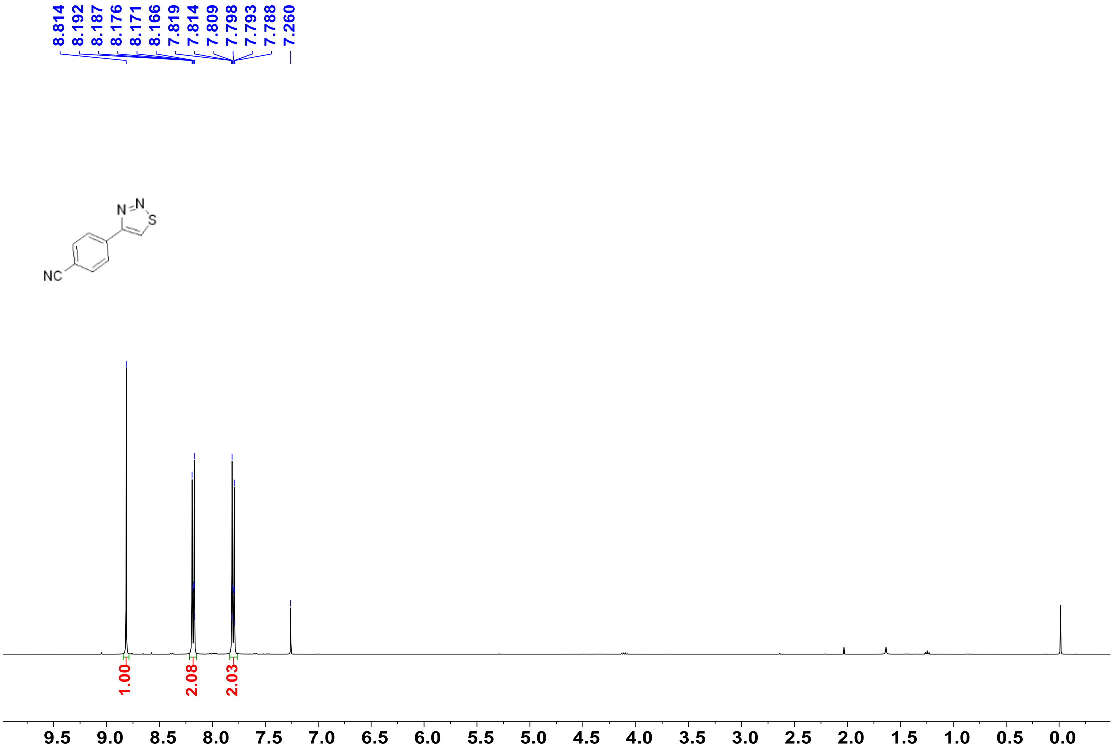


^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

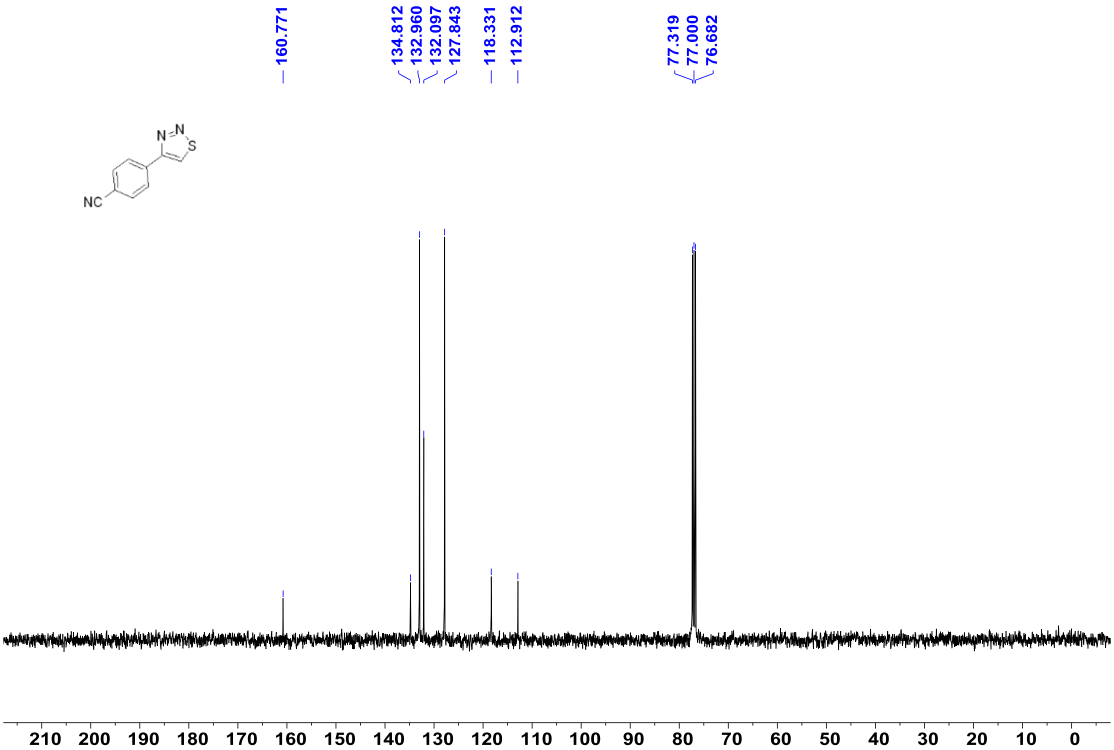


4-(1,2,3-Thiadiazol-4-yl)benzonitrile (1n)

^{1}H MNR (400 MHz, $CDCl_3$)

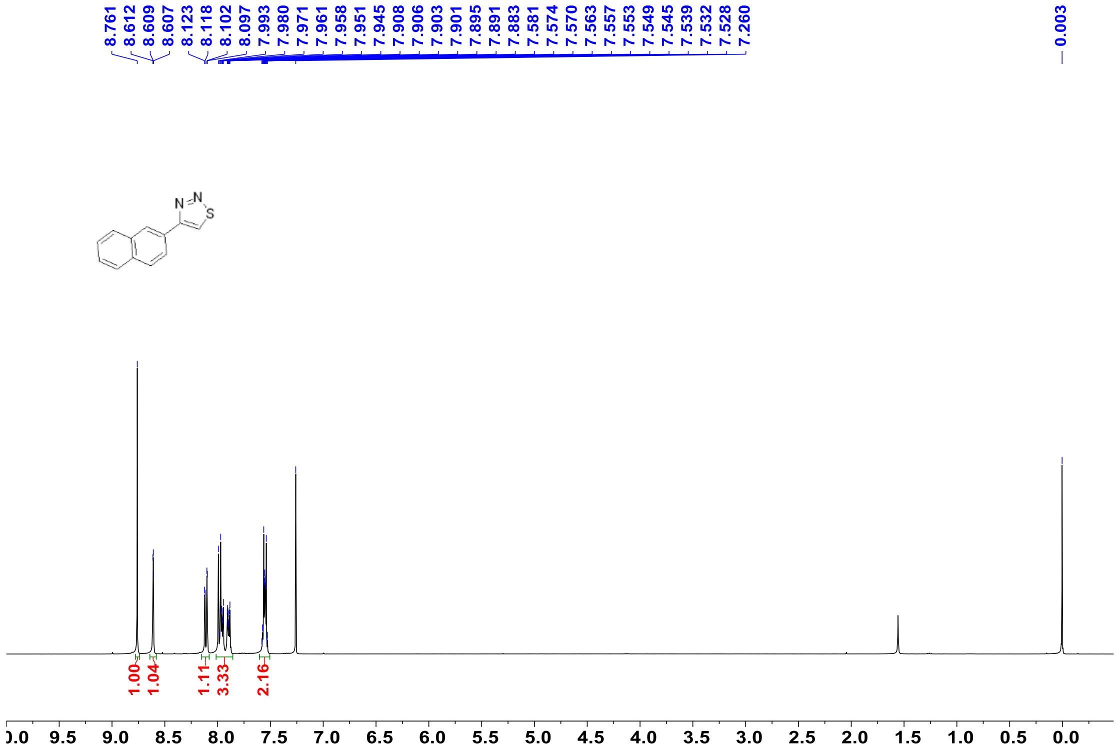


^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

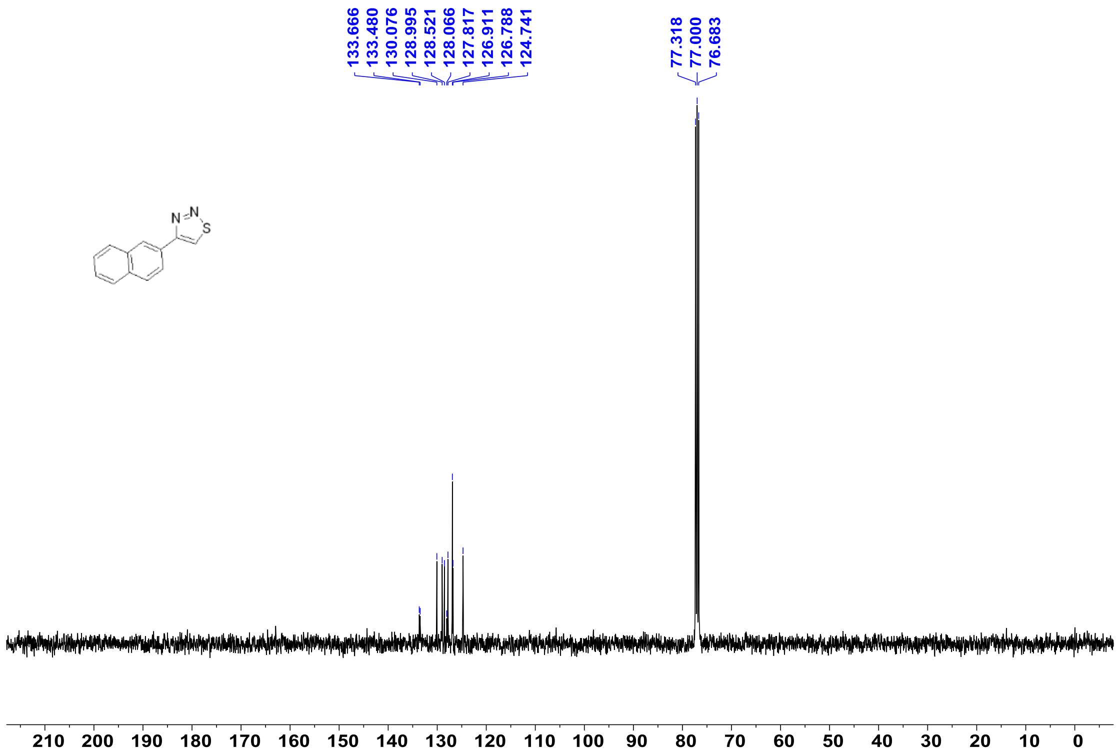


4-(Naphthalen-2-yl)-1,2,3-thiadiazole (1p)

[1]H MNR (400 MHz, $CDCl_3$)

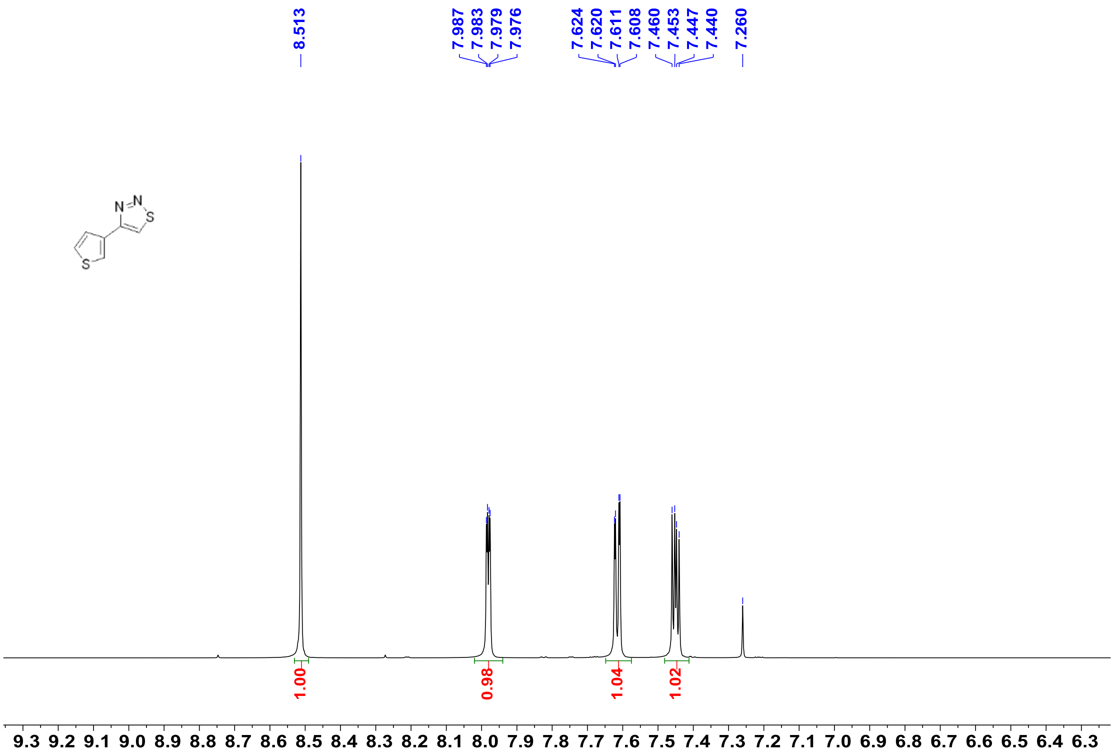


[13]C NMR{[1]H} (101 MHz, $CDCl_3$)

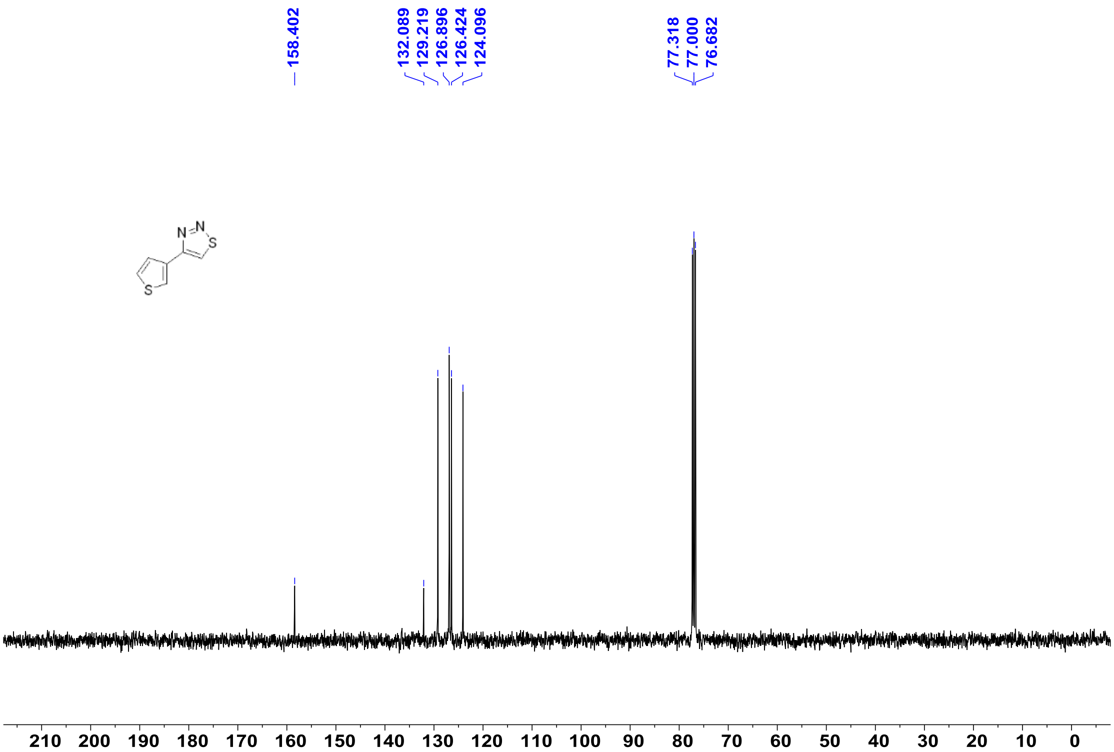


4-(Thiophen-3-yl)-1,2,3-thiadiazole (1q)

^{1}H MNR (400 MHz, $CDCl_3$)

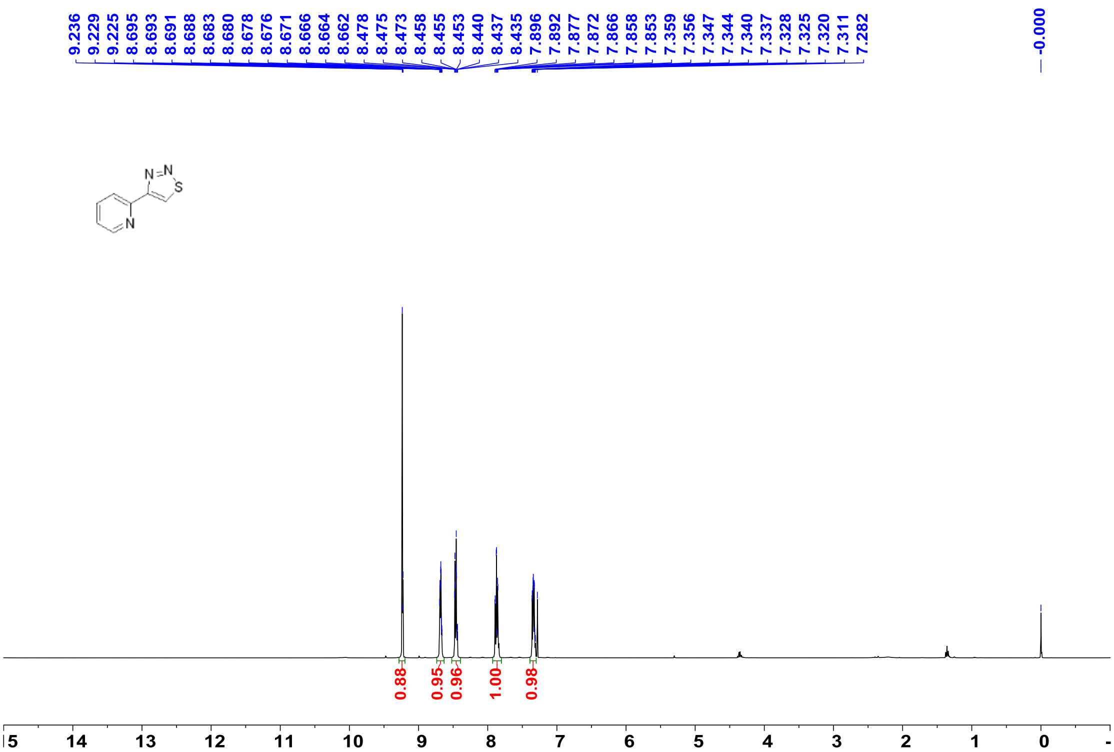


^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

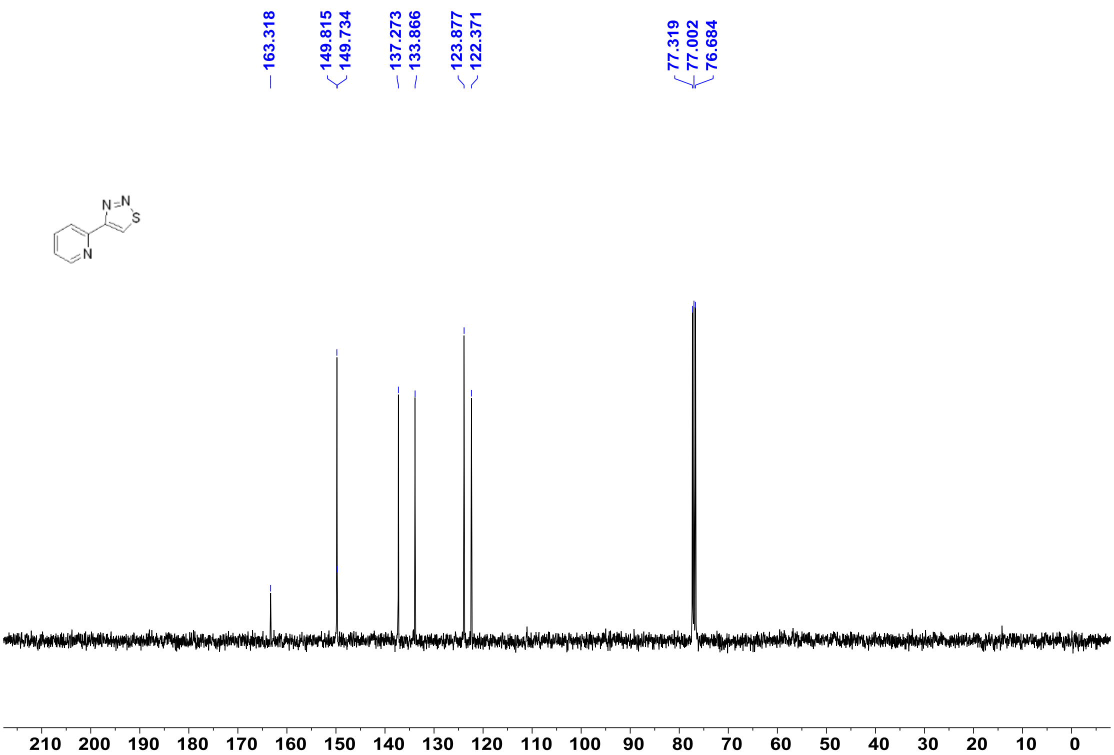


4-(Pyridin-2-yl)-1,2,3-thiadiazole (1r)

^1H MNR (400 MHz, $CDCl_3$)

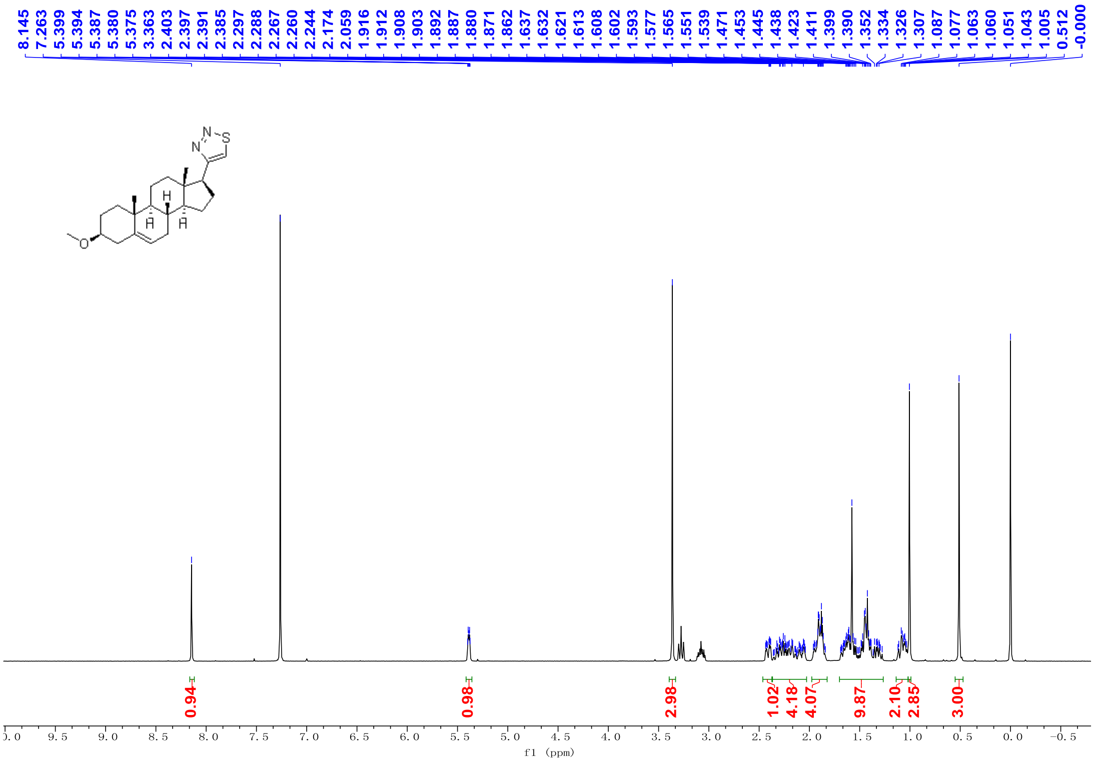


^{13}C NMR{^1H} (101 MHz, $CDCl_3$)

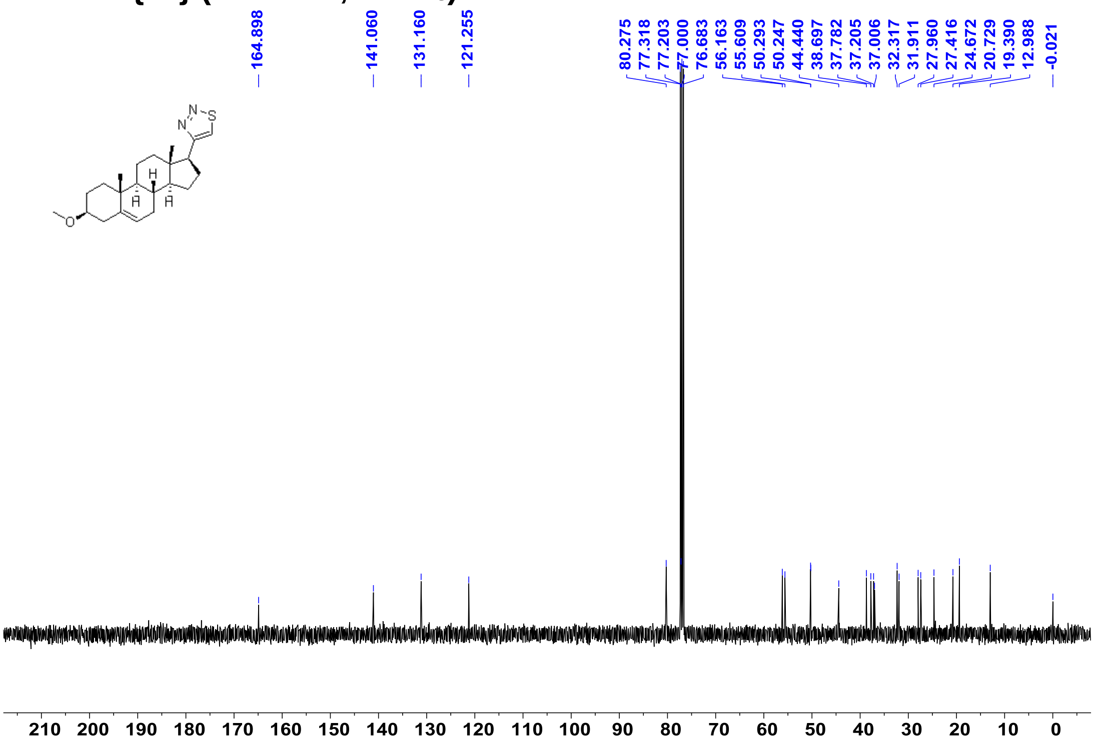


4-((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-Methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-1,2,3-thiadiazole (1v)

^{1}H MNR (400 MHz, CDCl$_3$)



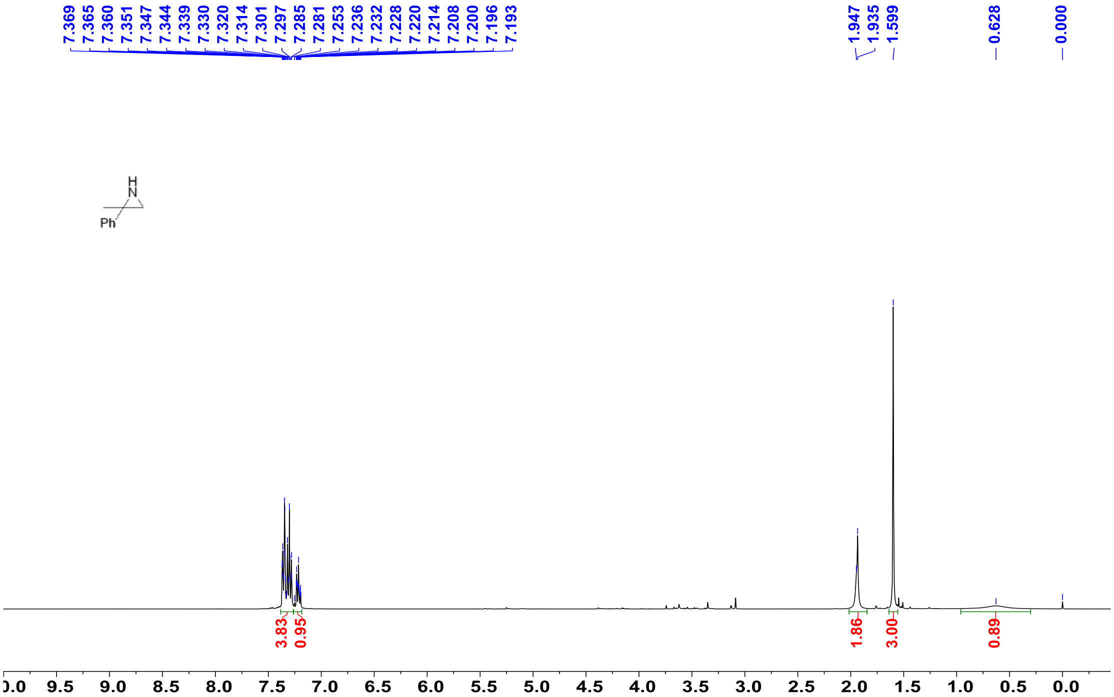
^{13}C NMR{^{1}H} (101 MHz, CDCl$_3$)



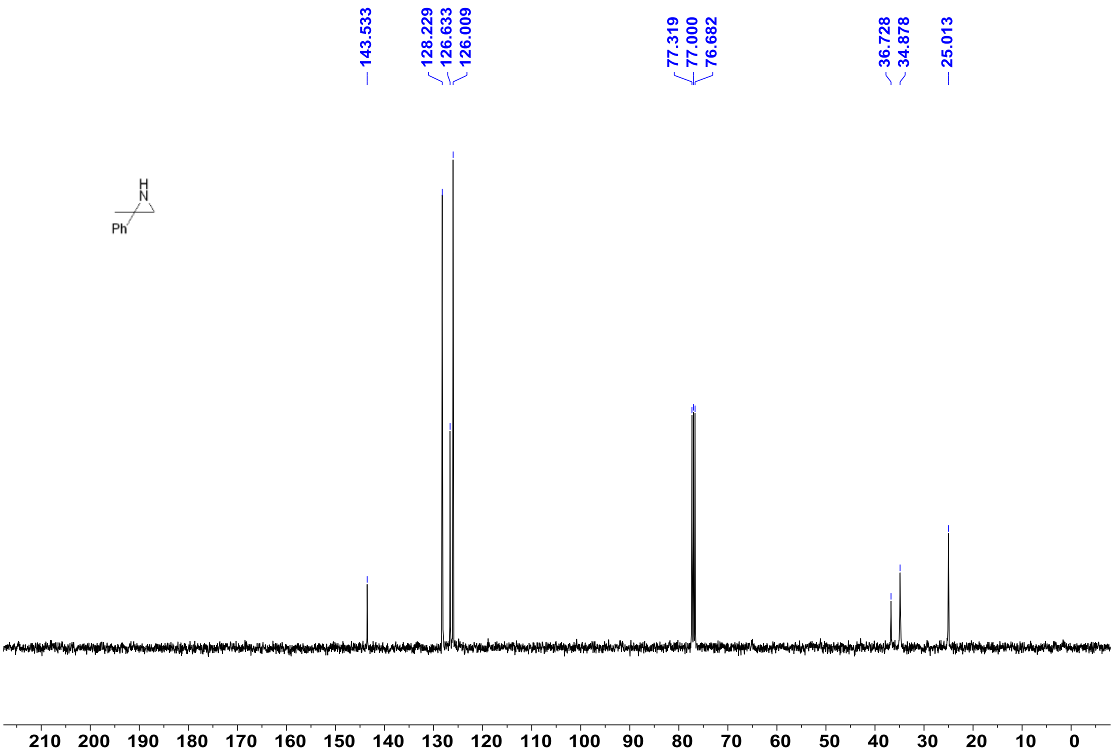
Copies of NMR spectra of synthesized 2,2-disubstituted aziridines 2

2-Methyl-2-phenylaziridine (2n)

^{1}H MNR (400 MHz, $CDCl_3$)

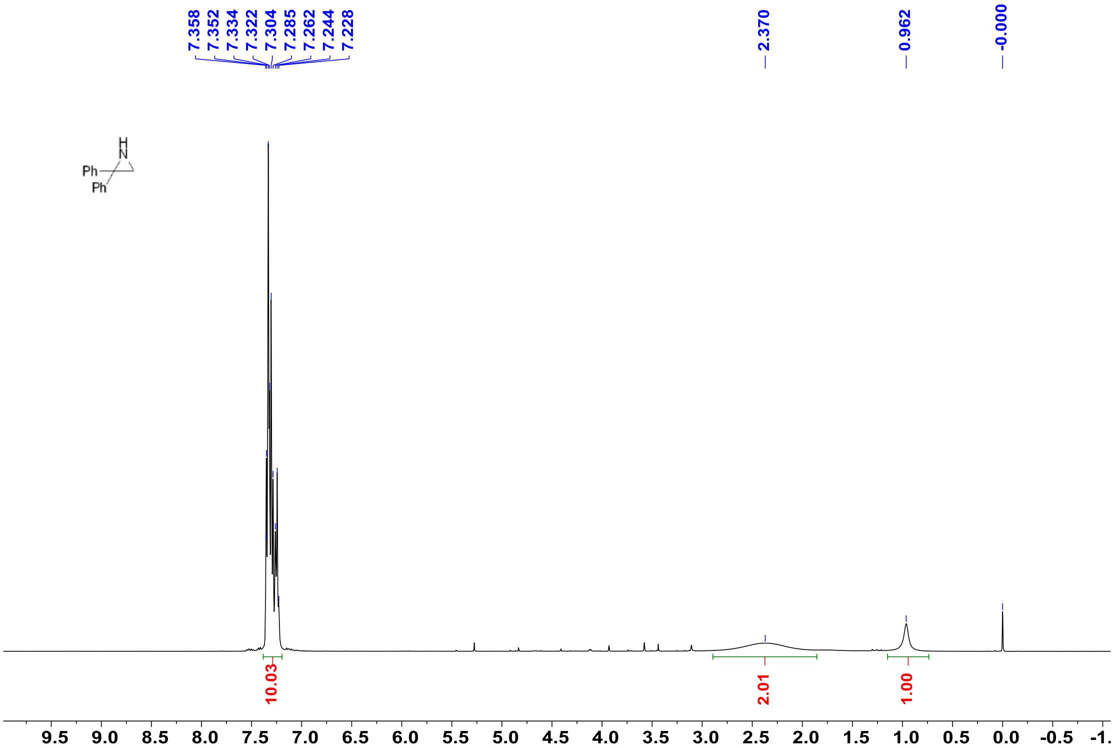


^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

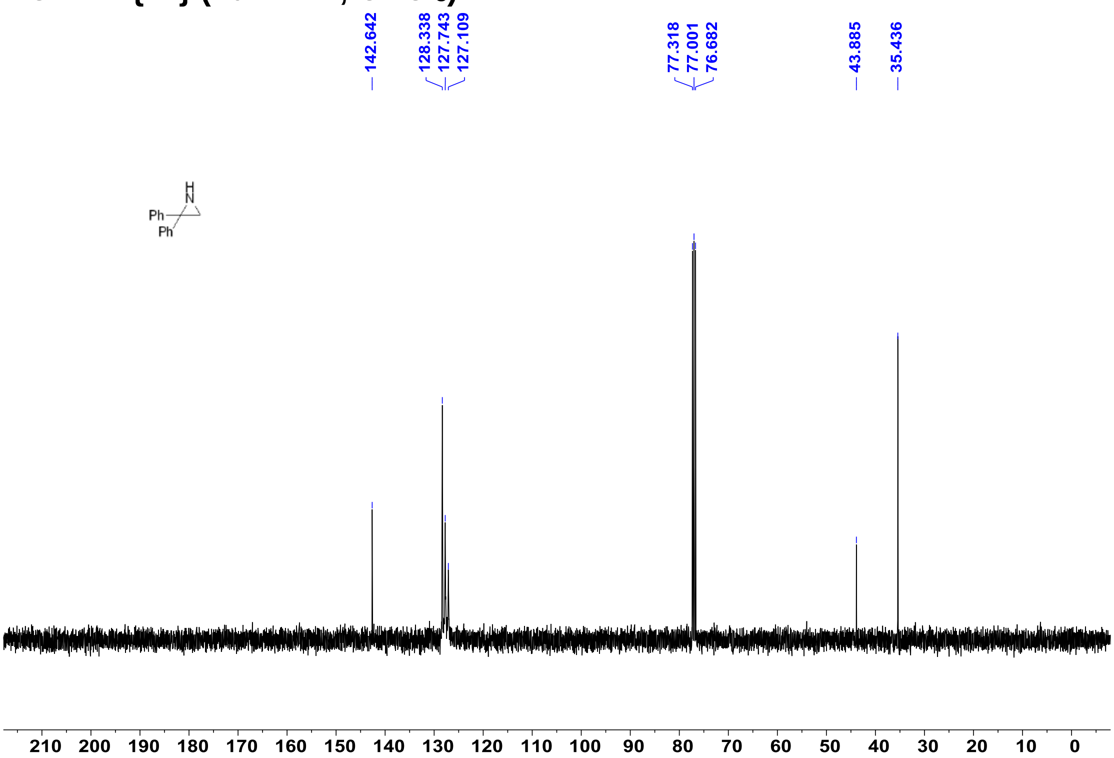


2,2-Diphenylaziridine (2o)

^{1}H MNR (400 MHz, $CDCl_3$)



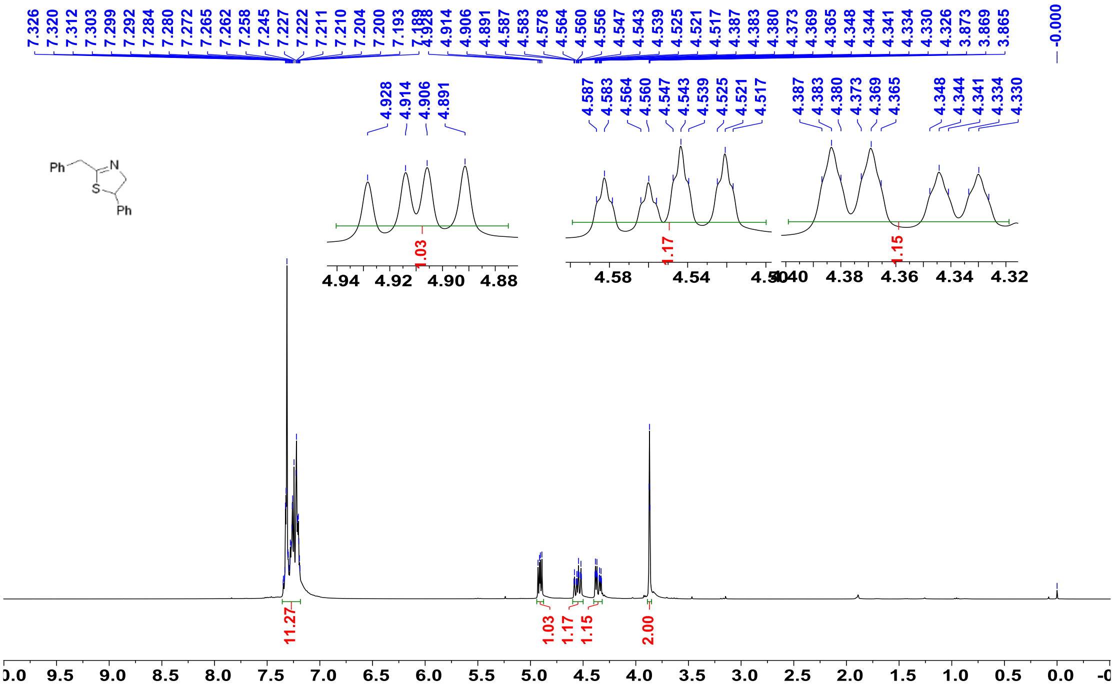
^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)



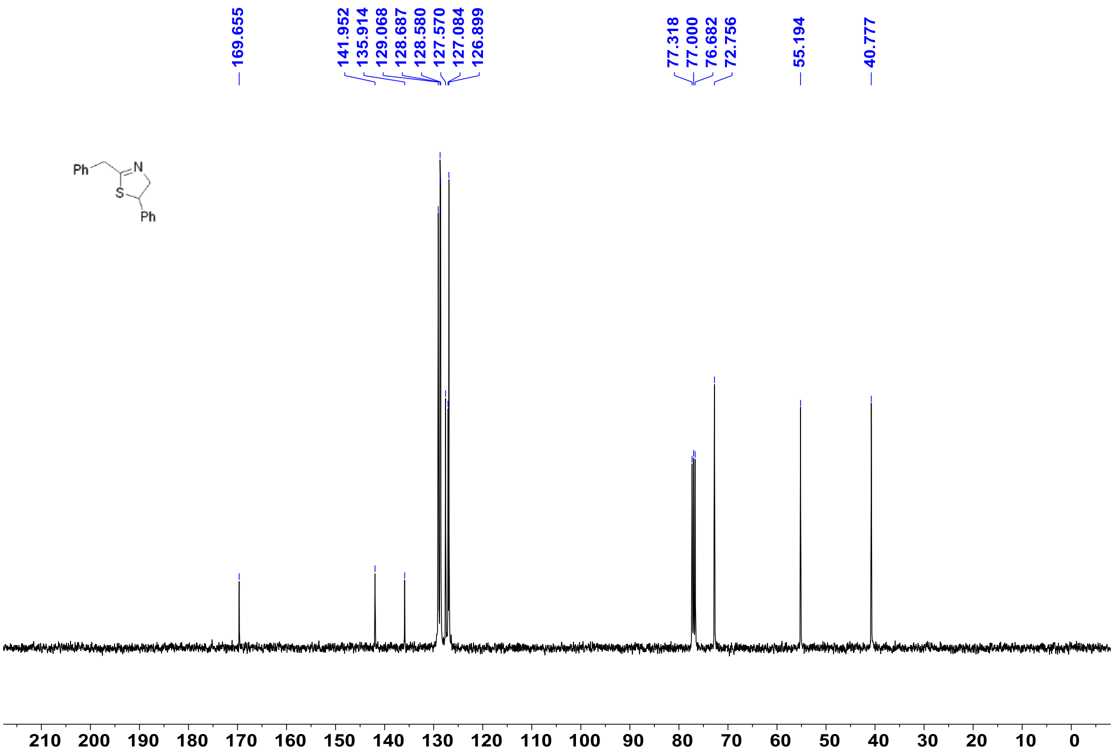
Copies of NMR spectra of thiazolines 3

2-Benzyl-4-phenyl-4,5-dihydrothiazole (3aa)

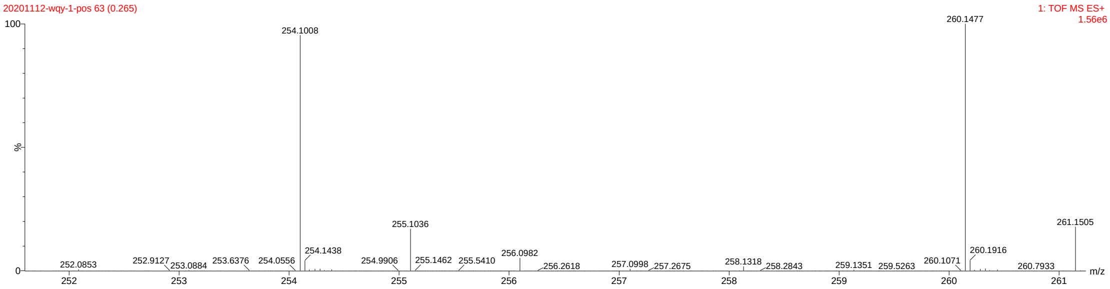
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

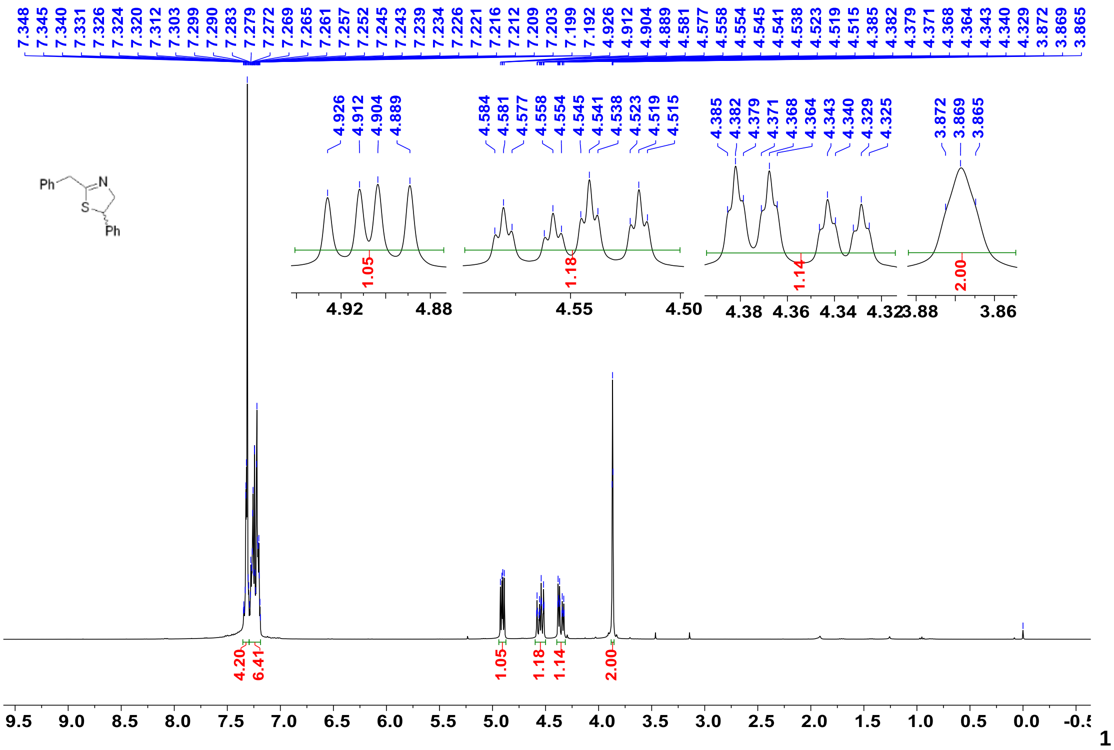


HRMS [M+H]+

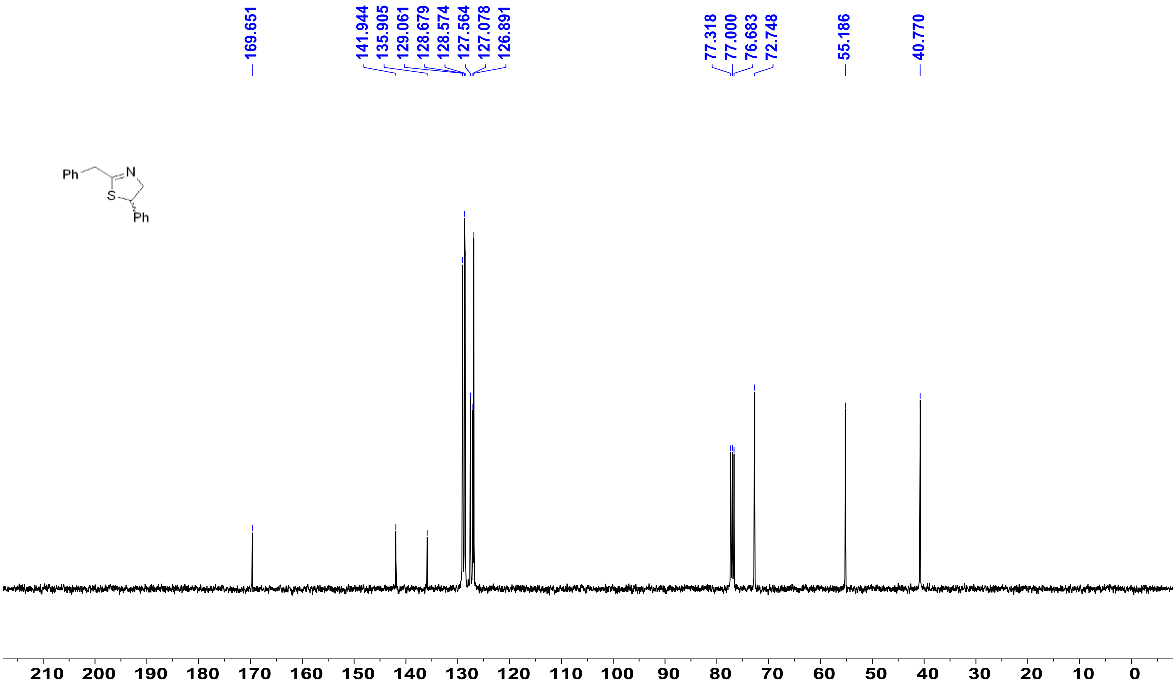


(*S*)-2-Benzyl-4-phenyl-4,5-dihydrothiazole ((*S*)-3aa)

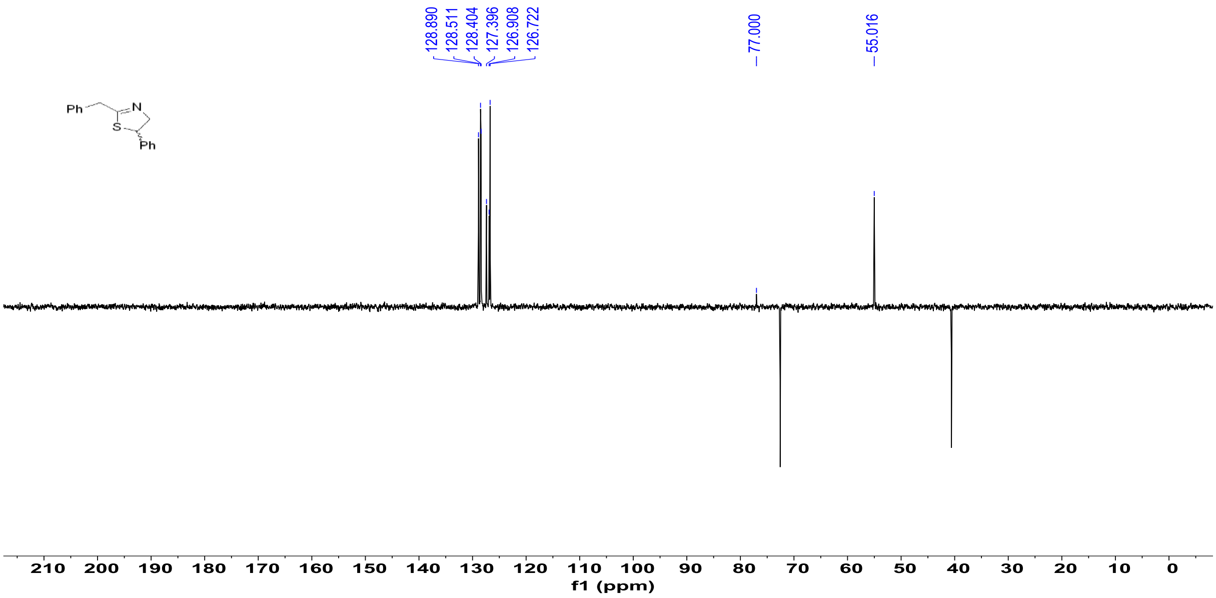
[1]H MNR (400 MHz, $CDCl_3$)



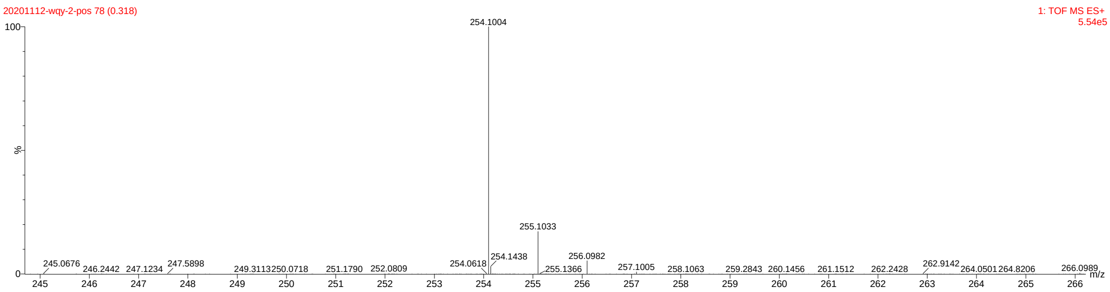
^{3}C NMR{^{1}H} (101 MHz, $CDCl_3$)



DEPT 135 ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

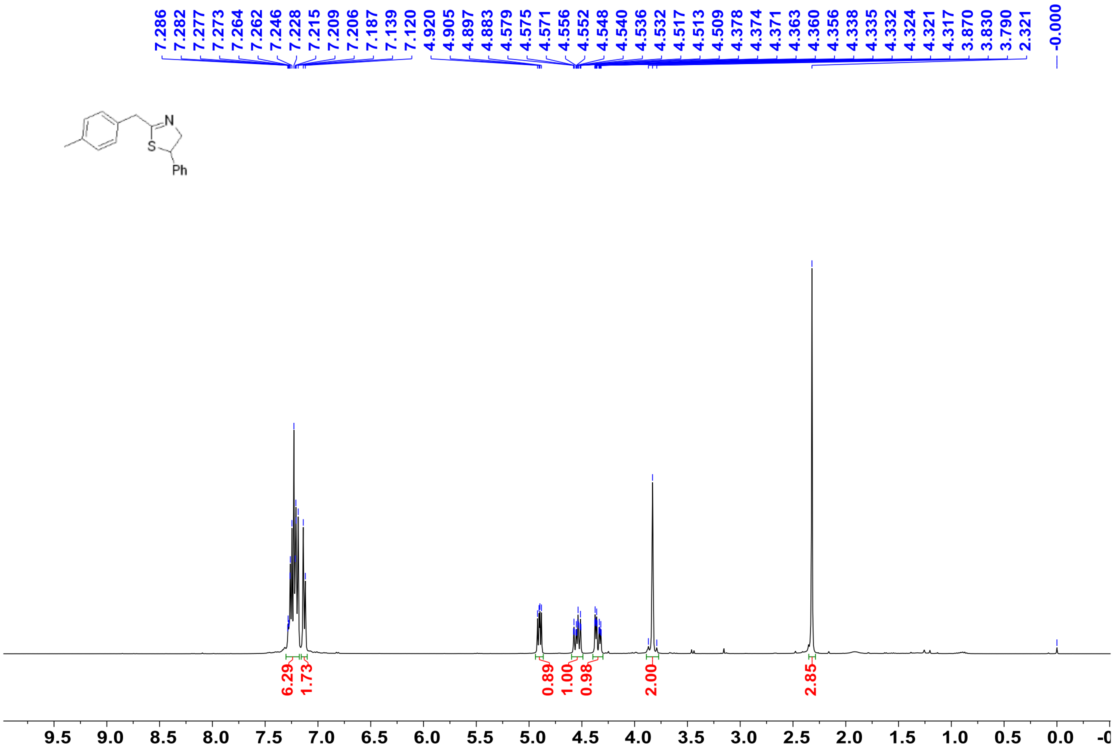


HRMS $[M+H]^+$

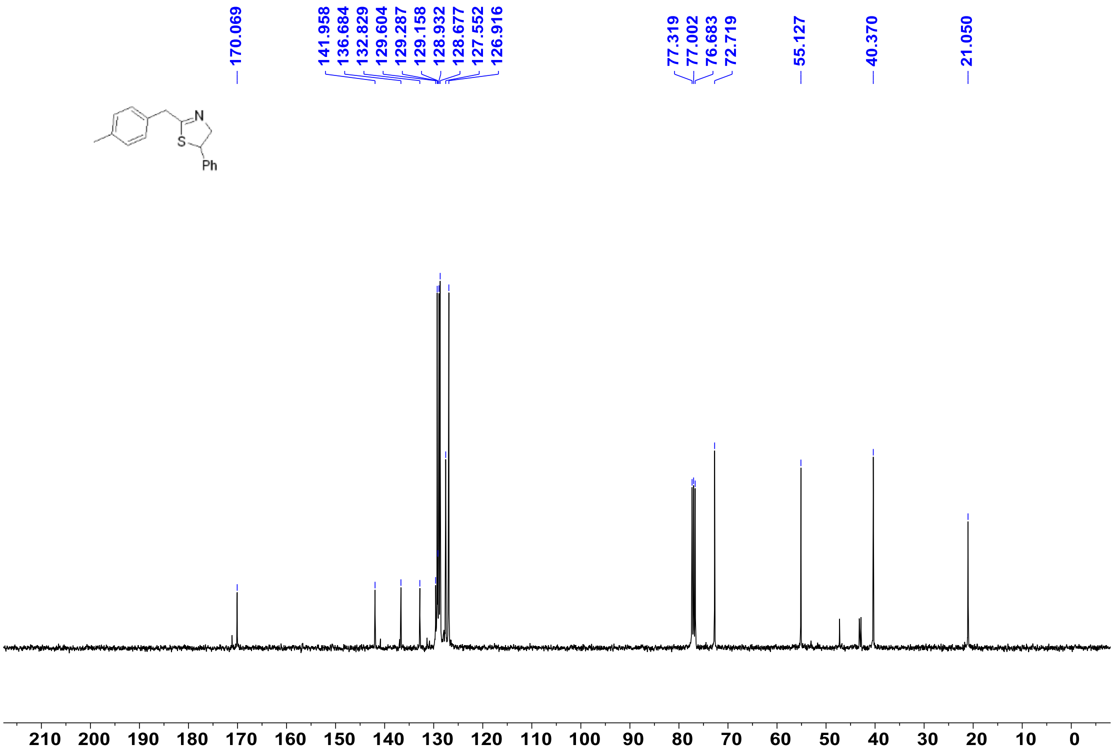


2-(4-Methylbenzyl)-5-phenyl-4,5-dihydrothiazole (3ba)

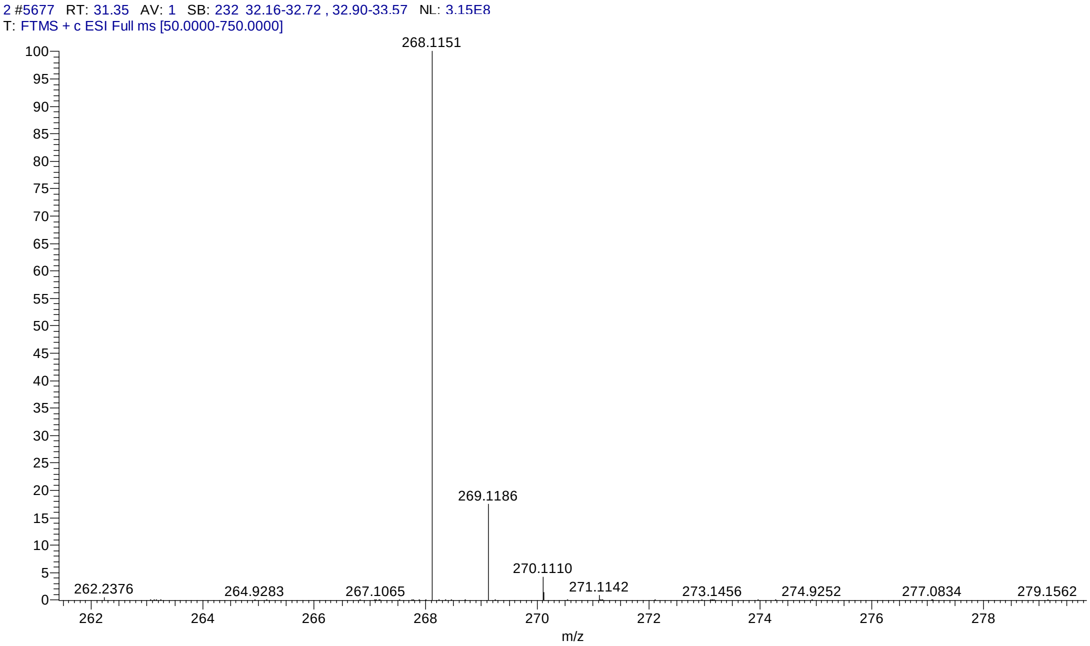
^{1}H MNR (400 MHz, CDCl$_3$)



^{13}C NMR{^{1}H} (101 MHz, CDCl$_3$)

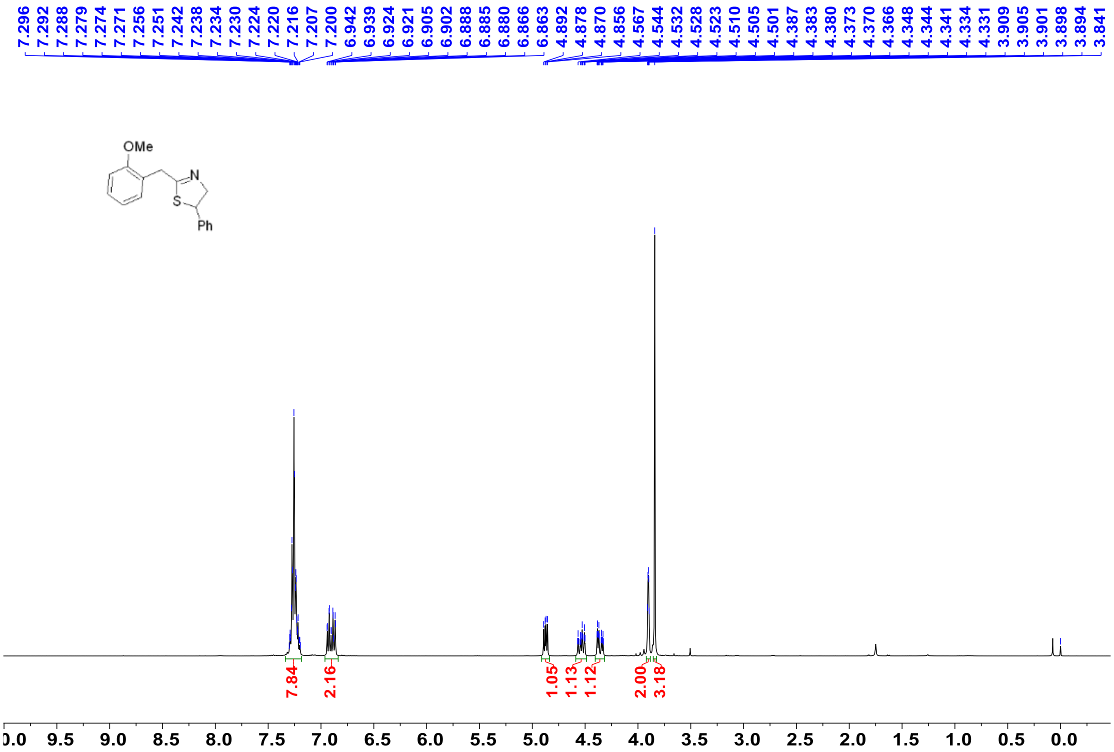


HRMS [M+H]+

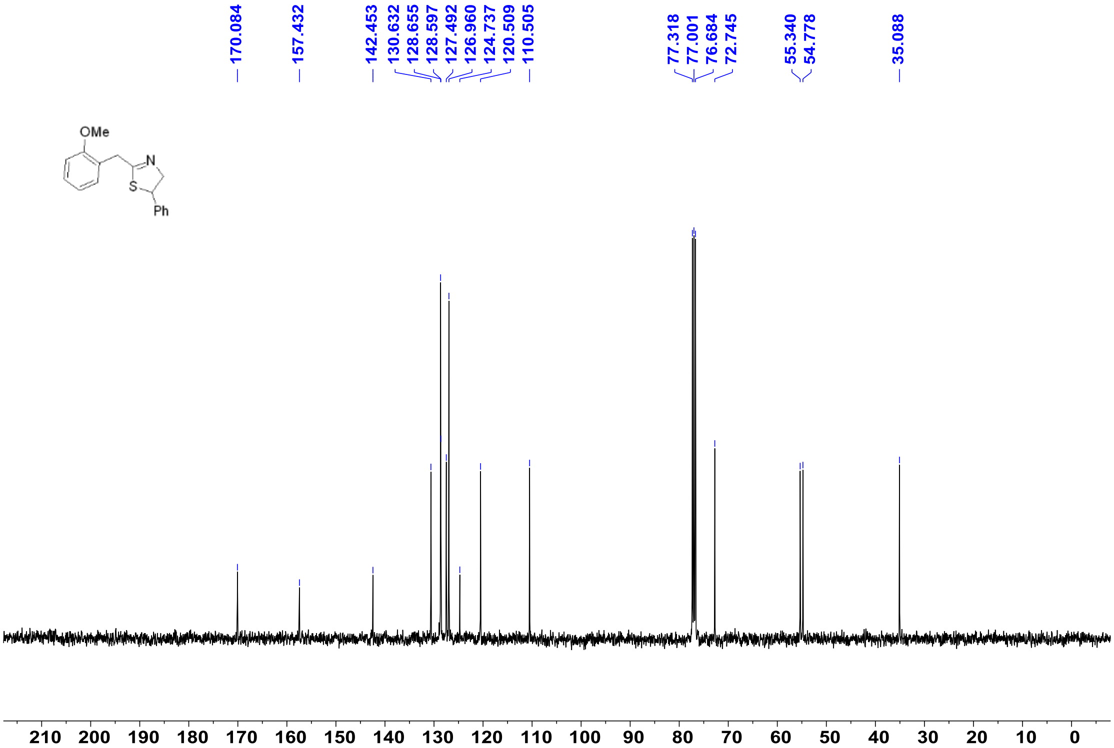


2-(2-Methoxybenzyl)-5-phenyl-4,5-dihydrothiazole (3ca)

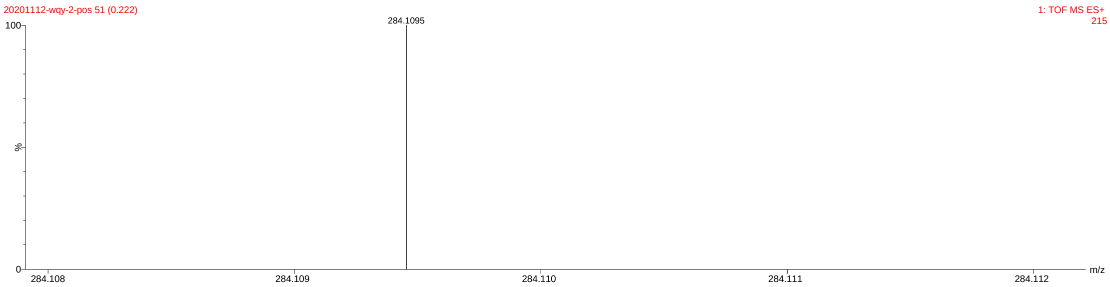
1H MNR (400 MHz, CDCl3)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

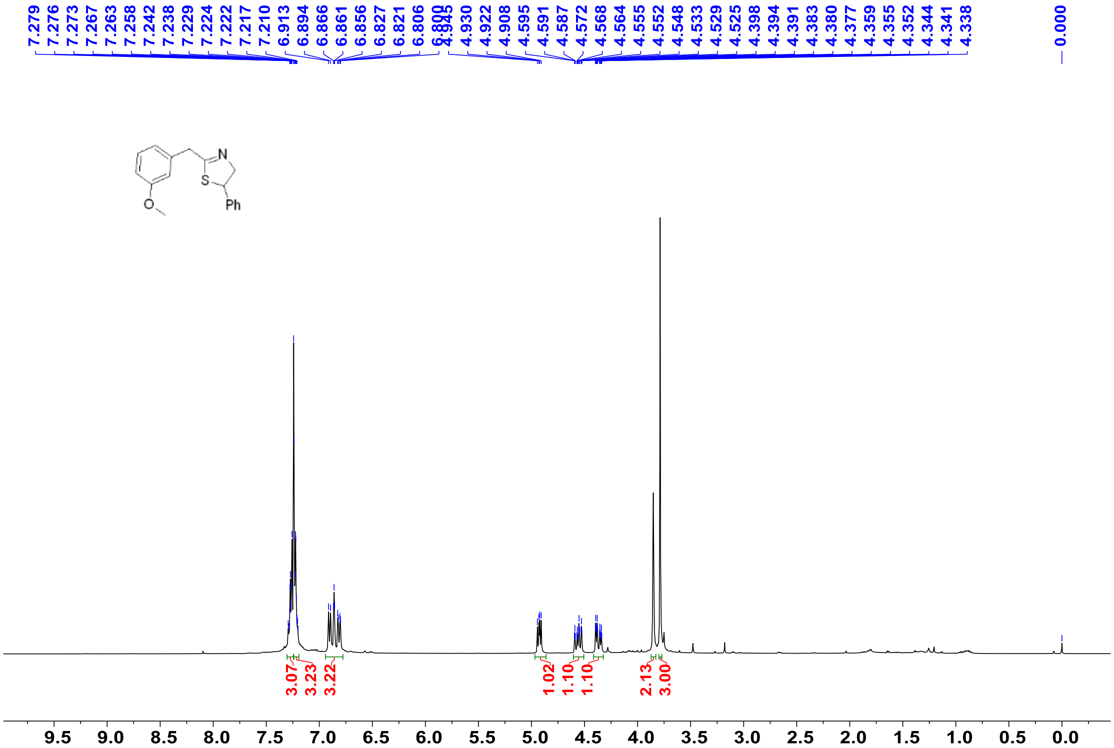


HRMS [M+H]+

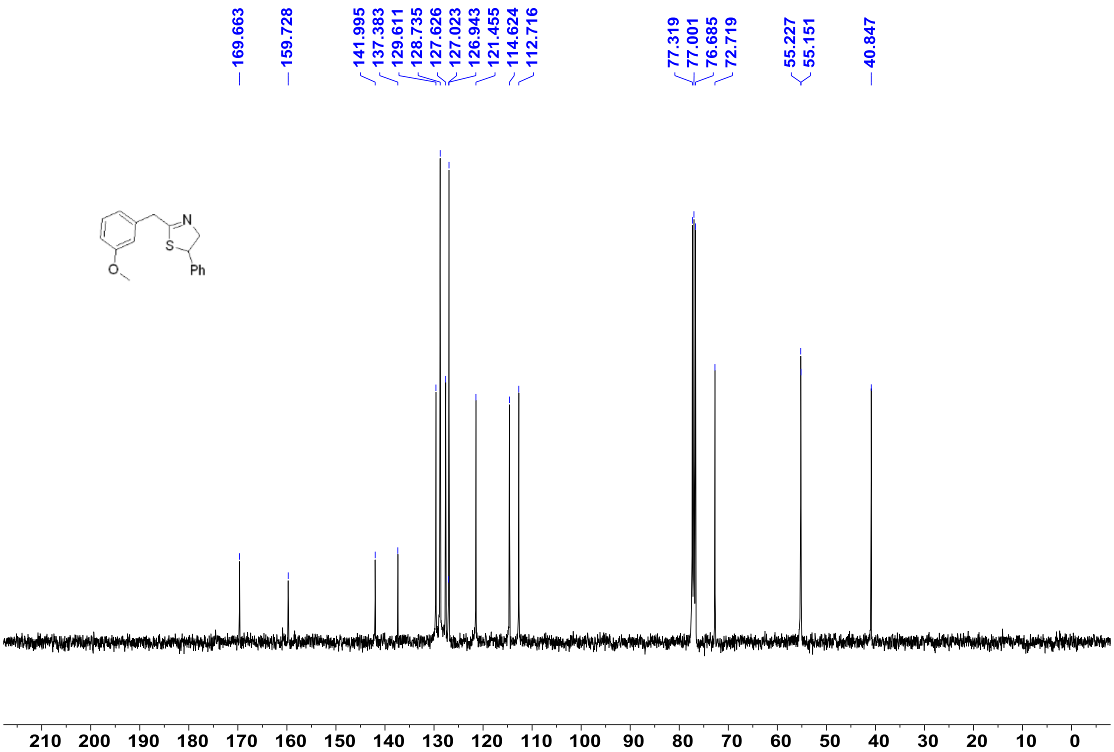


2-(3-Methoxybenzyl)-5-phenyl-4,5-dihydrothiazole (3da)

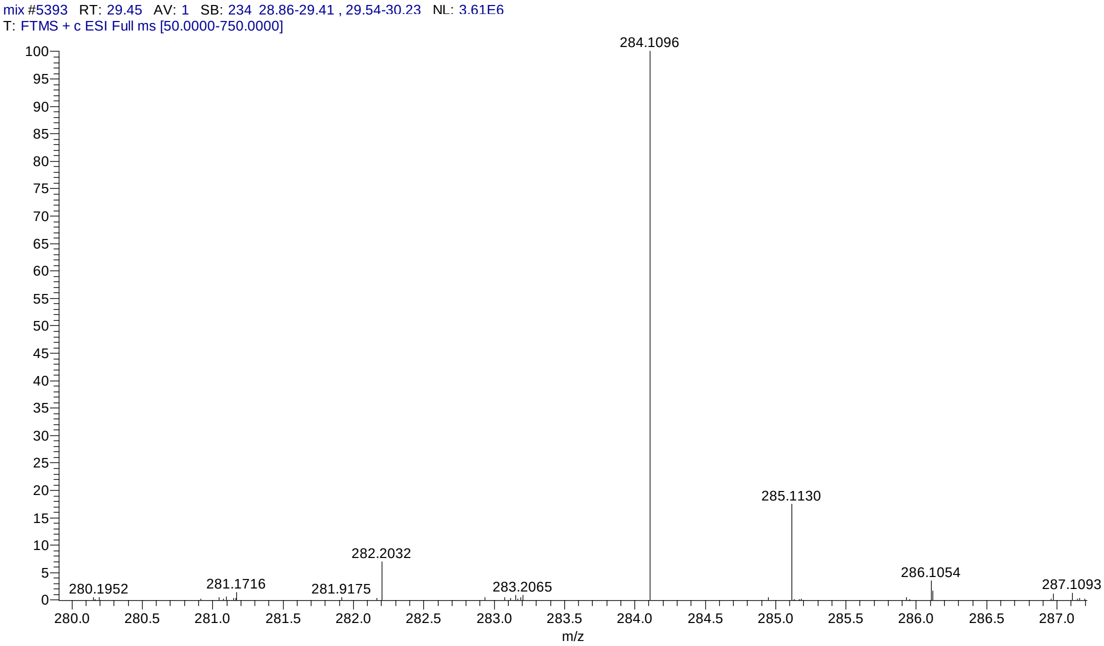
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

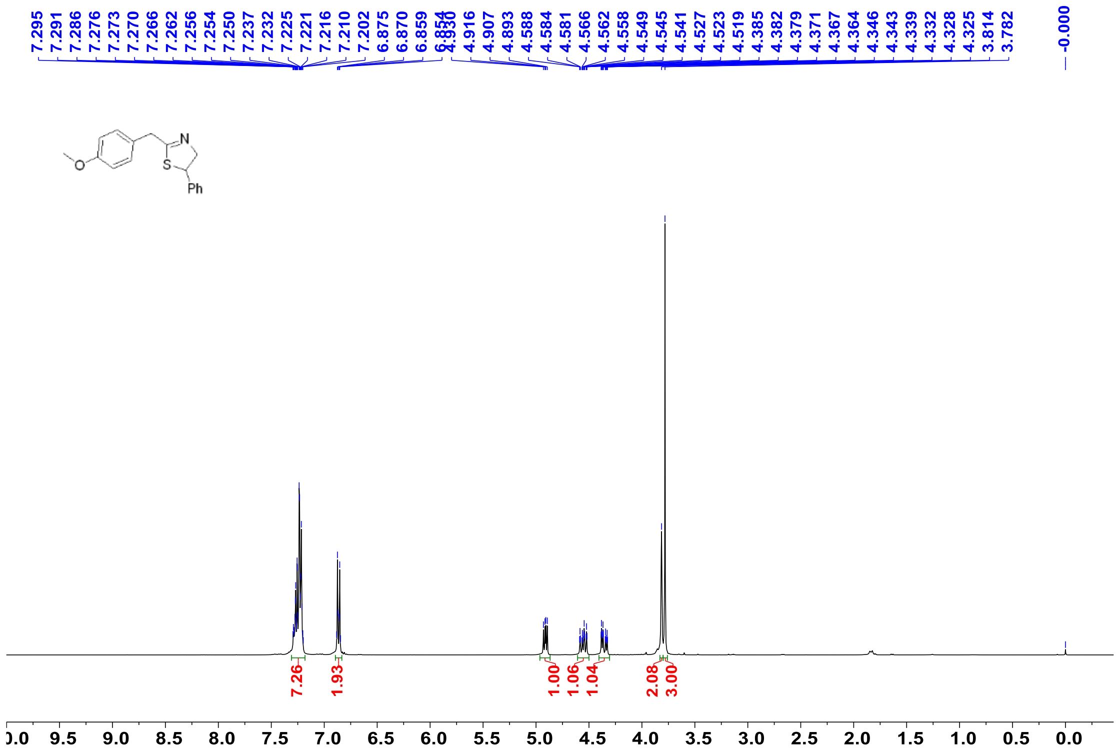


HRMS $[M+H]^+$

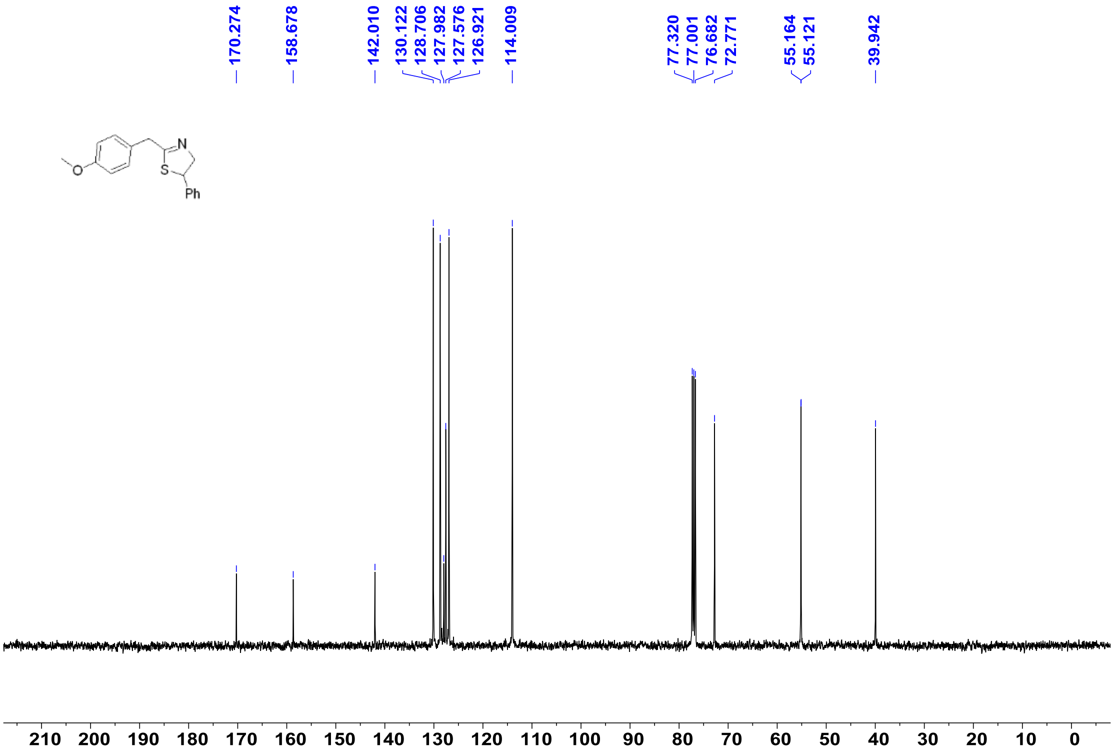


2-(4-Methoxybenzyl)-5-phenyl-4,5-dihydrothiazole (3ea)

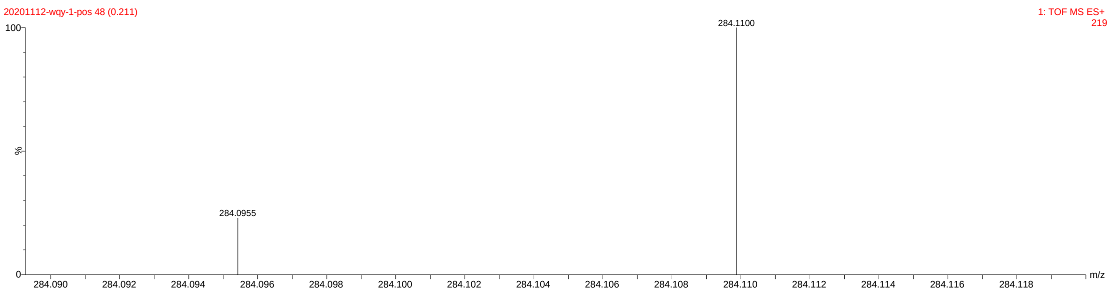
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, CDCl$_3$)

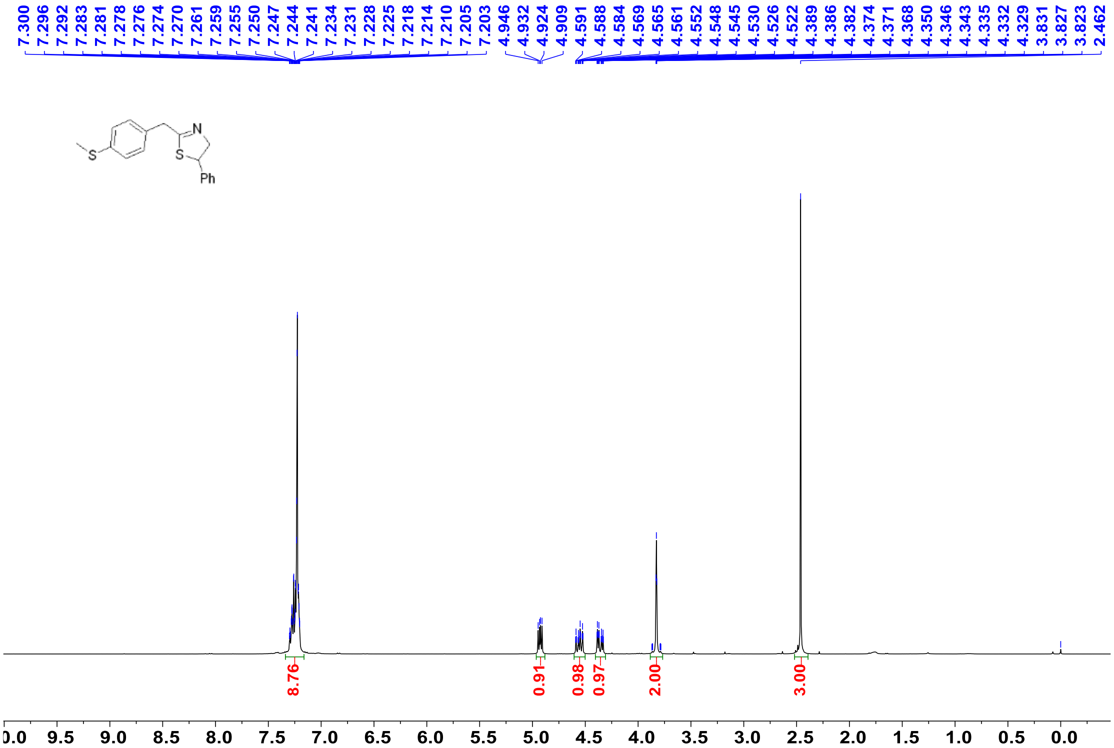


HRMS [M+H]$^+$

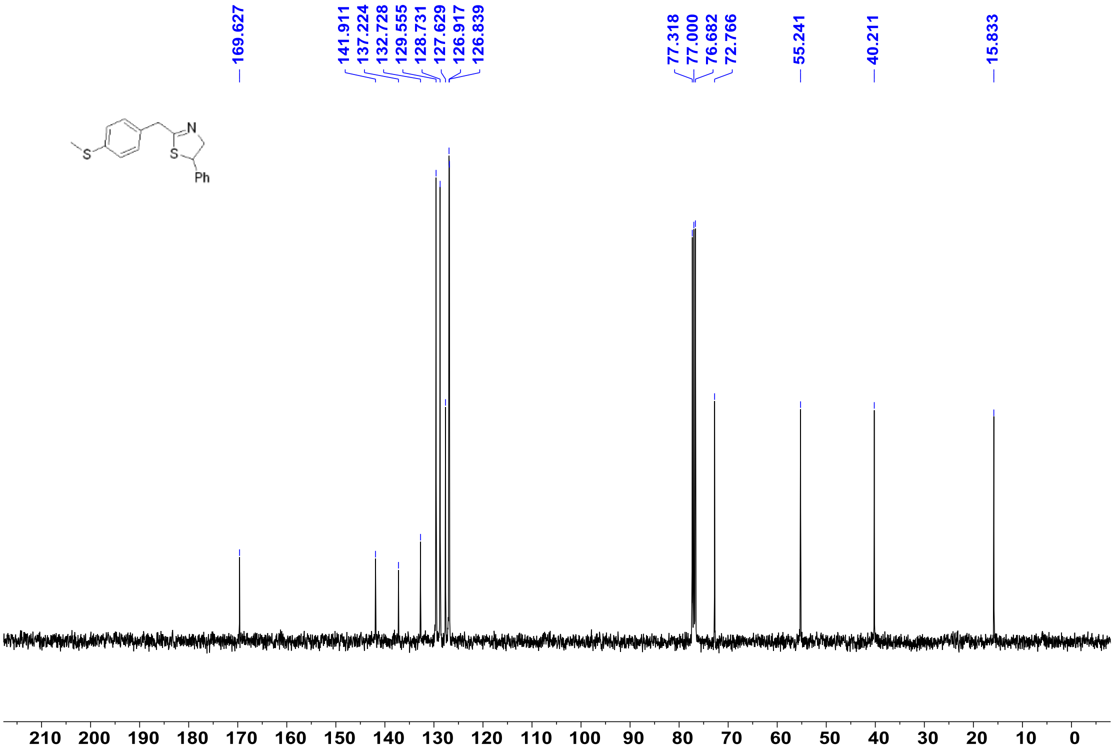


2-(4-(Methylthio)benzyl)-5-phenyl-4,5-dihydrothiazole (3fa)

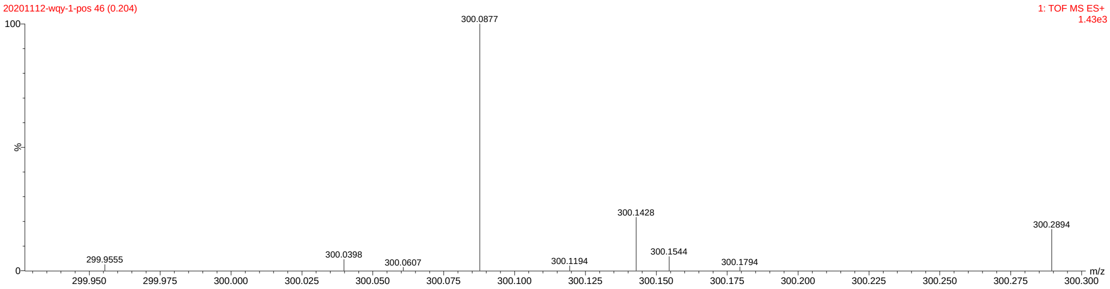
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

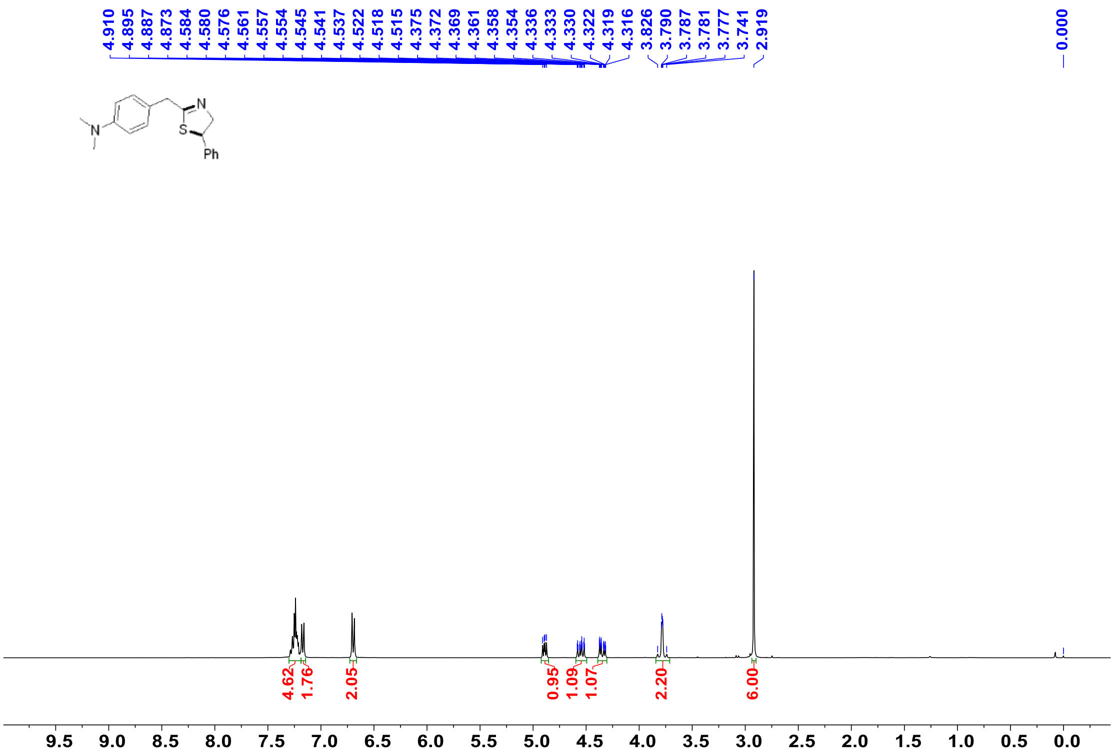


HRMS [M+H]$^+$

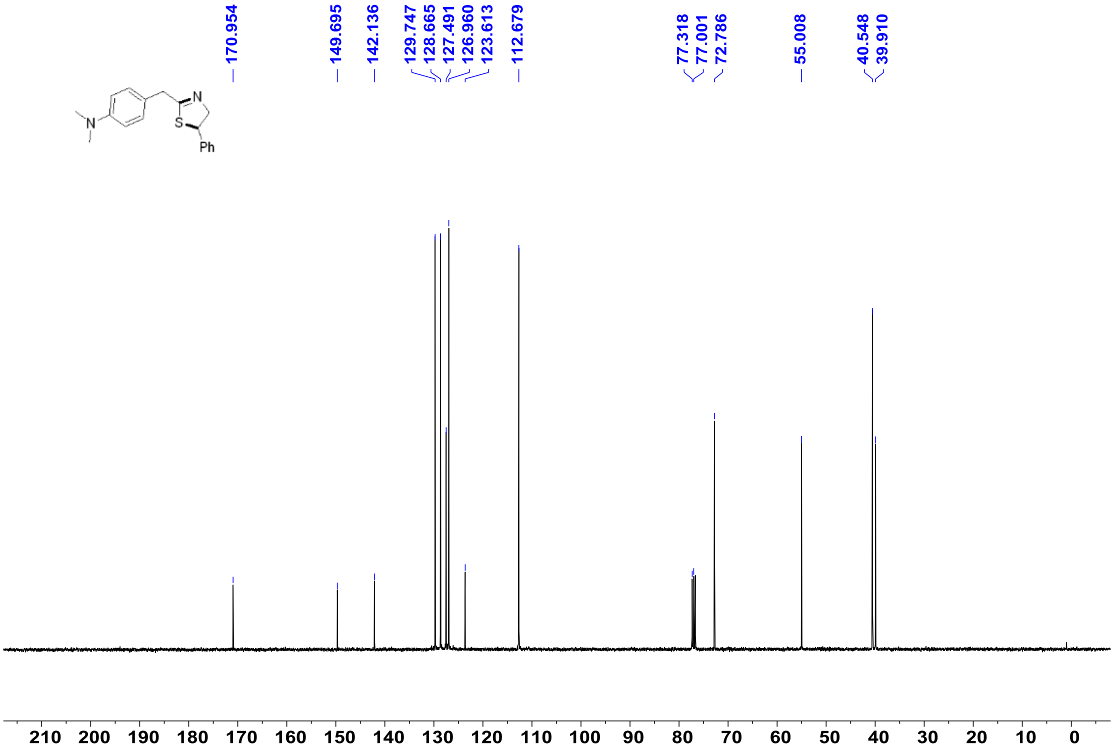


(*N,N*-Dimethyl-4-((5-phenyl-4,5-dihydrothiazol-2-yl)methyl)aniline (3ga)

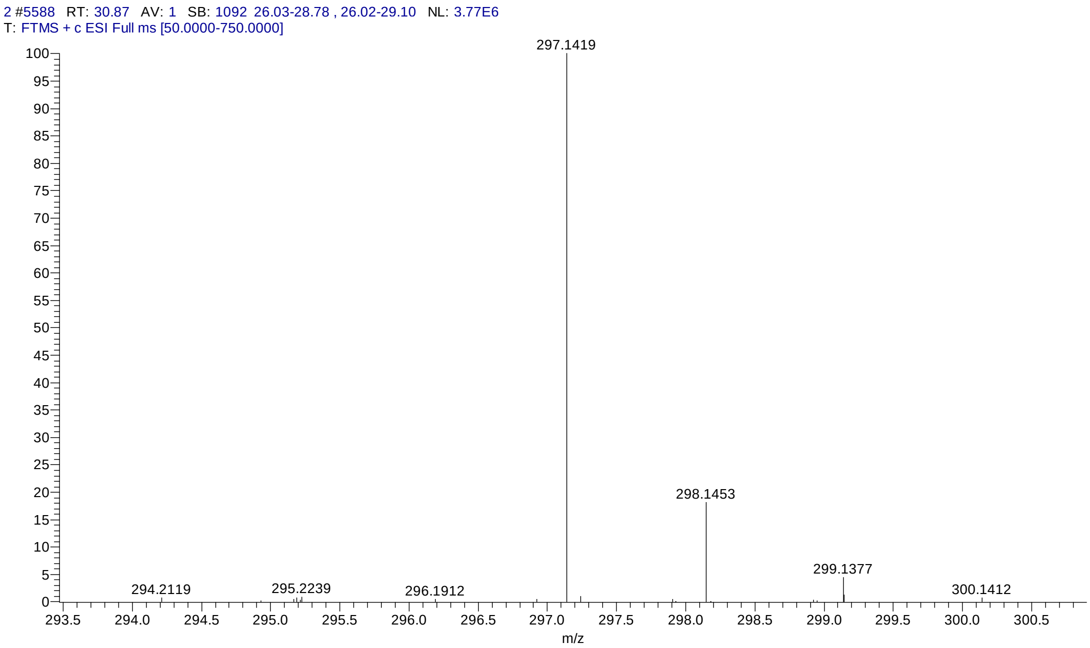
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

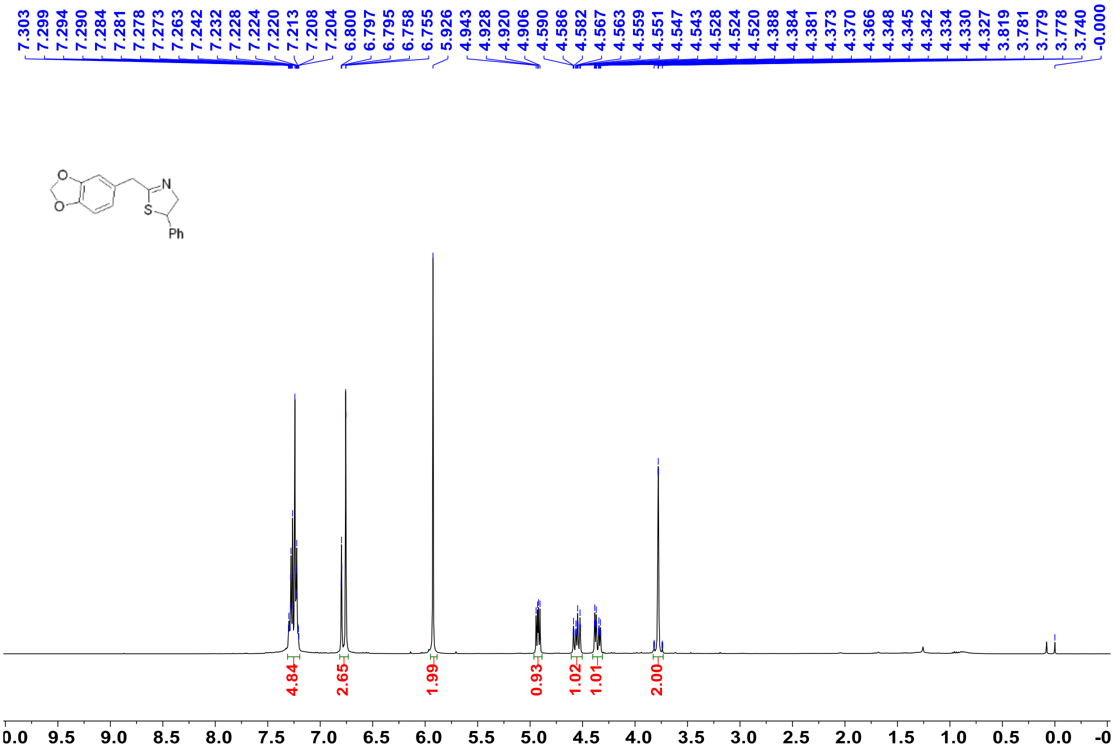


HRMS [M+H]$^+$

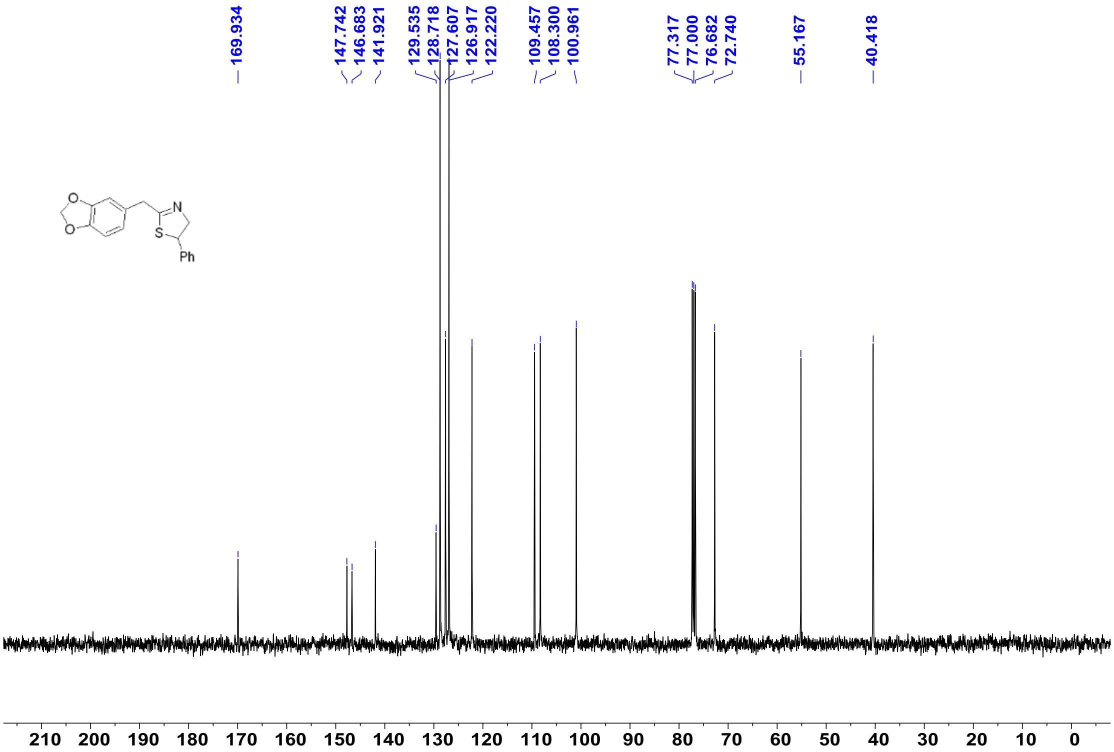


2-(Benzo[*d*][1,3]dioxol-5-ylmethyl)-5-phenyl-4,5-dihydrothiazole (3ha)

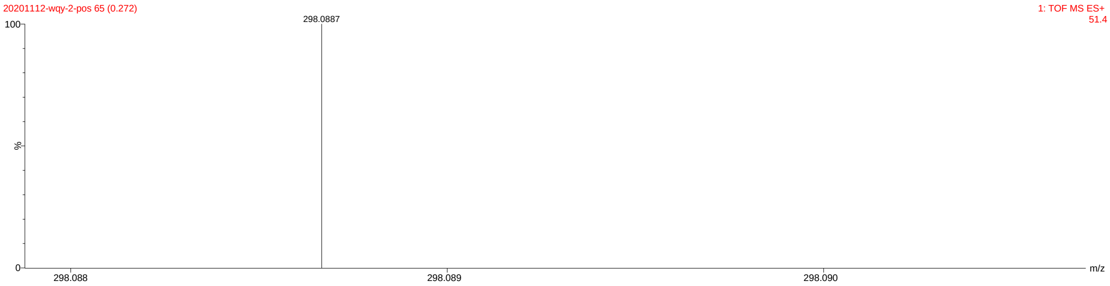
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

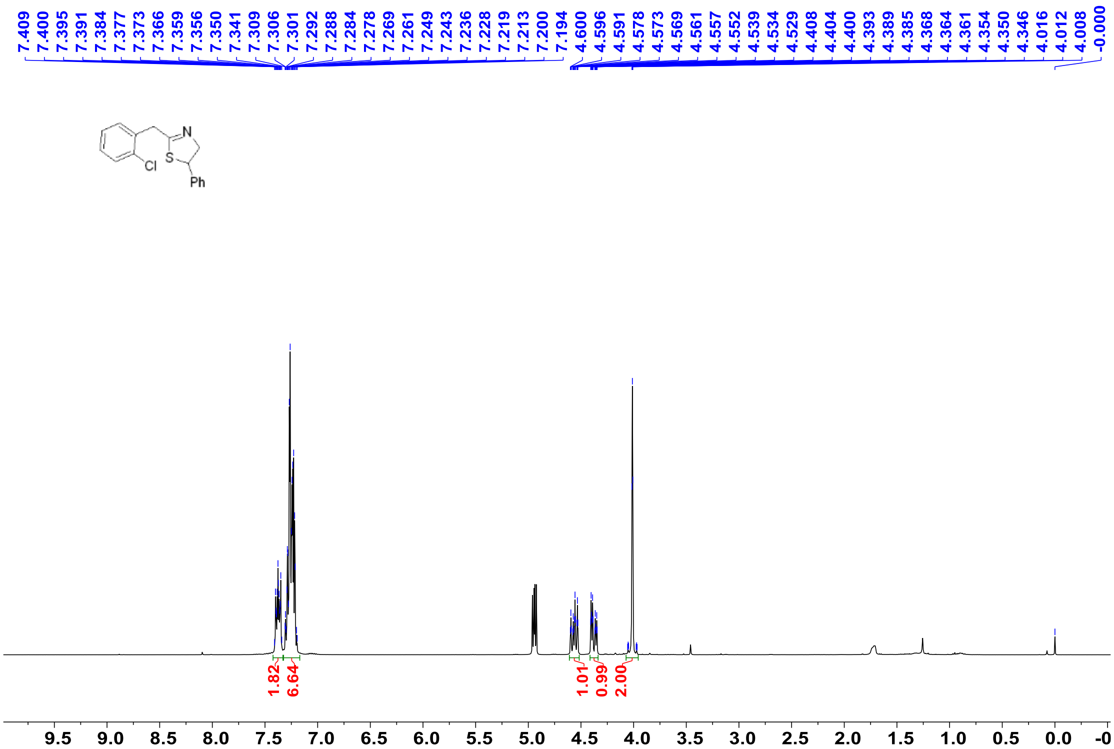


HRMS [M+H]$^+$

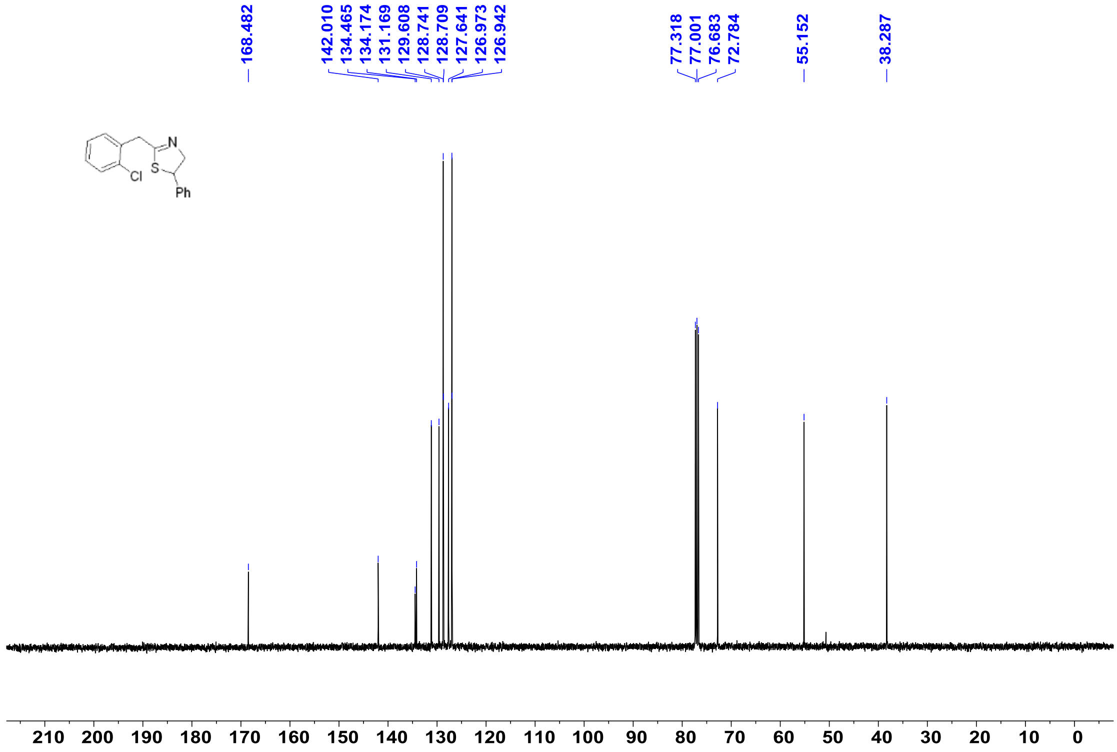


2-(2-Chlorobenzyl)-5-phenyl-4,5-dihydrothiazole (3ia)

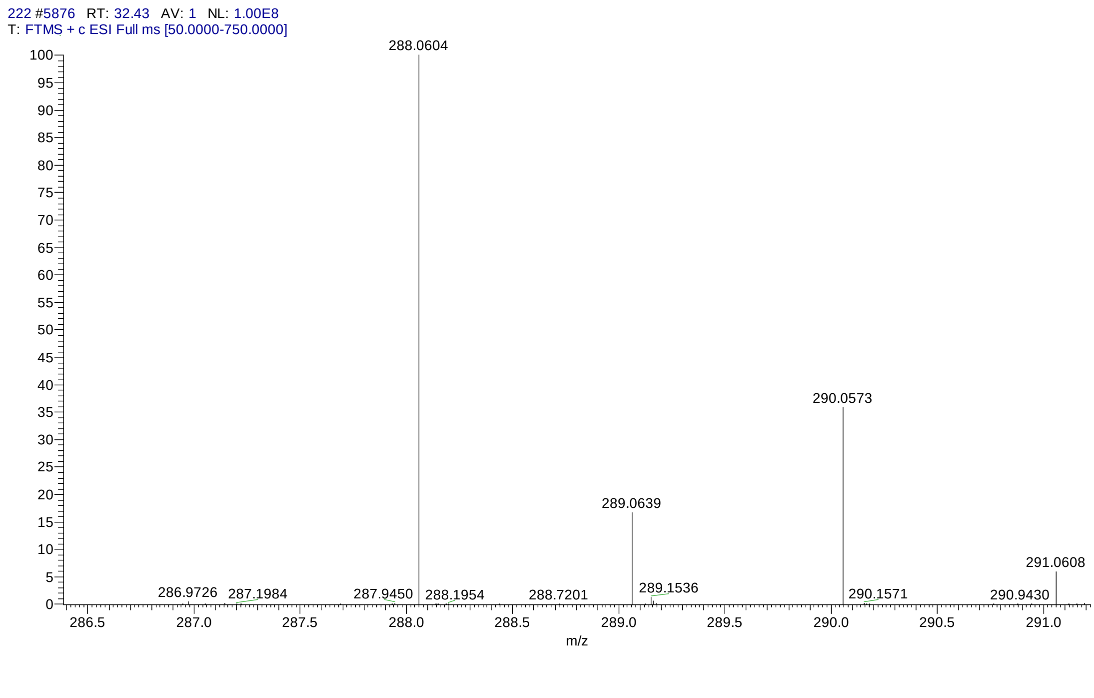
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

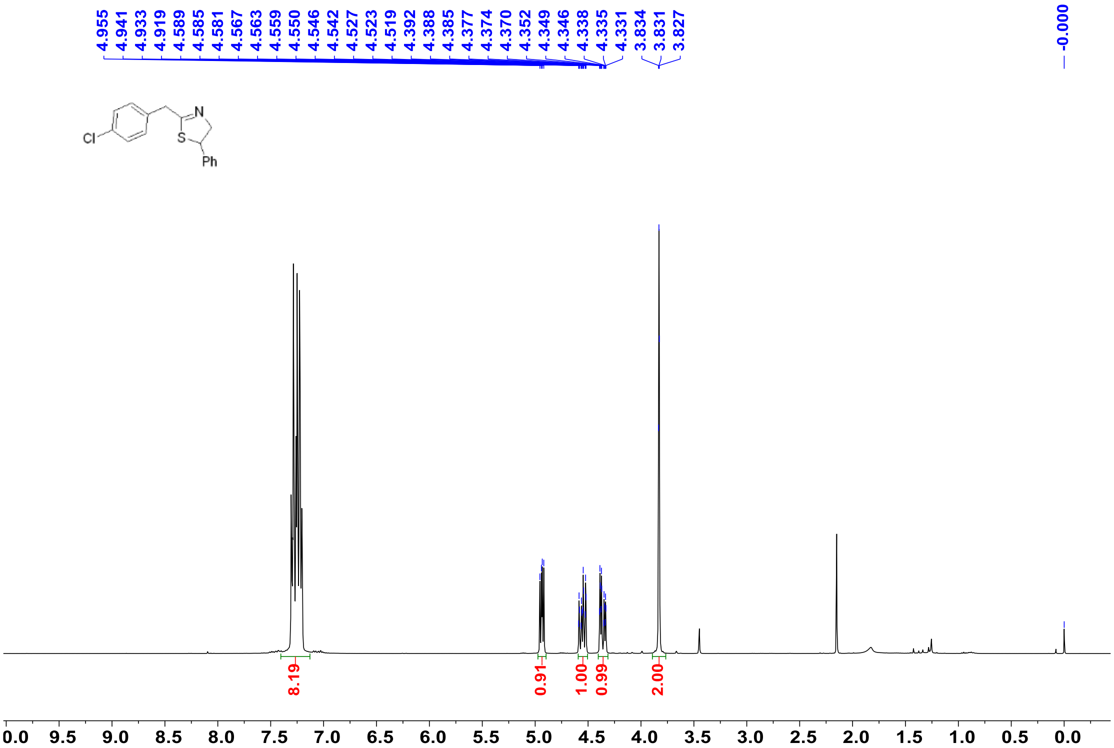


HRMS [M+H]+

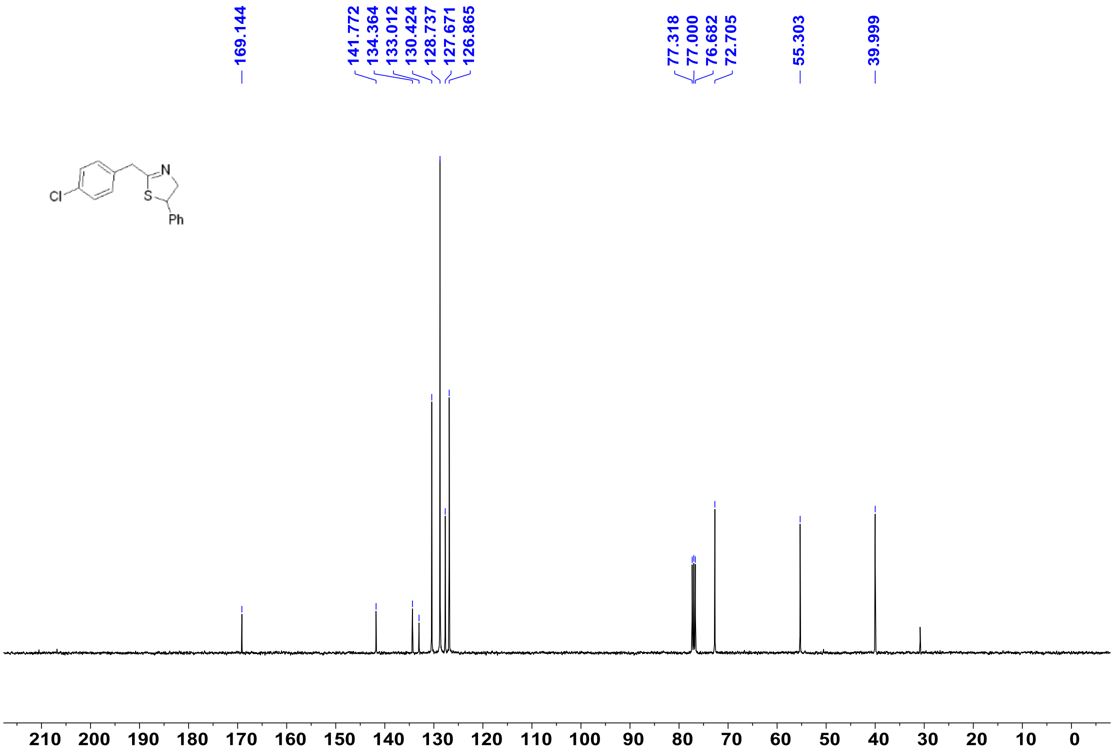


2-(4-Chlorobenzyl)-5-phenyl-4,5-dihydrothiazole (3ja)

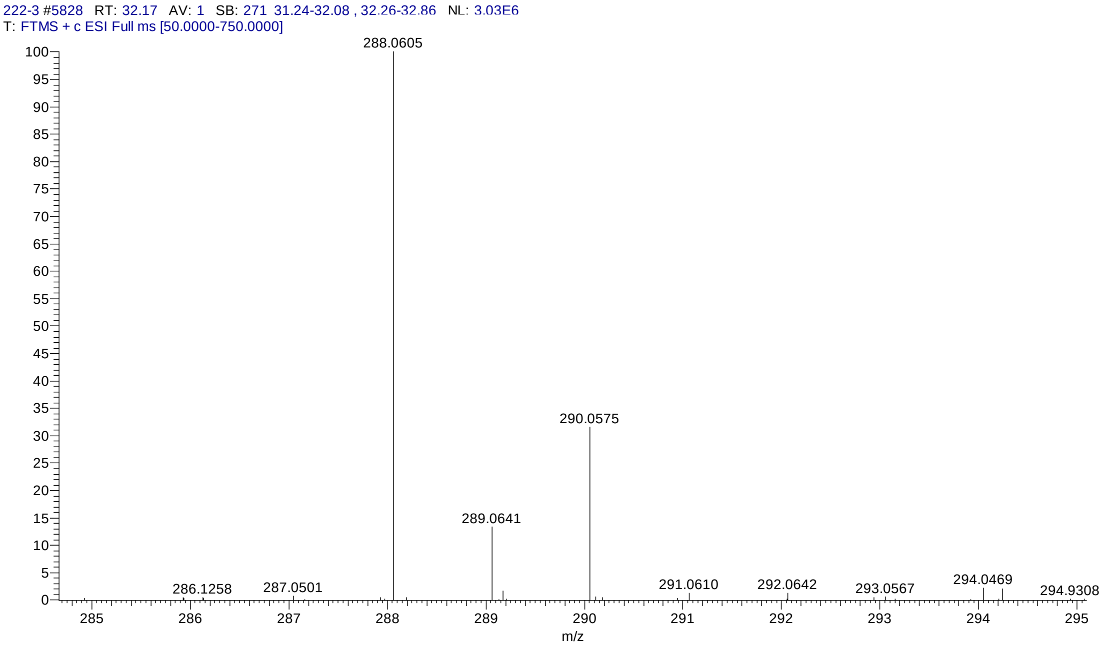
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

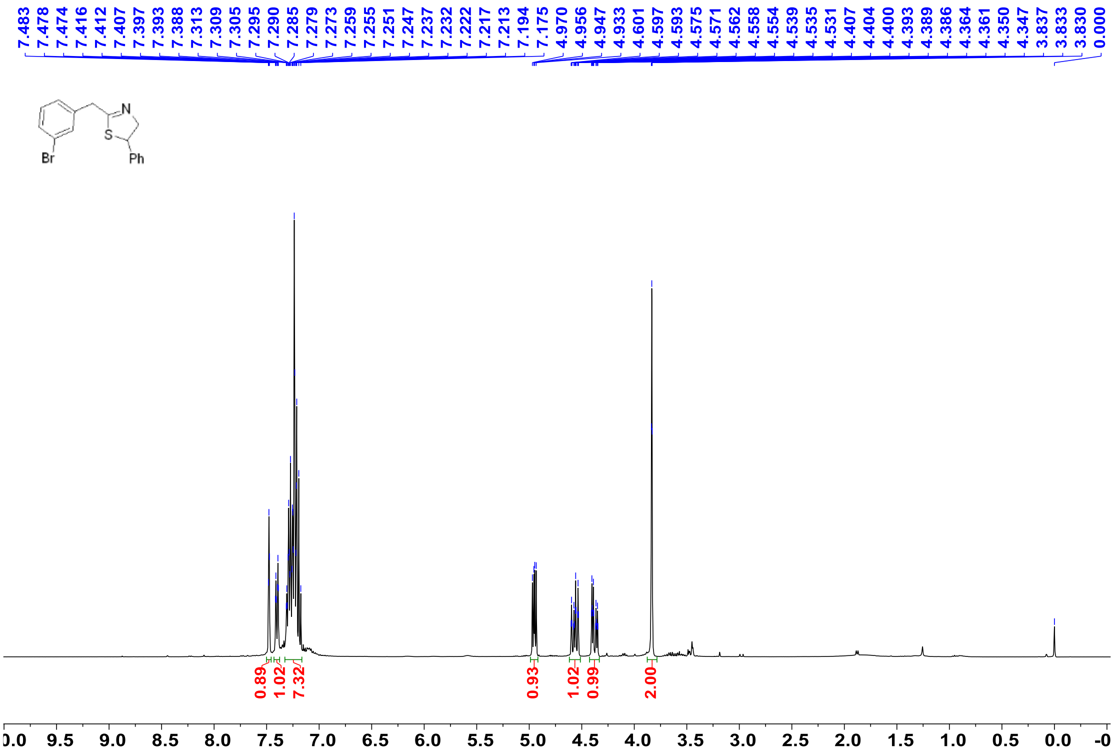


HRMS [M+H]+

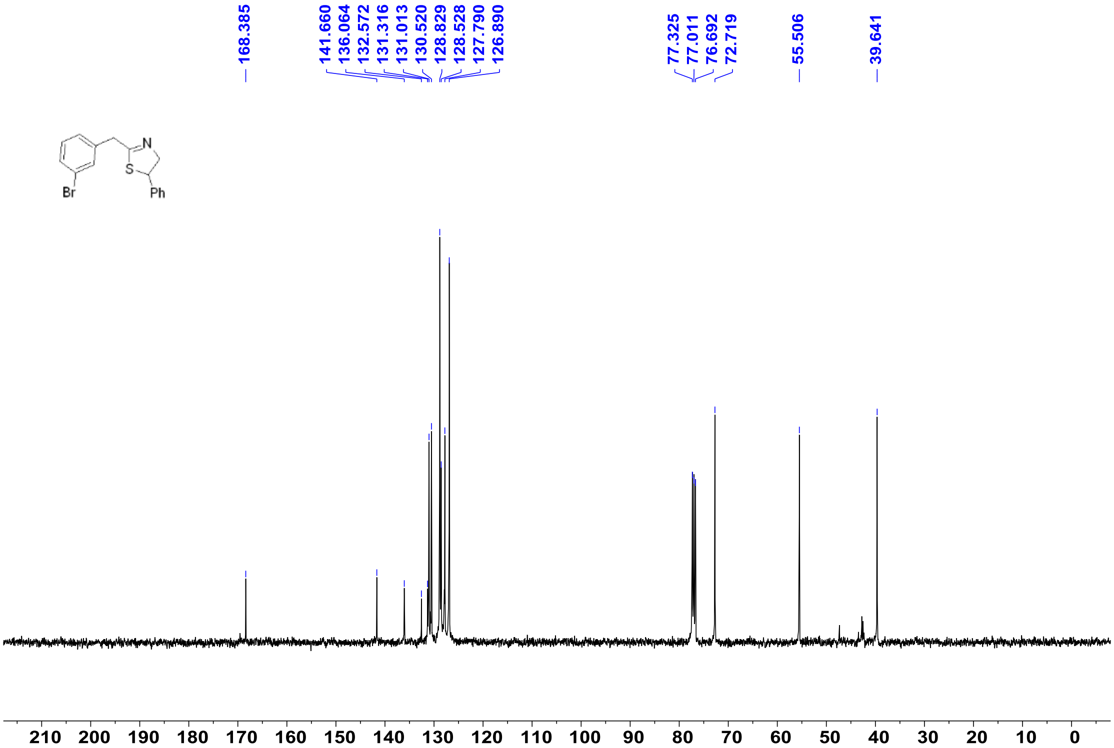


2-(3-Bromobenzyl)-5-phenyl-4,5-dihydrothiazole (3ka)

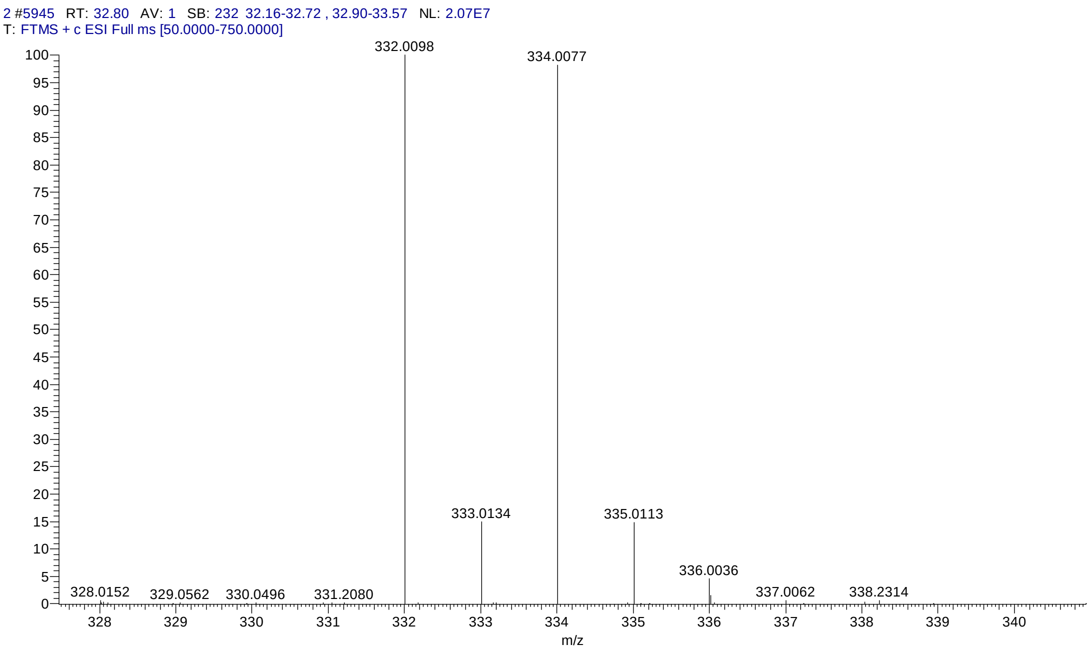
1H MNR (400 MHz, CDCl3)



^{13}C NMR{^1H} (101 MHz, $CDCl_3$)

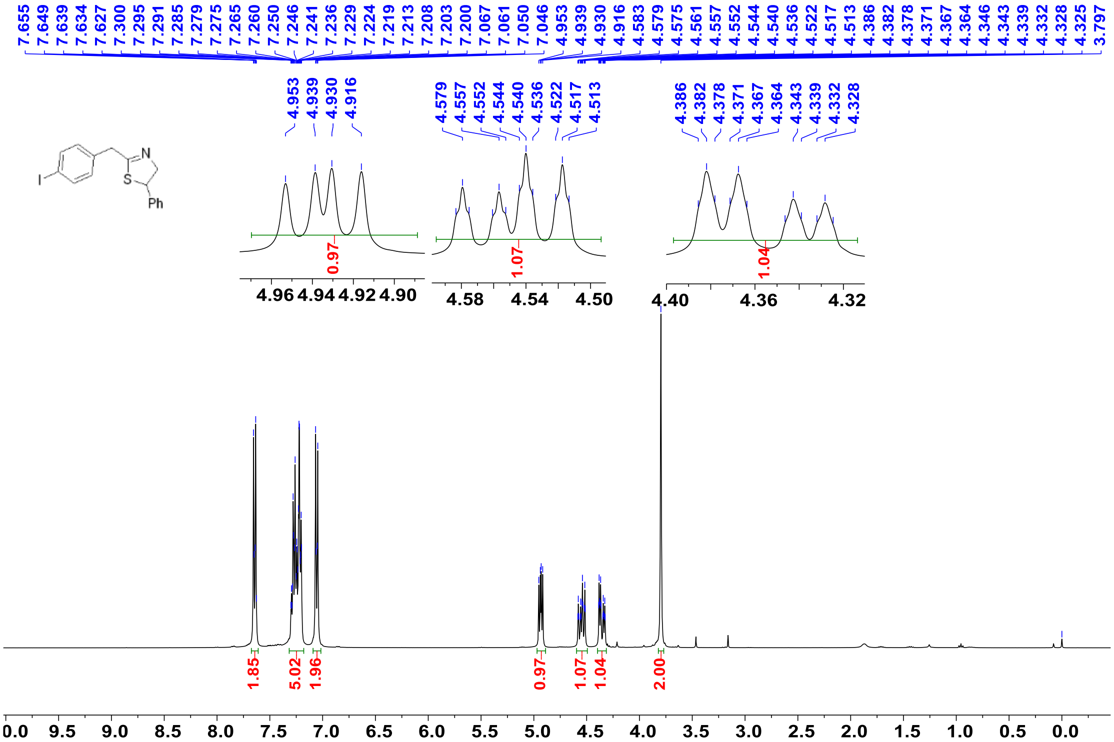


HRMS [M+H]+

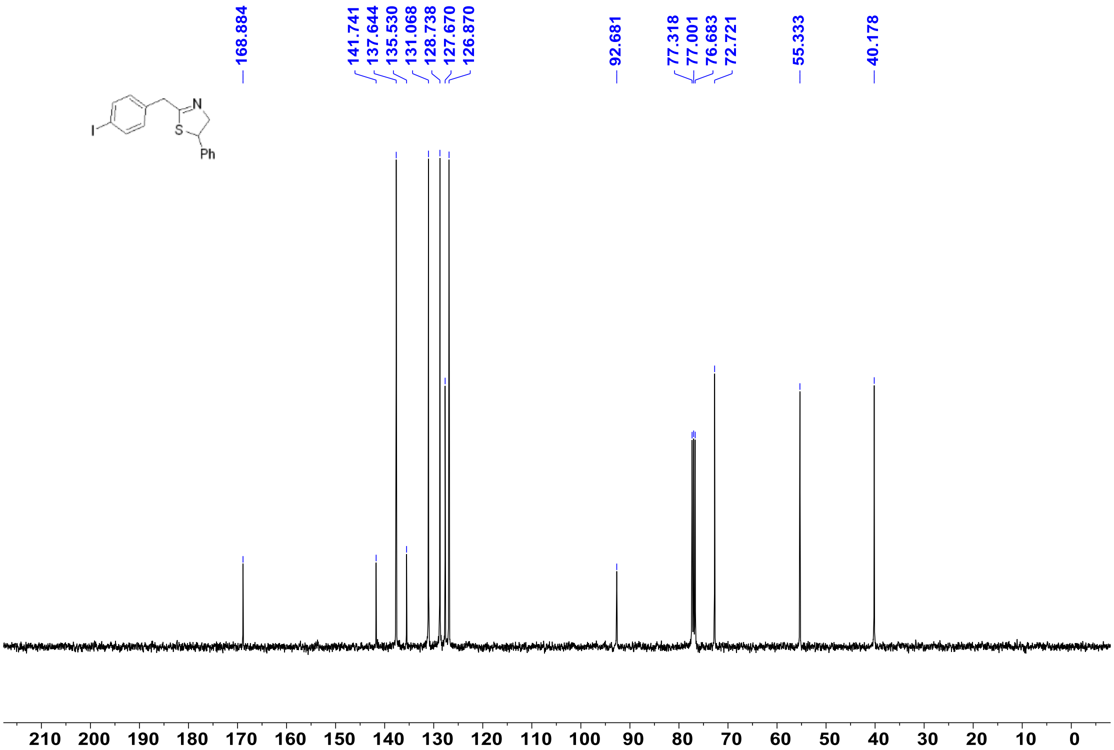


2-(4-Iodobenzyl)-5-phenyl-4,5-dihydrothiazole (3la)

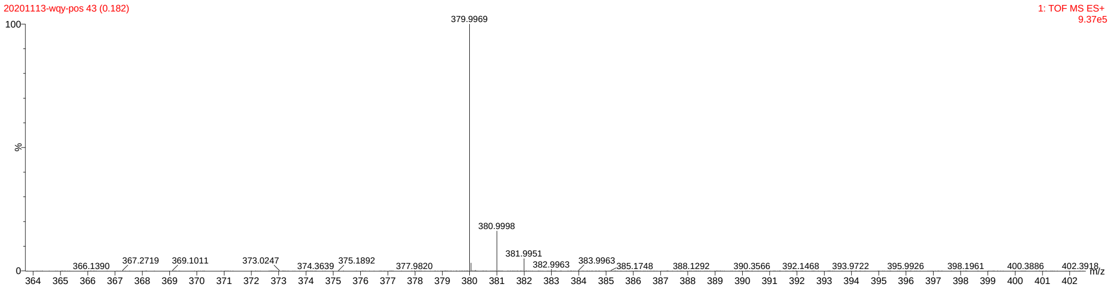
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

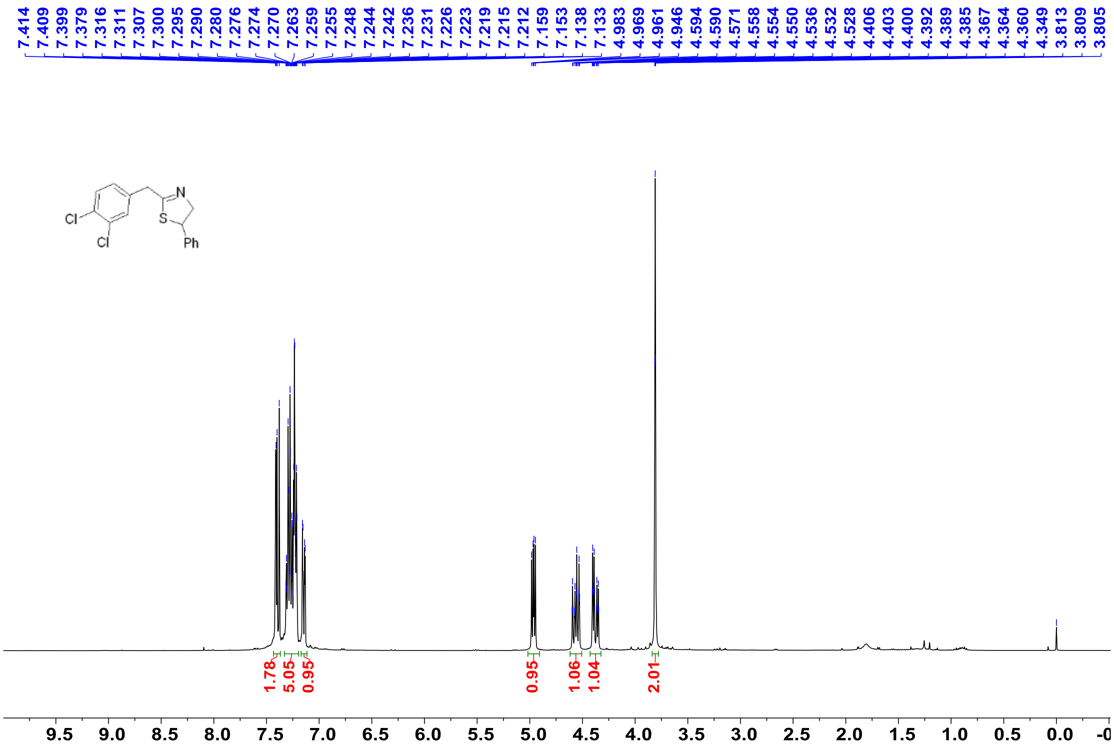


HRMS [M+H]+

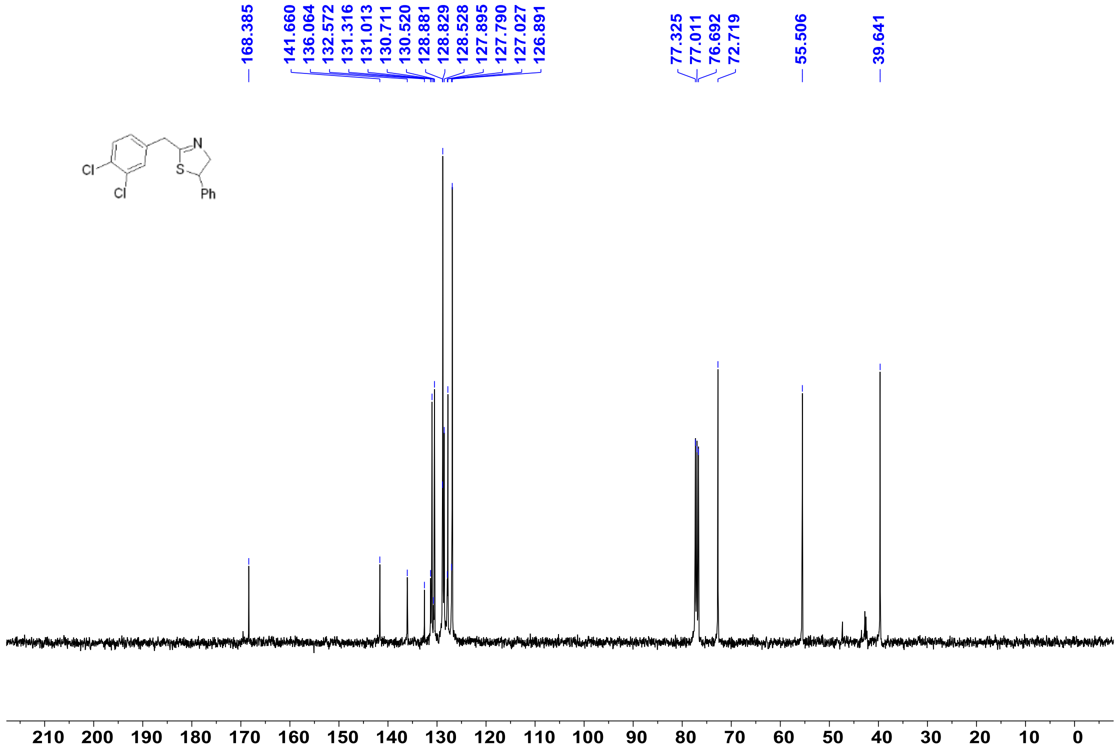


2-(3,4-Dichlorobenzyl)-5-phenyl-4,5-dihydrothiazole (3ma)

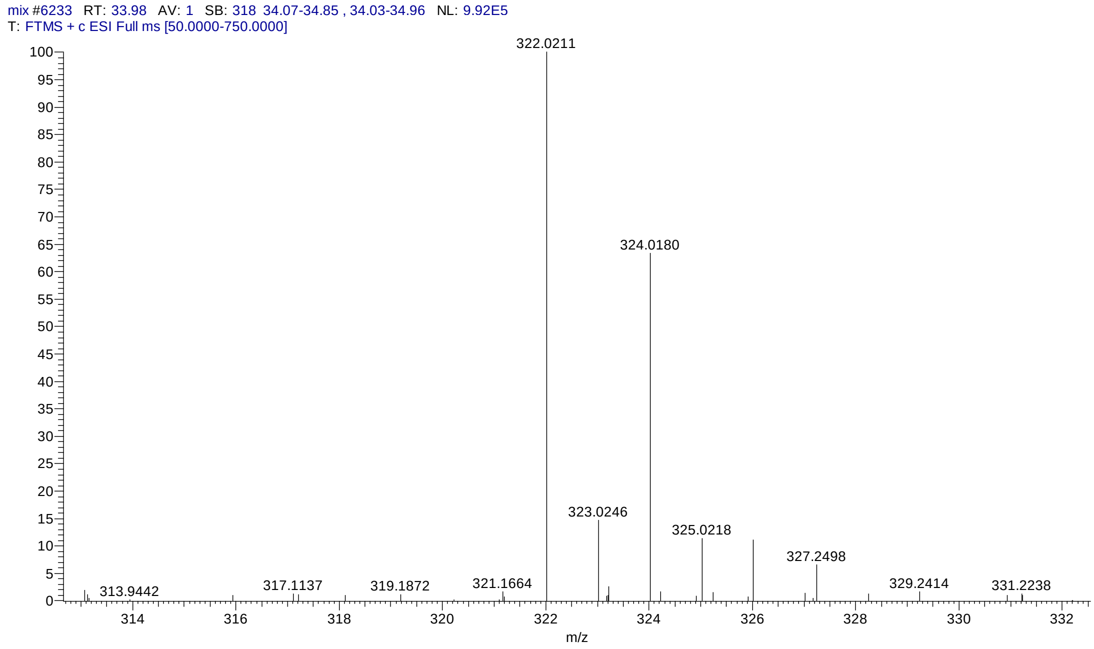
1H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

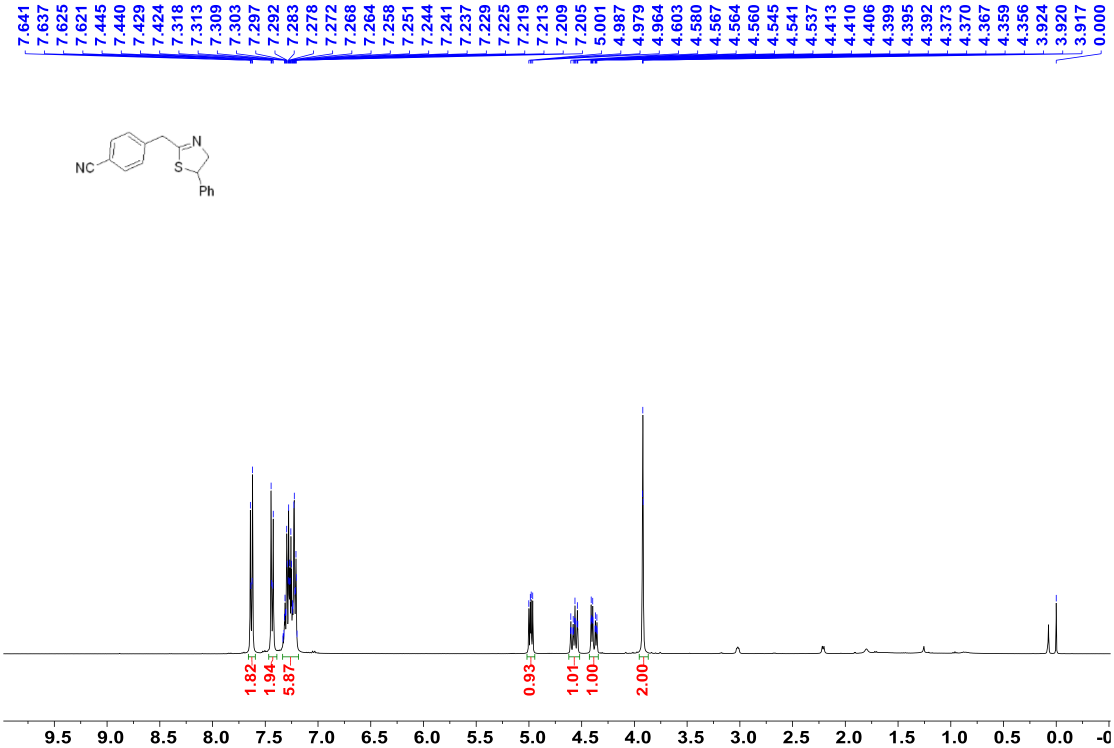


HRMS [M+H]+

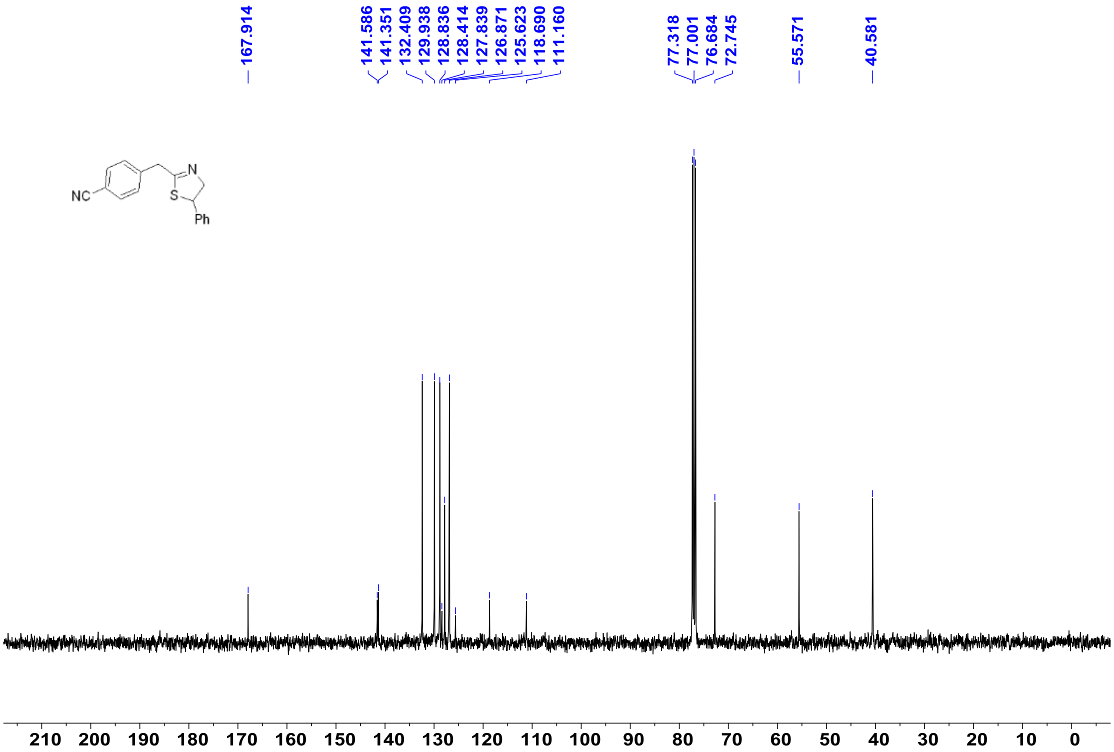


4-((5-Phenyl-4,5-dihydrothiazol-2-yl)methyl)benzonitrile (3na)

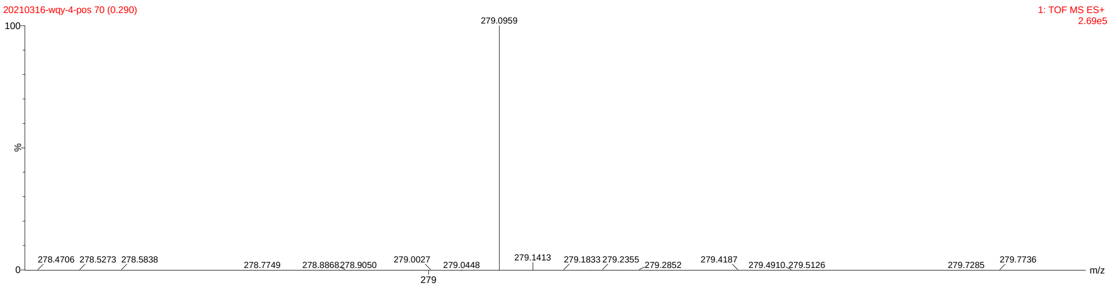
[1]H MNR (400 MHz, $CDCl_3$)



[13]C NMR{[1]H} (101 MHz, $CDCl_3$)

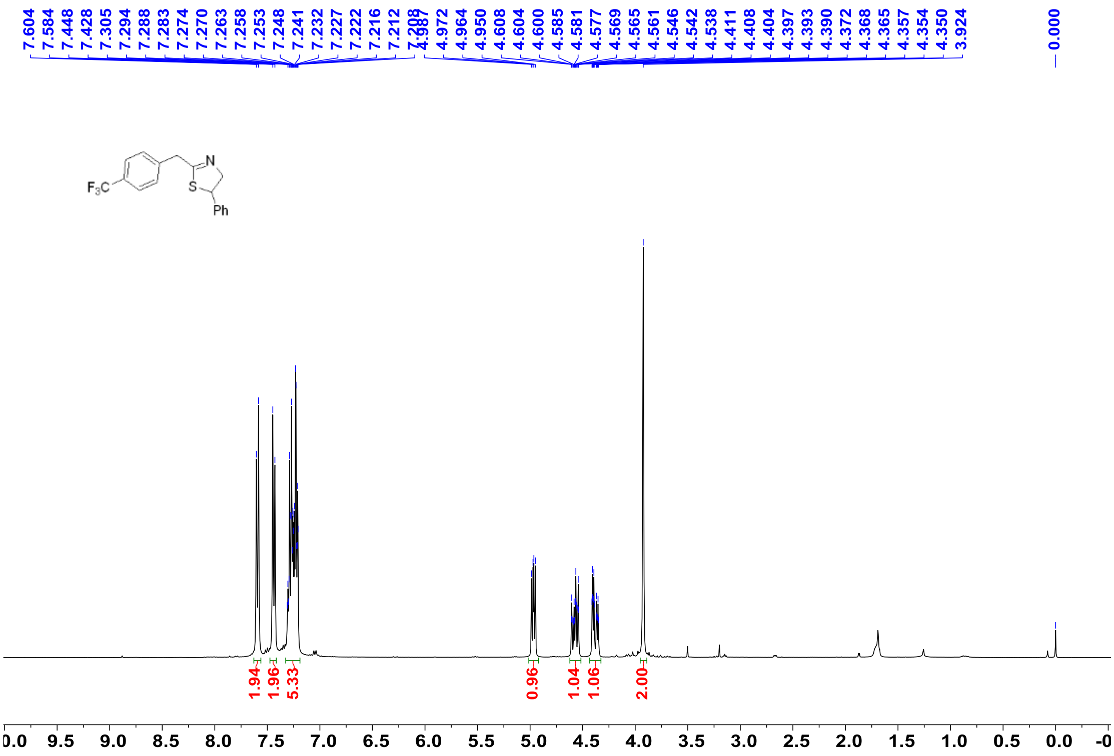


HRMS $[M+H]^+$

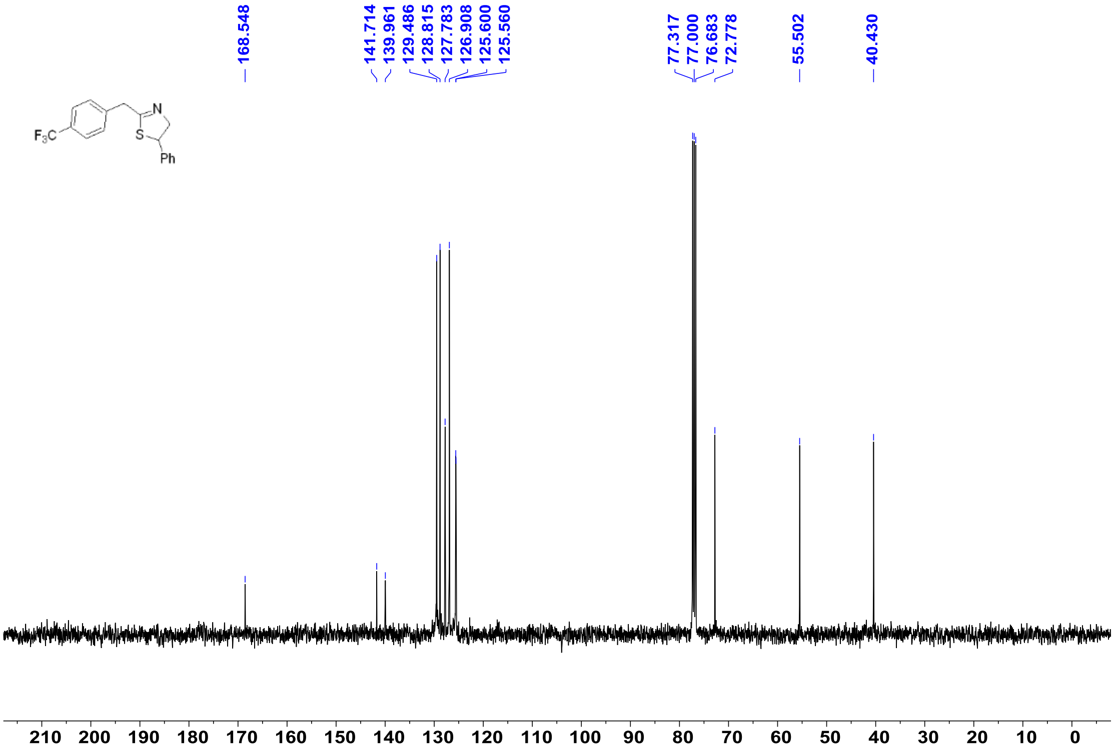


5-Phenyl-2-(4-(trifluoromethyl)benzyl)-4,5-dihydrothiazole (3oa)

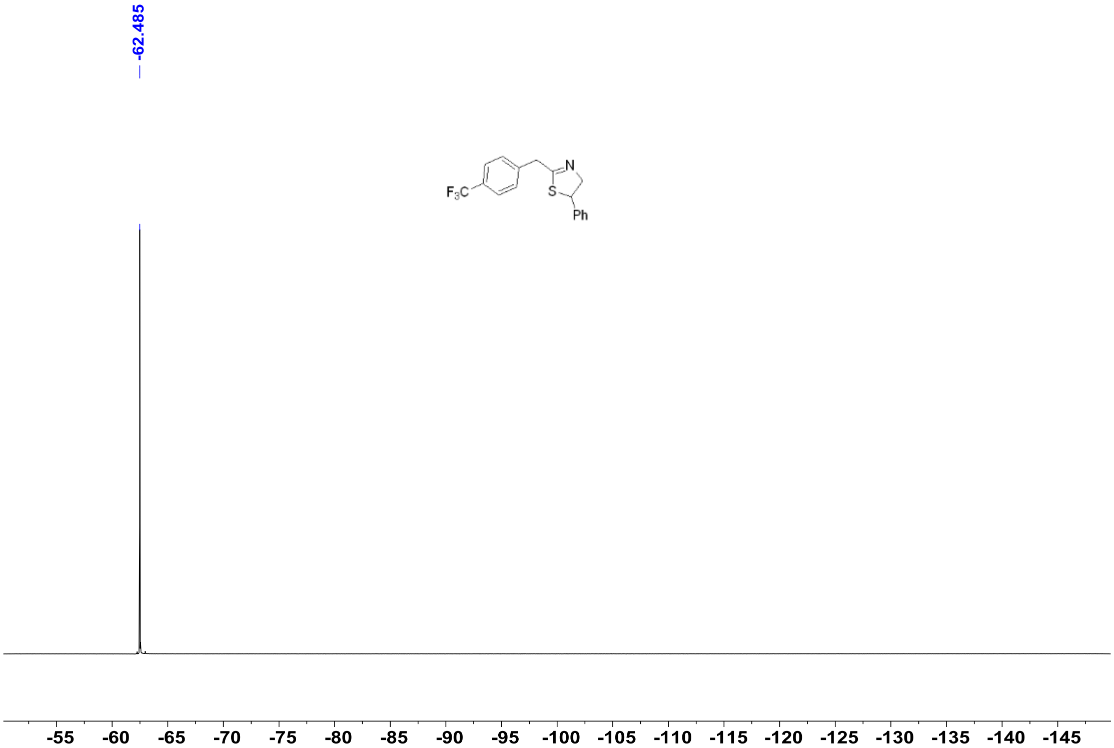
^1H MNR (400 MHz, $CDCl_3$)



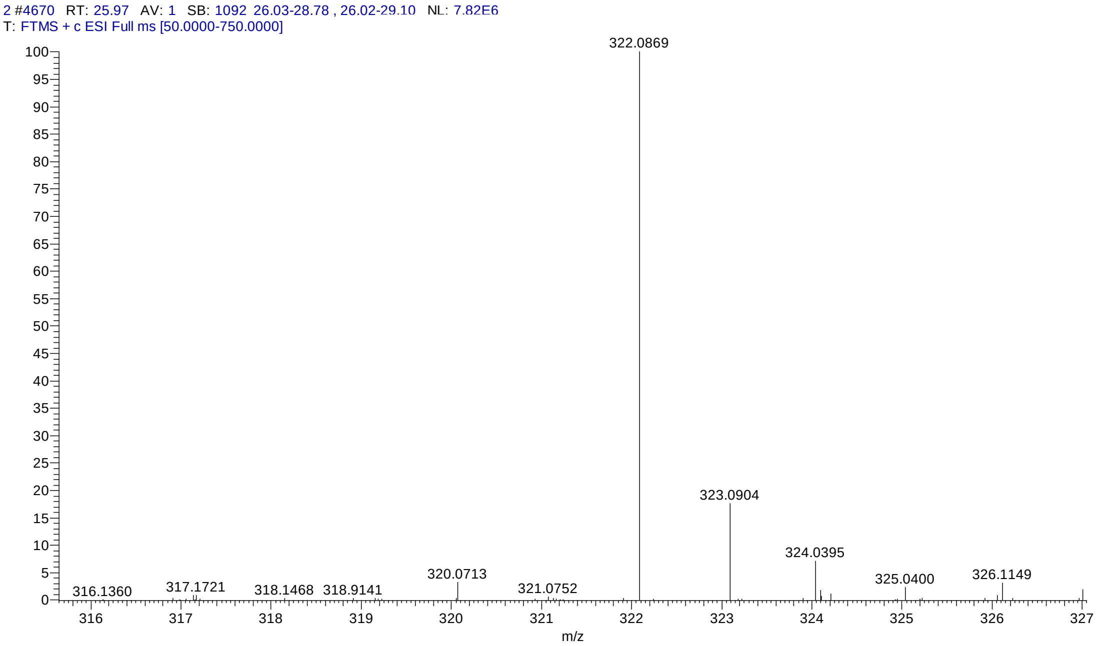
^{13}C NMR{^1H} (101 MHz, $CDCl_3$)



^{19}F NMR{^1H } (376 MHz, $CDCl_3$)

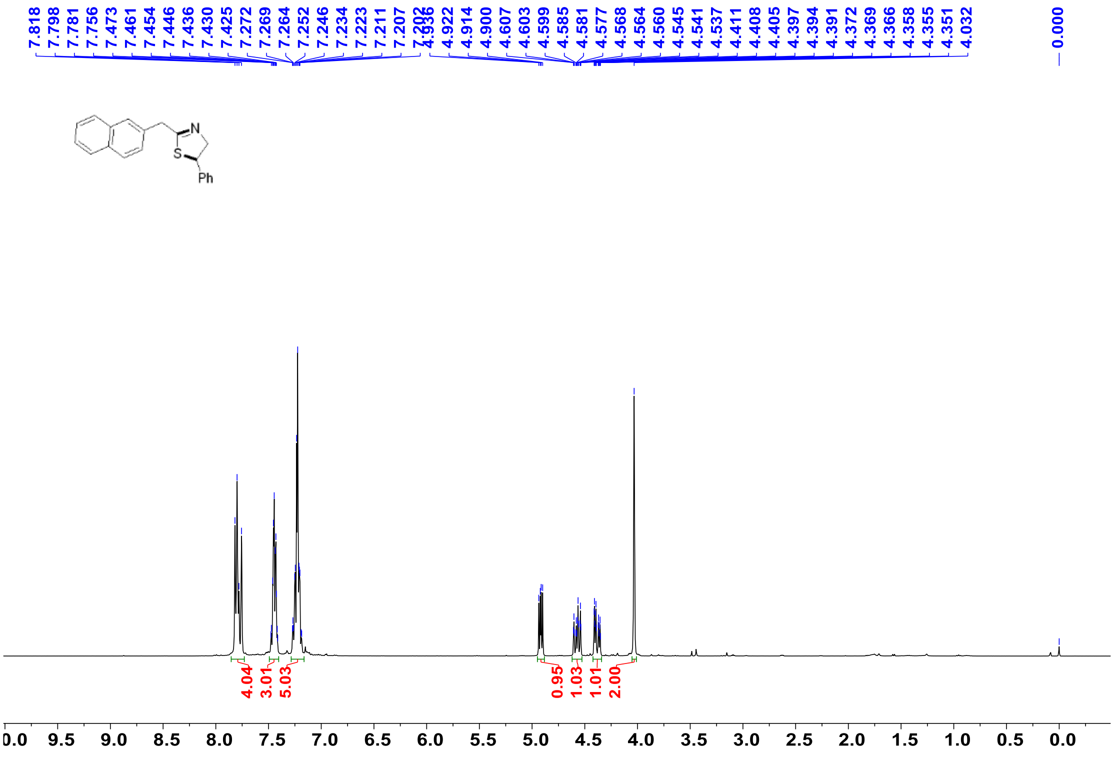


HRMS $[M+H]^+$

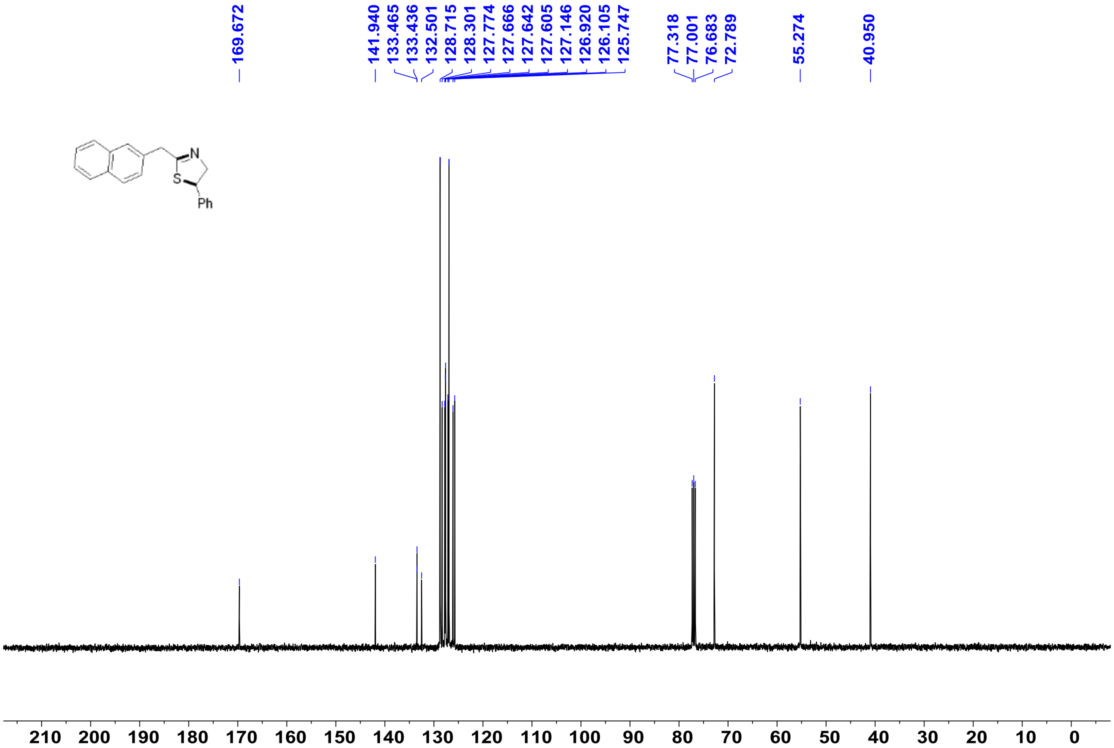


2-(Naphthalen-2-ylmethyl)-5-phenyl-4,5-dihydrothiazole (3pa)

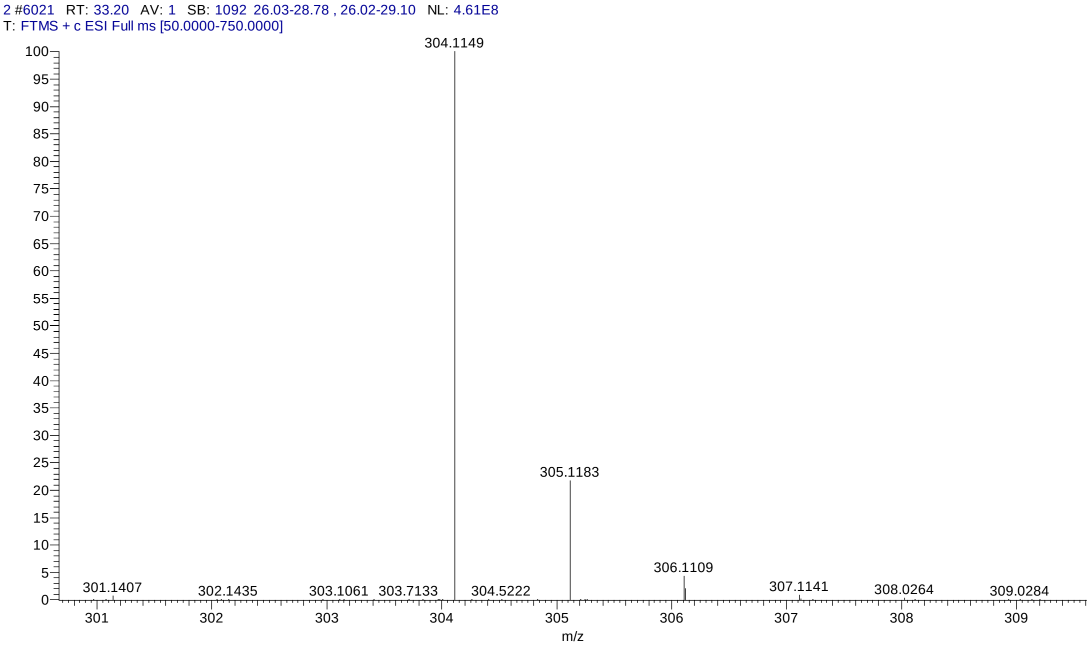
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

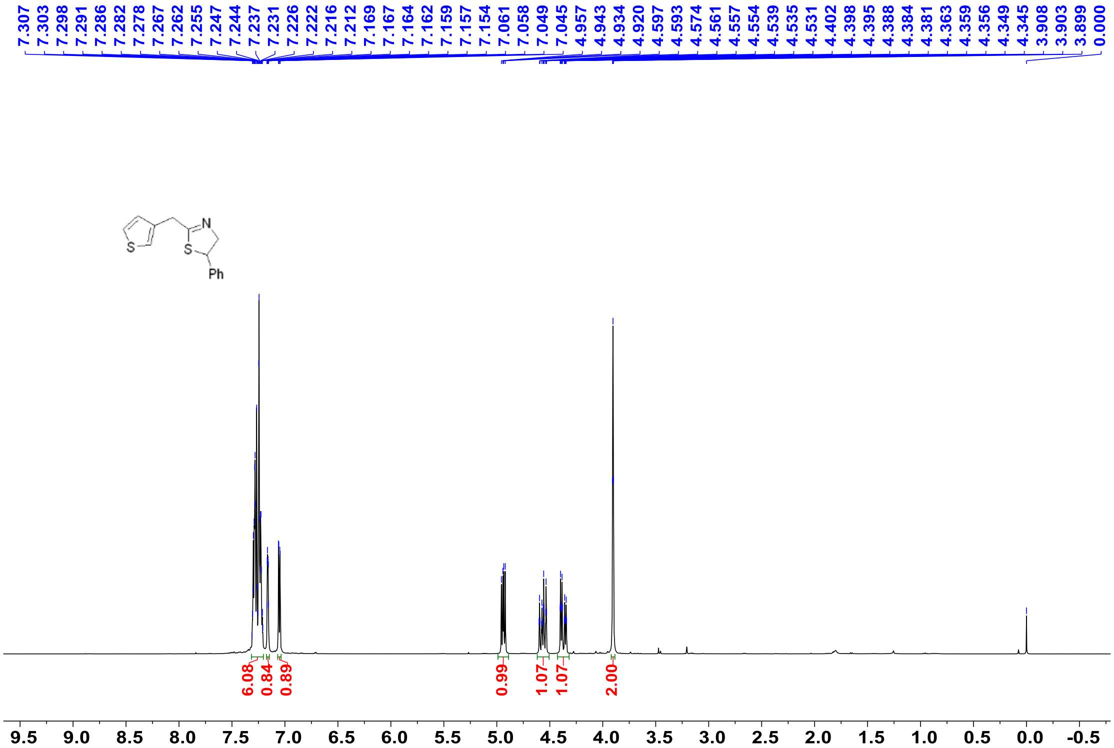


HRMS [M+H]+

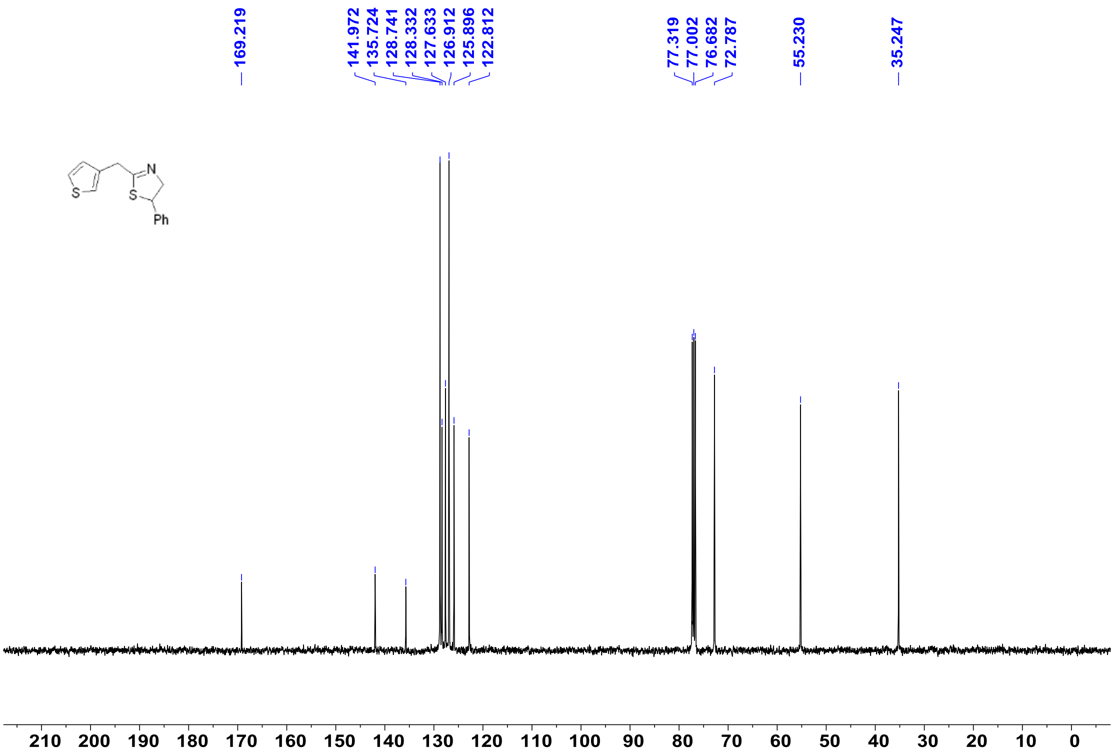


5-Phenyl-2-(thiophen-3-ylmethyl)-4,5-dihydrothiazole (3qa)

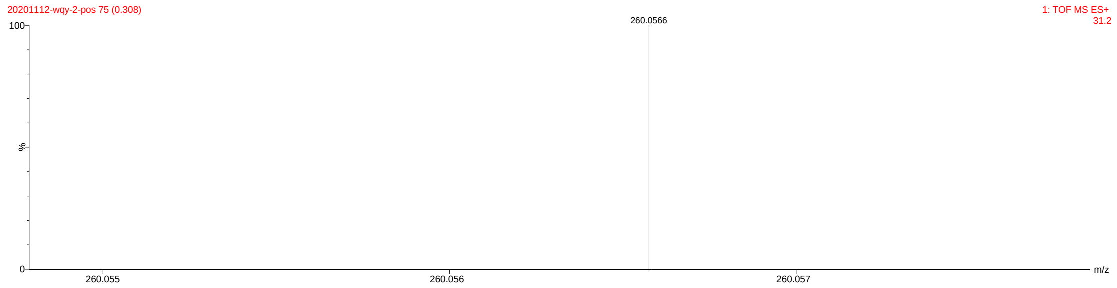
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

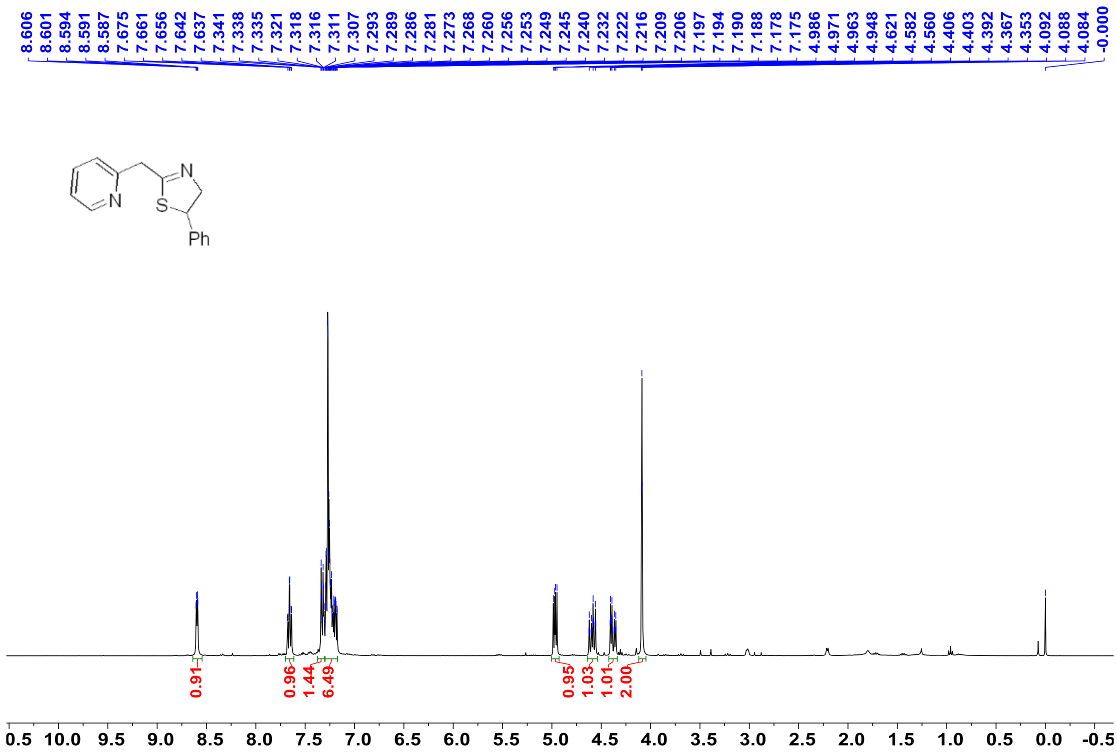


HRMS $[M+H]^+$

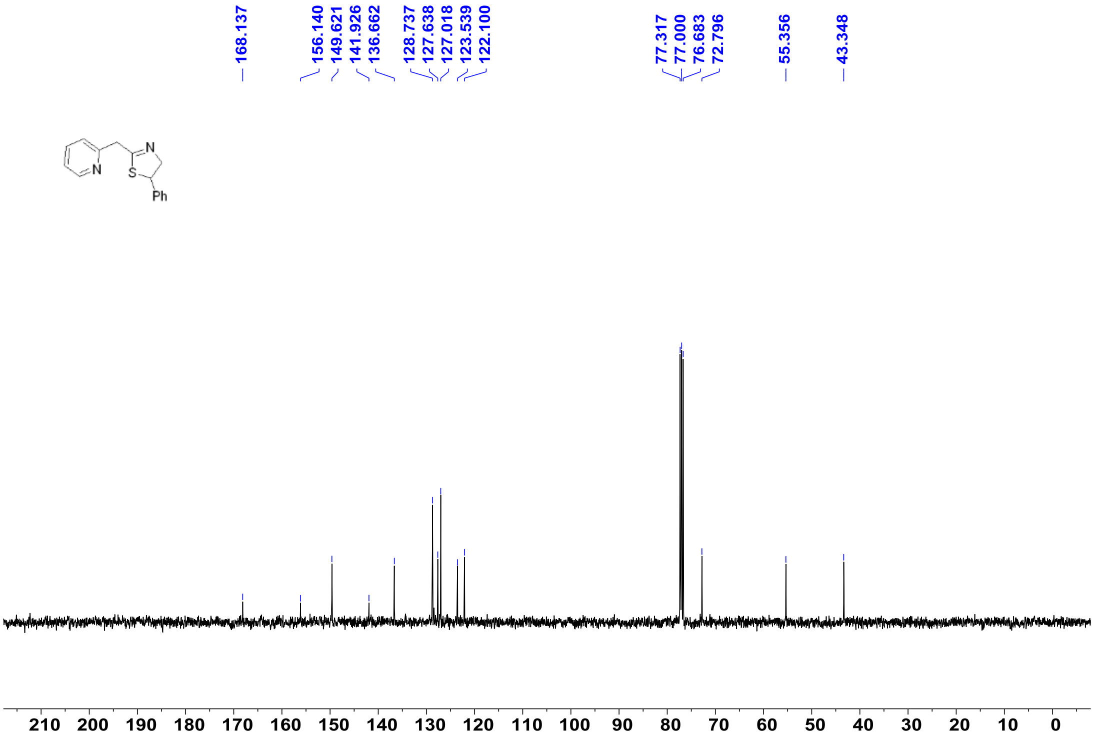


4-Phenyl-2-(pyridin-2-ylmethyl)-4,5-dihydrothiazole (3ra)

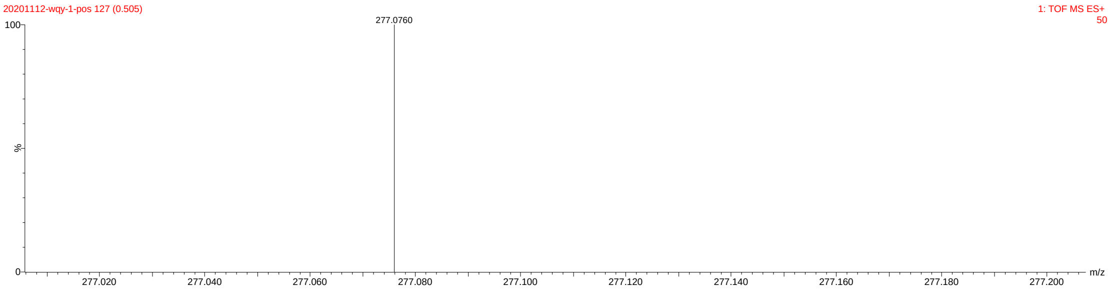
^1H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

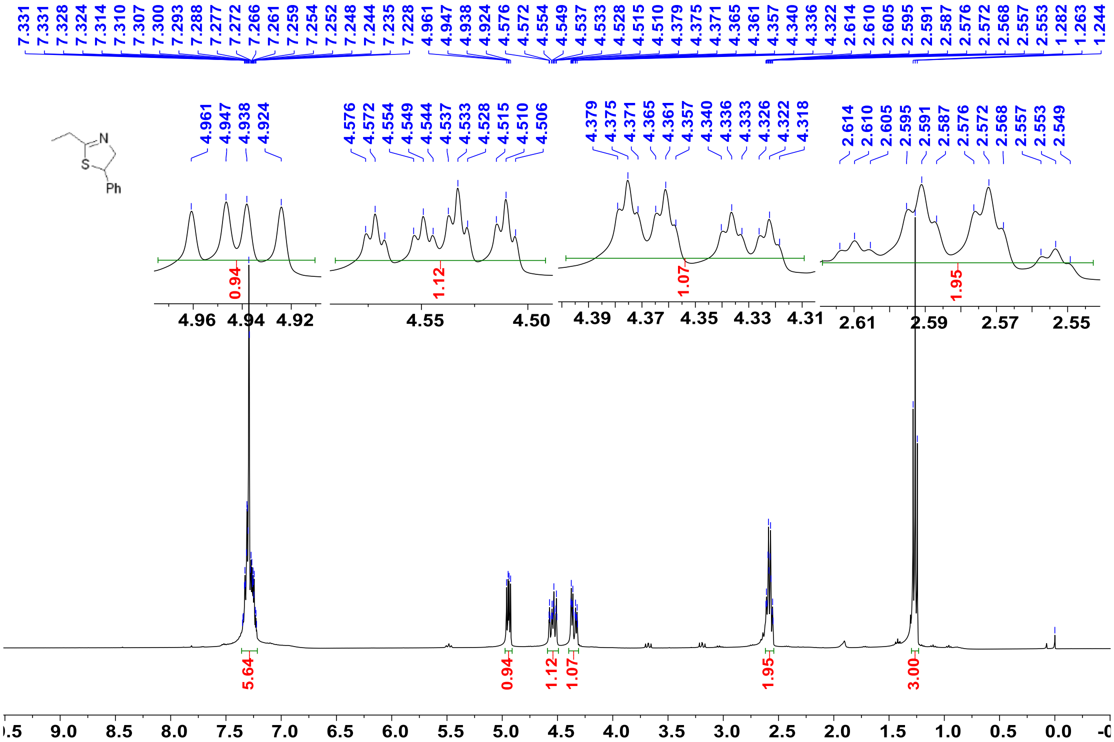


HRMS [M+H]+

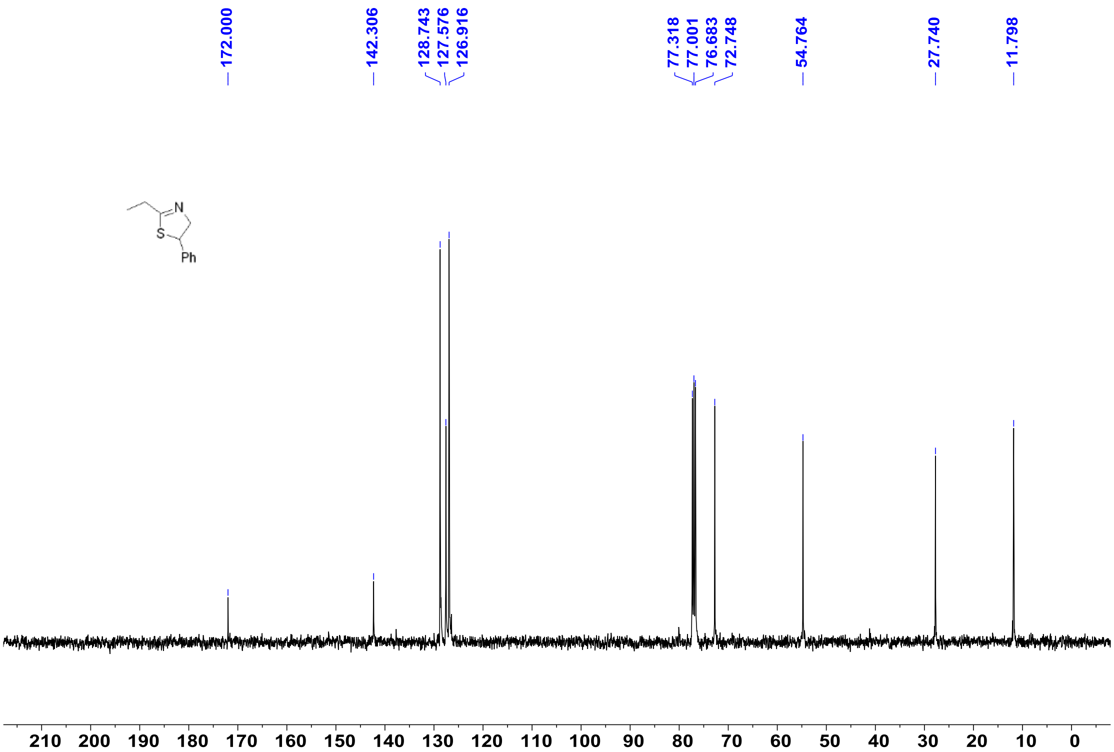


2-Ethyl-5-phenyl-4,5-dihydrothiazole (3sa)

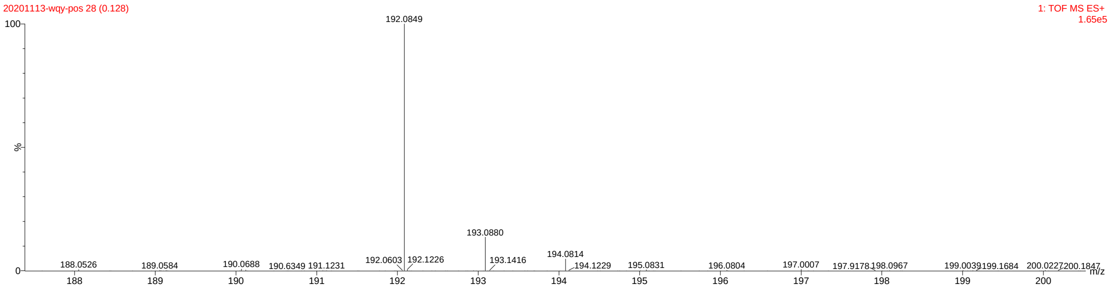
[1]H MNR (400 MHz, $CDCl_3$)



[13]C NMR{[1]H} (101 MHz, $CDCl_3$)

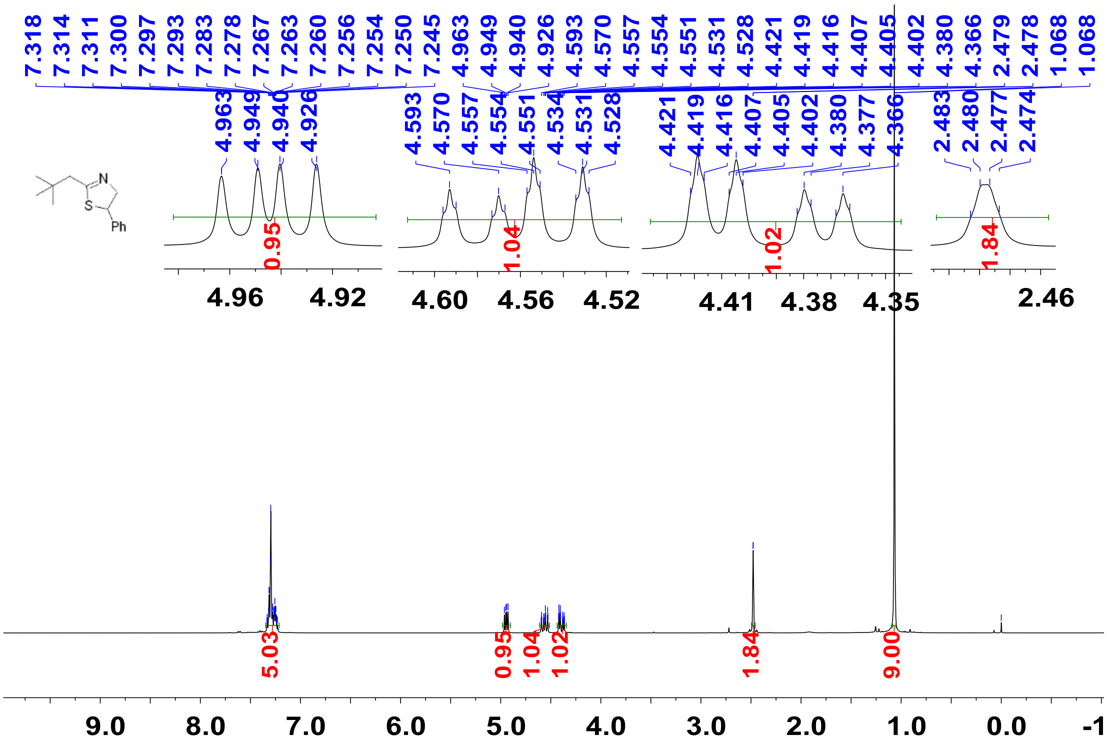


HRMS [M+H]+

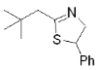


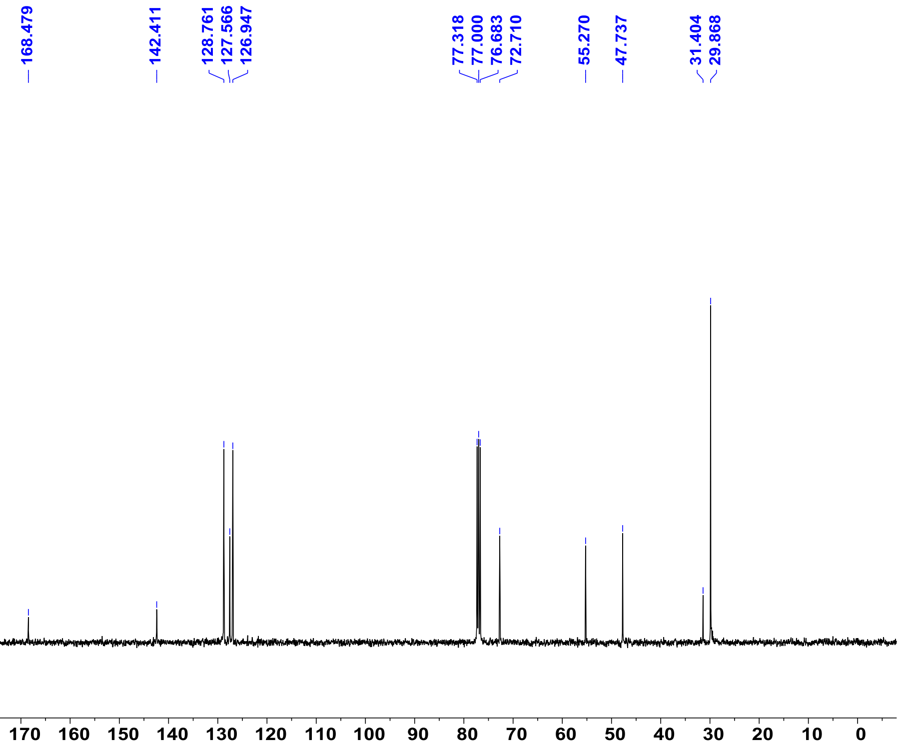
2-Neopentyl-5-phenyl-4,5-dihydrothiazole (3ta)

[1]H MNR (400 MHz, $CDCl_3$)

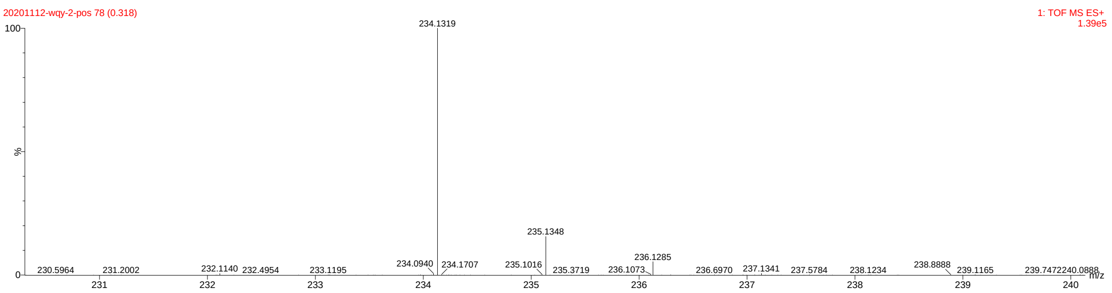


^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)



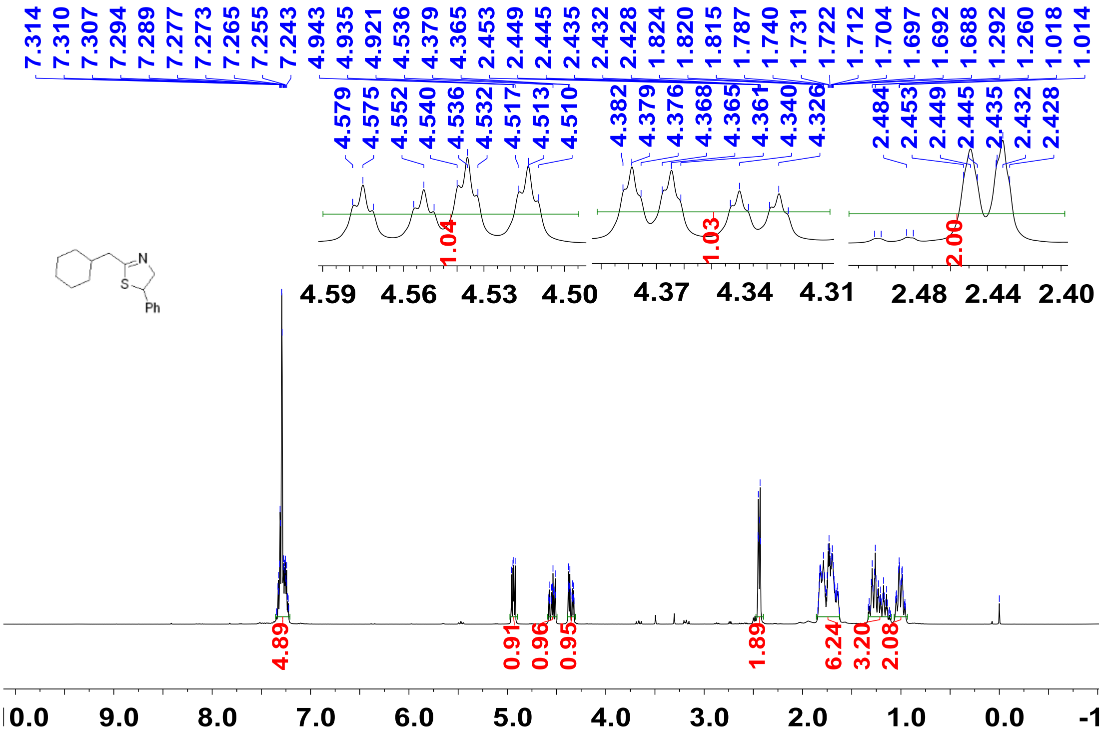


HRMS [M+H]$^+$

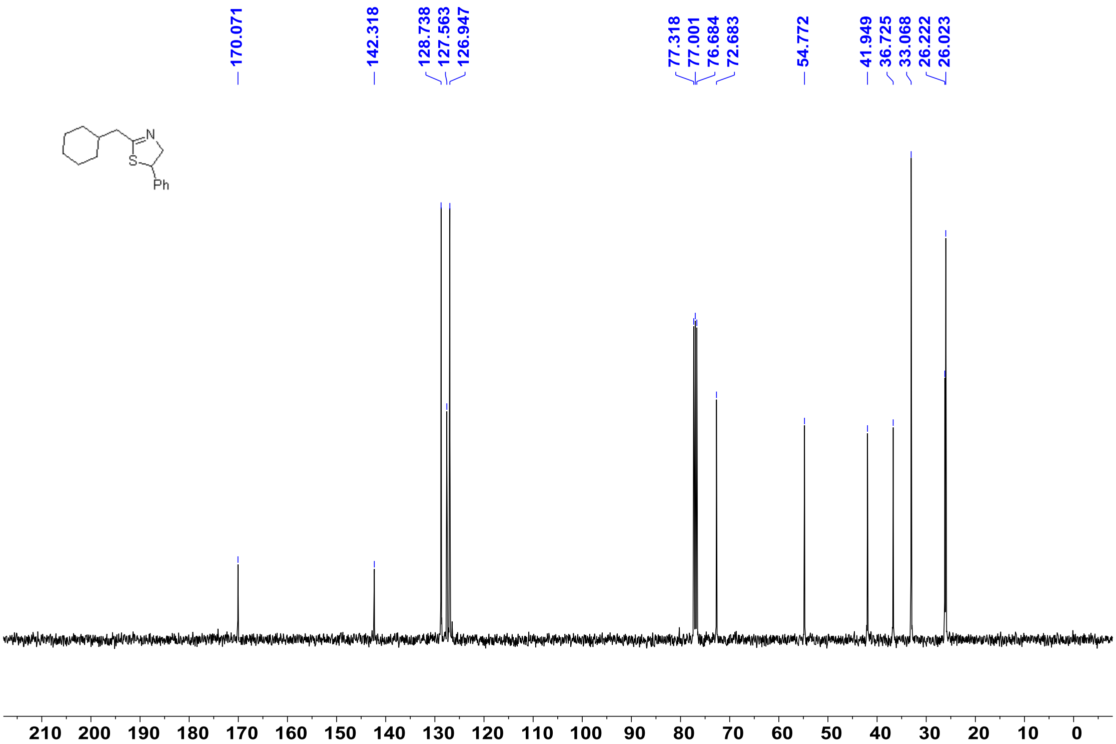


2-(Cyclohexylmethyl)-5-phenyl-4,5-dihydrothiazole (3ua)

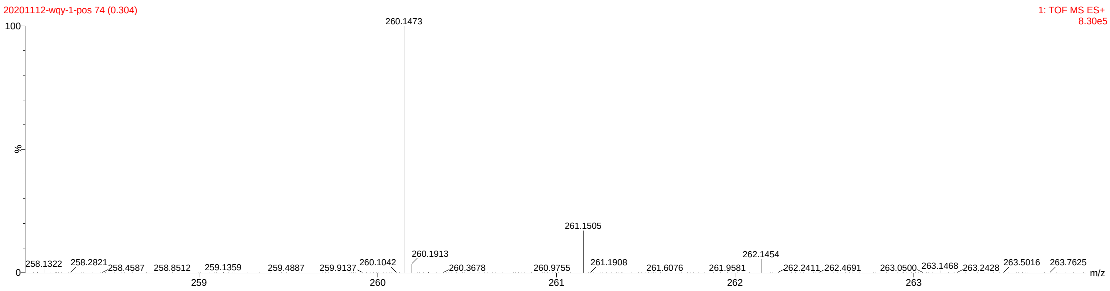
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

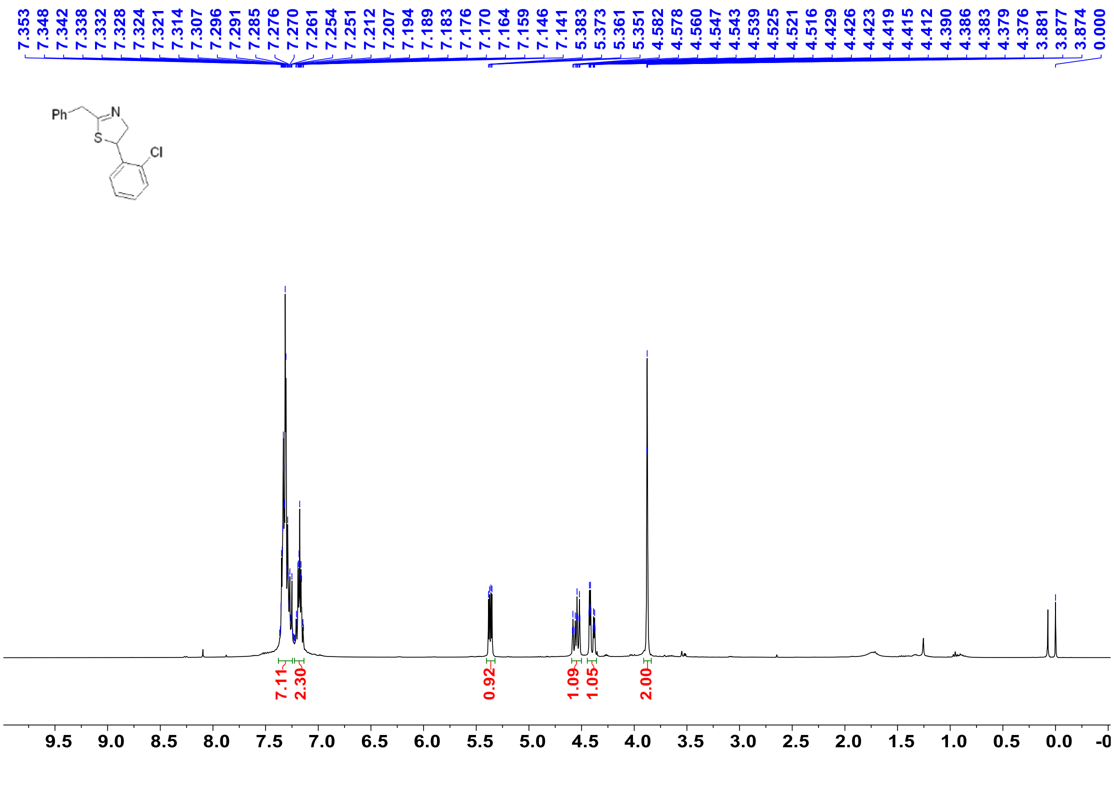


HRMS $[M+H]^+$

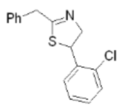


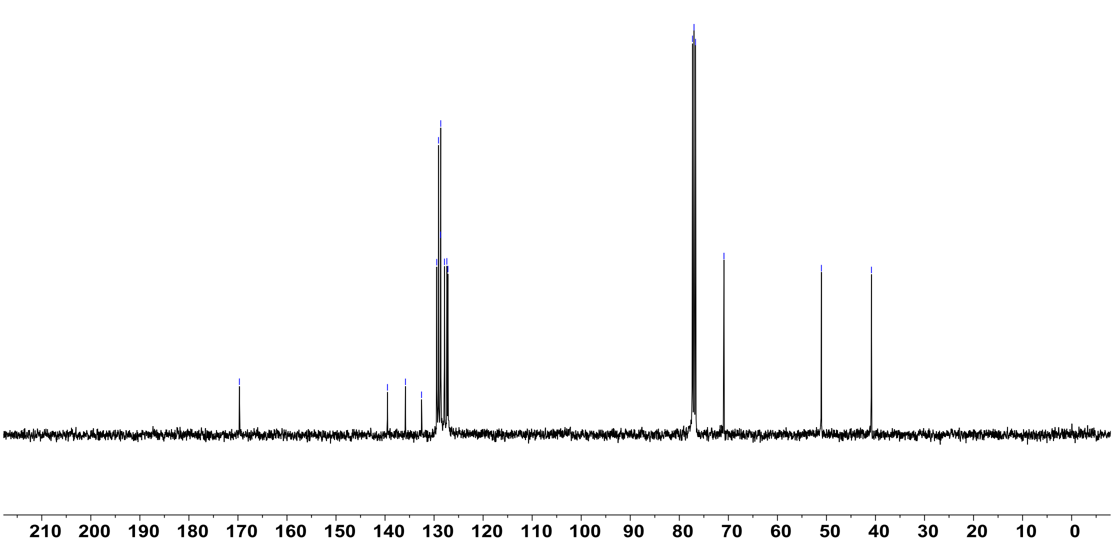
2-Benzyl-5-(2-chlorophenyl)-4,5-dihydrothiazole (3ab)

^1H MNR (400 MHz, $CDCl_3$)

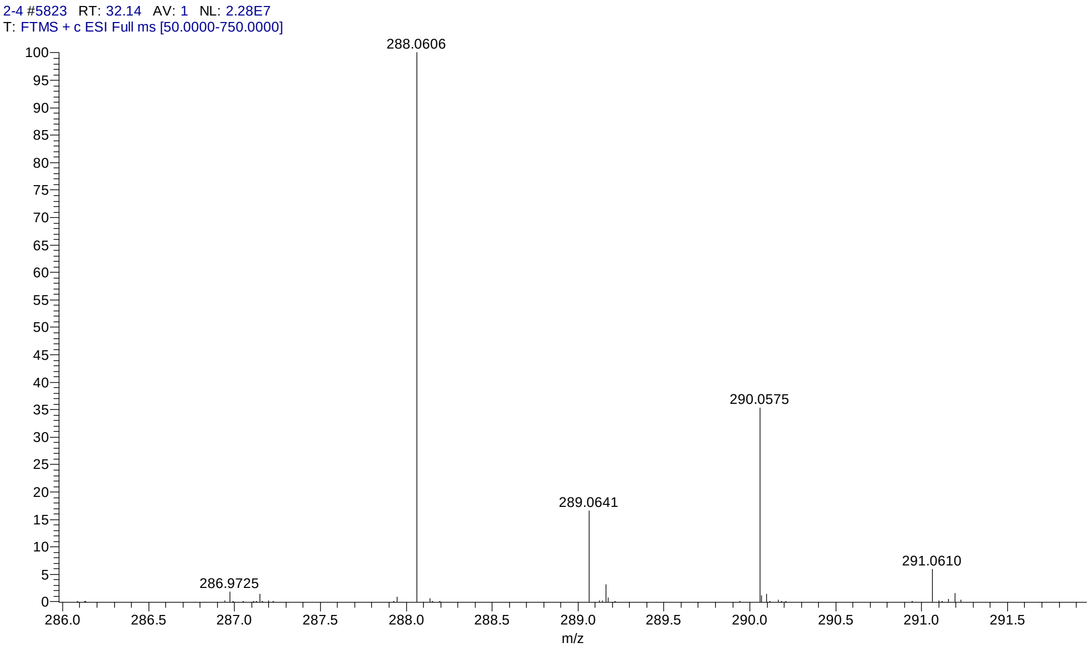


^{13}C NMR{^{1}H} (101 MHz, CDCl$_3$)



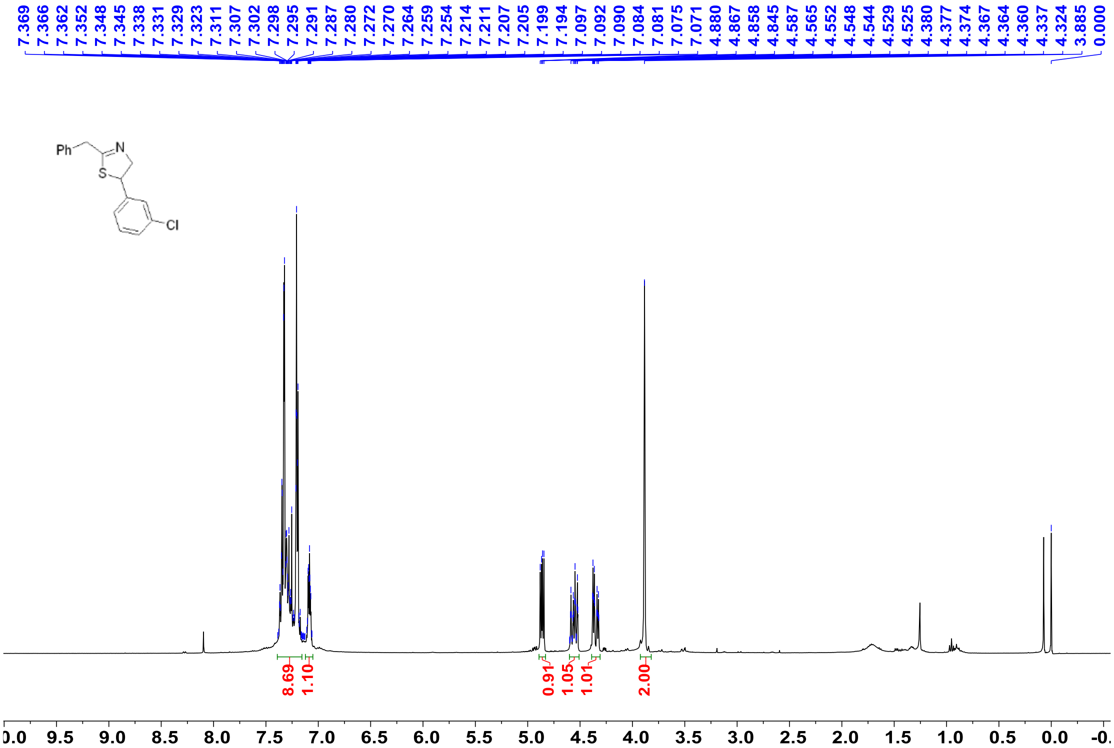


HRMS [M+H]$^+$

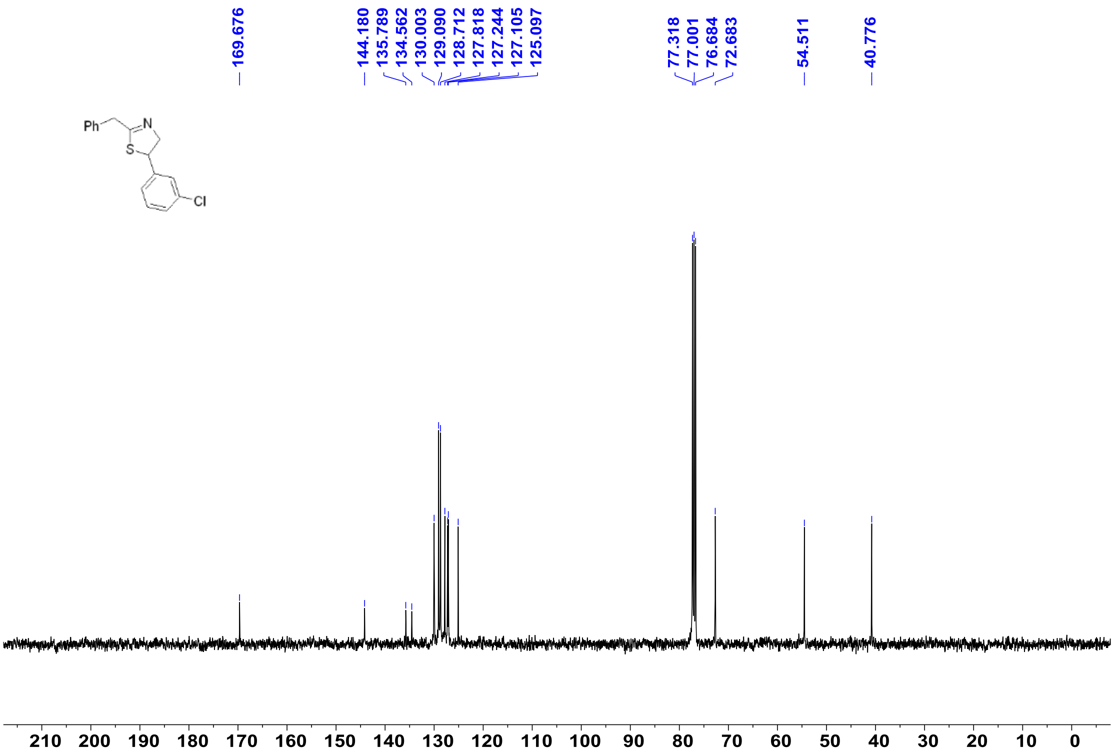


2-Benzyl-5-(3-chlorophenyl)-4,5-dihydrothiazole (3ac)

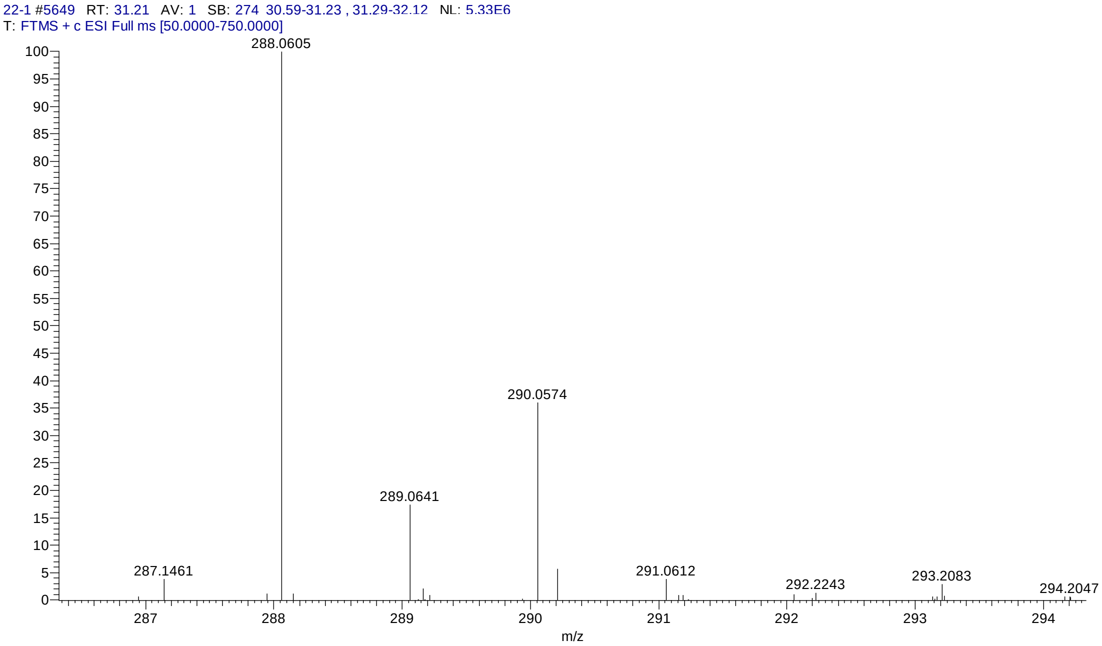
¹H MNR (400 MHz, CDCl₃)



¹³C NMR{¹H} (101 MHz, CDCl₃)

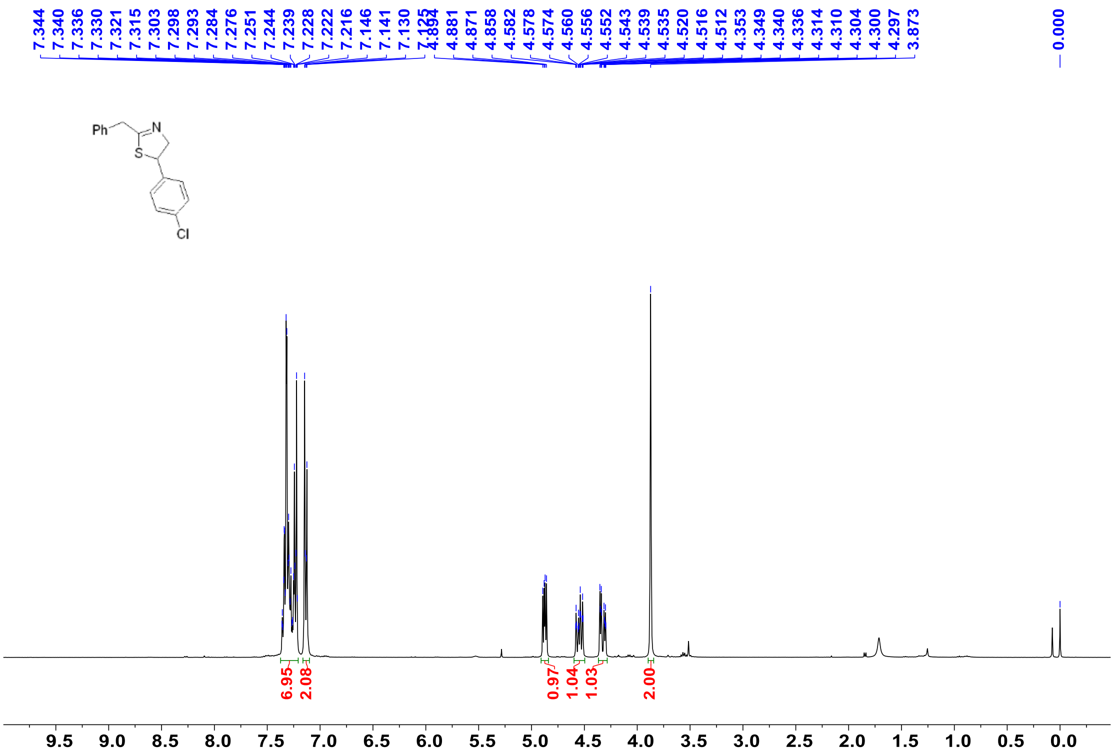


HRMS $[M+H]^+$

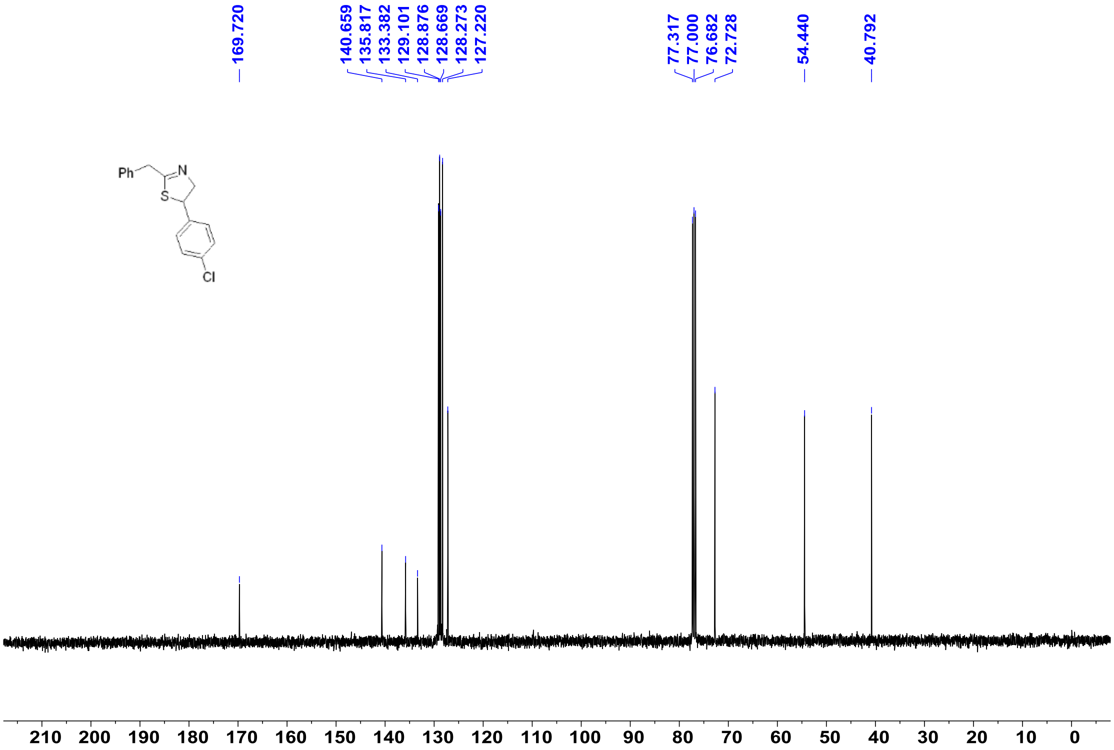


2-Benzyl-5-(4-chlorophenyl)-4,5-dihydrothiazole (3ad)

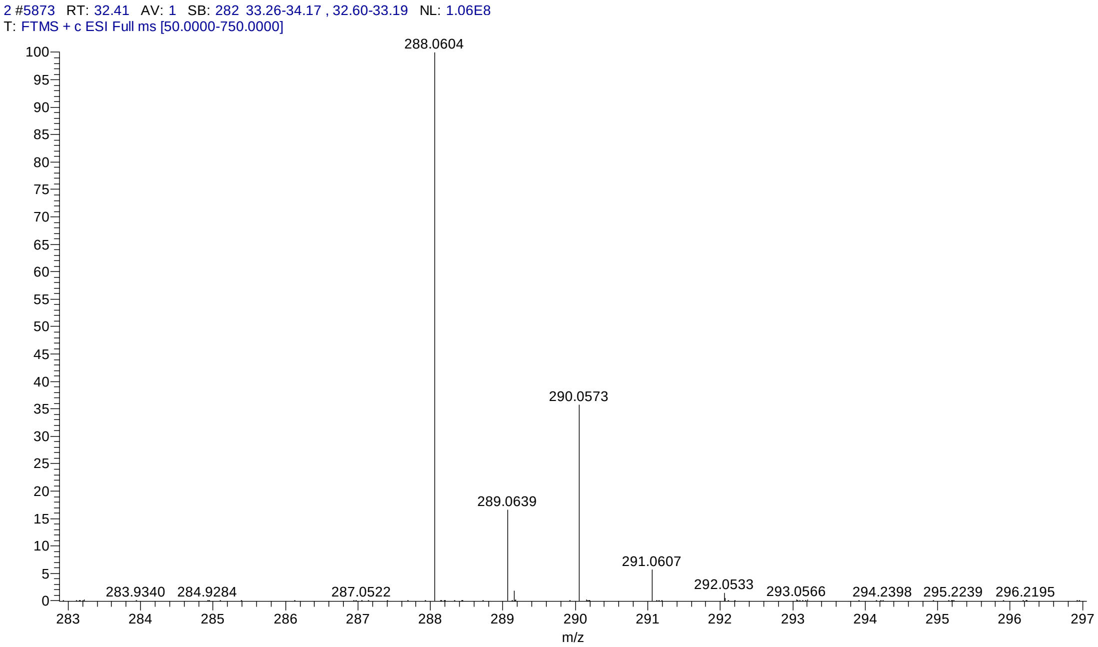
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

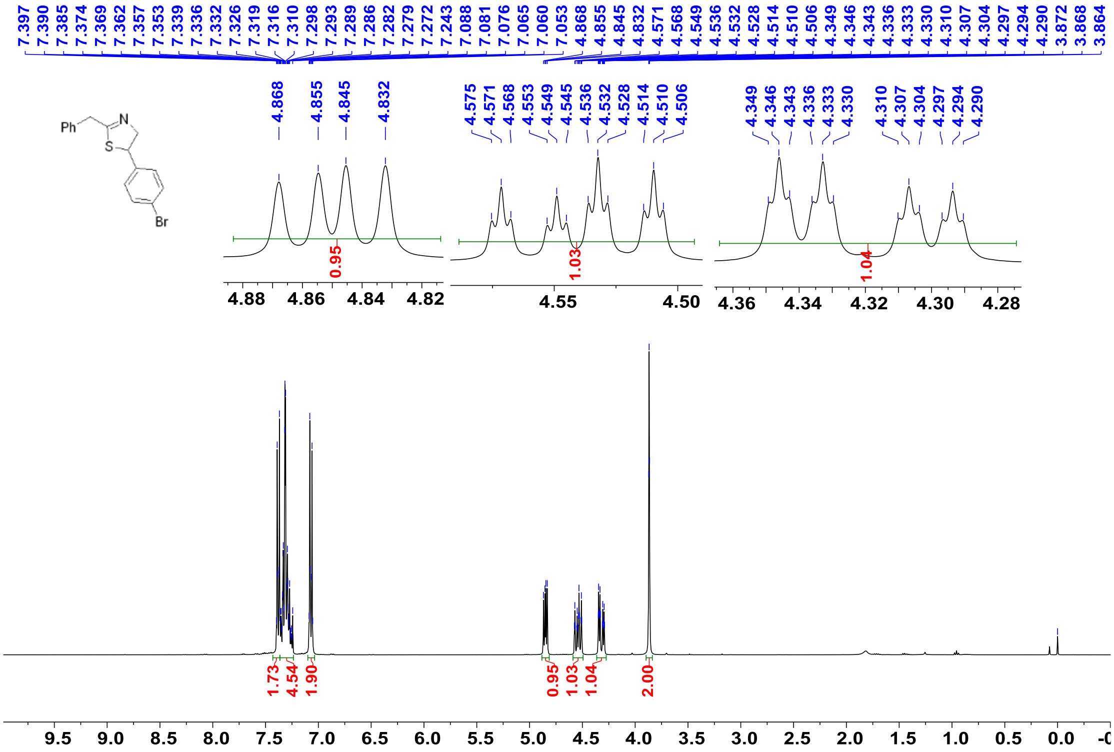


HRMS [M+H]$^{+}$

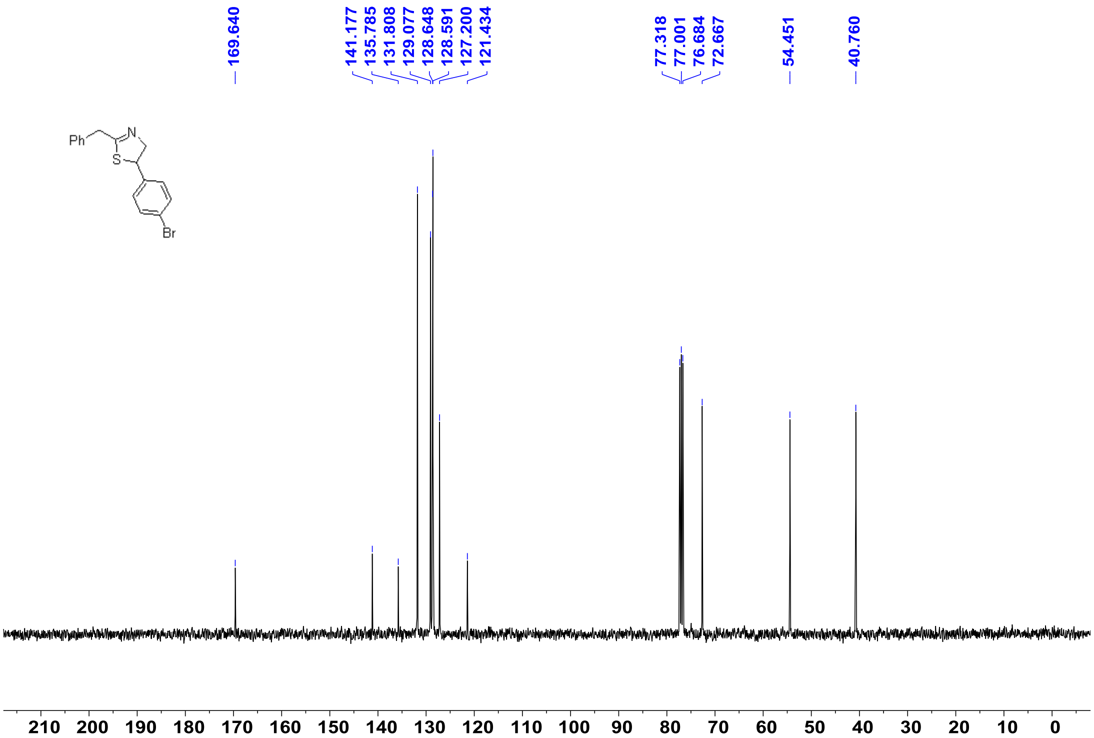


2-Benzyl-5-(4-bromophenyl)-4,5-dihydrothiazole (3ae)

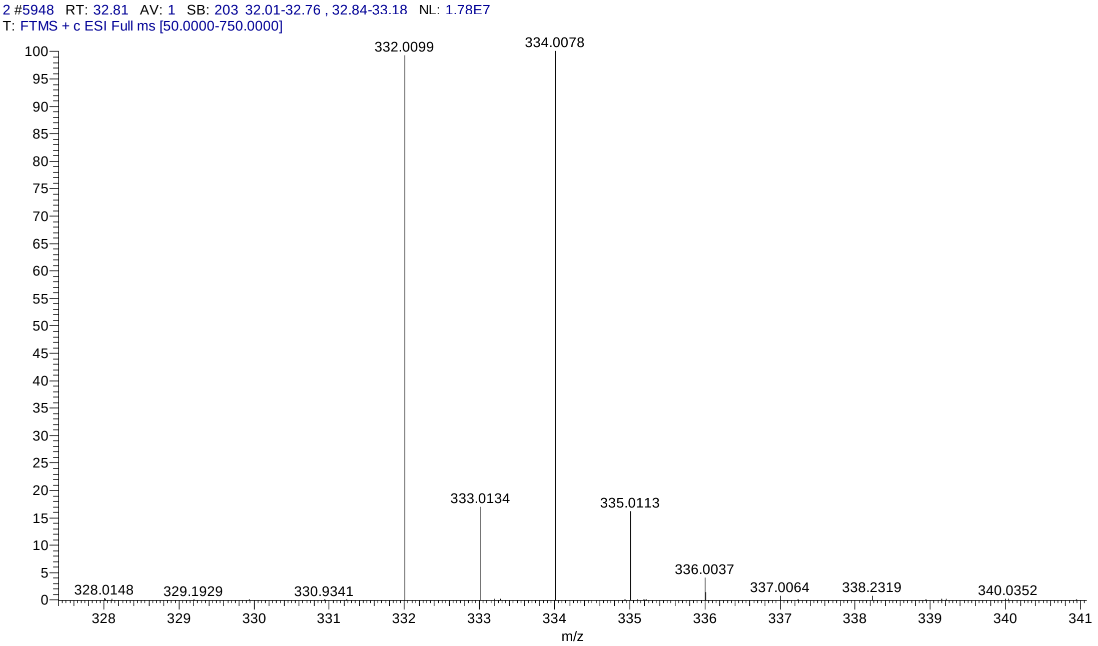
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

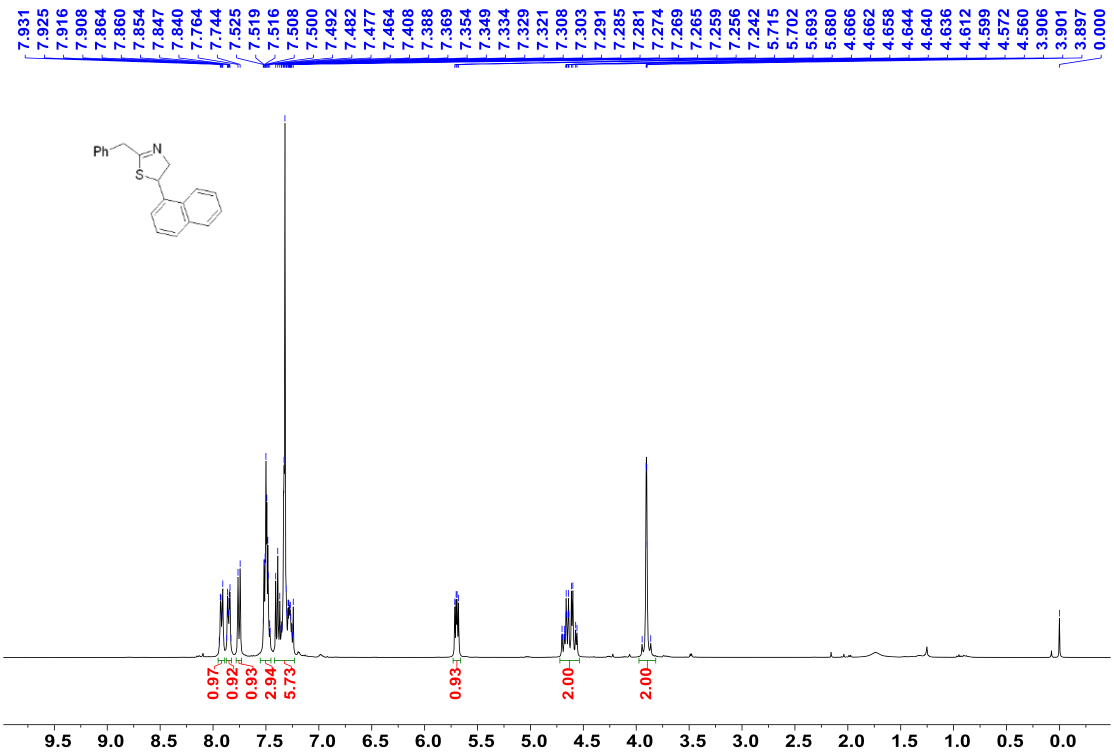


HRMS $[M+H]^+$

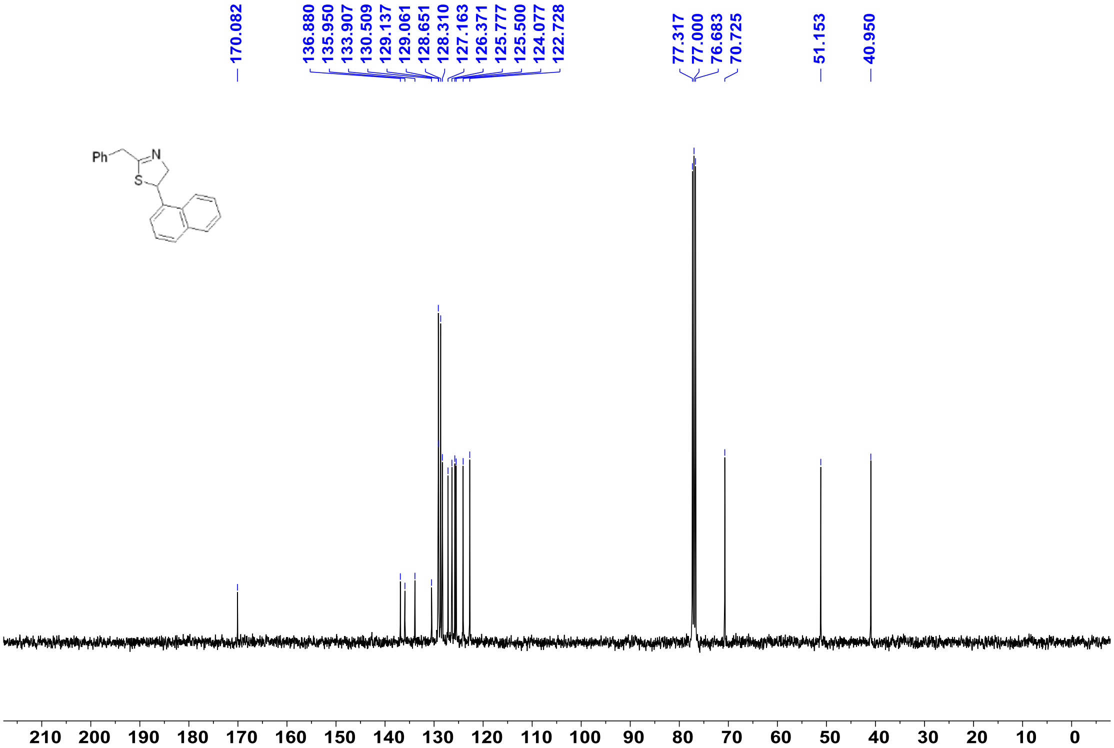


2-Benzyl-5-(naphthalen-1-yl)-4,5-dihydrothiazole (3af)

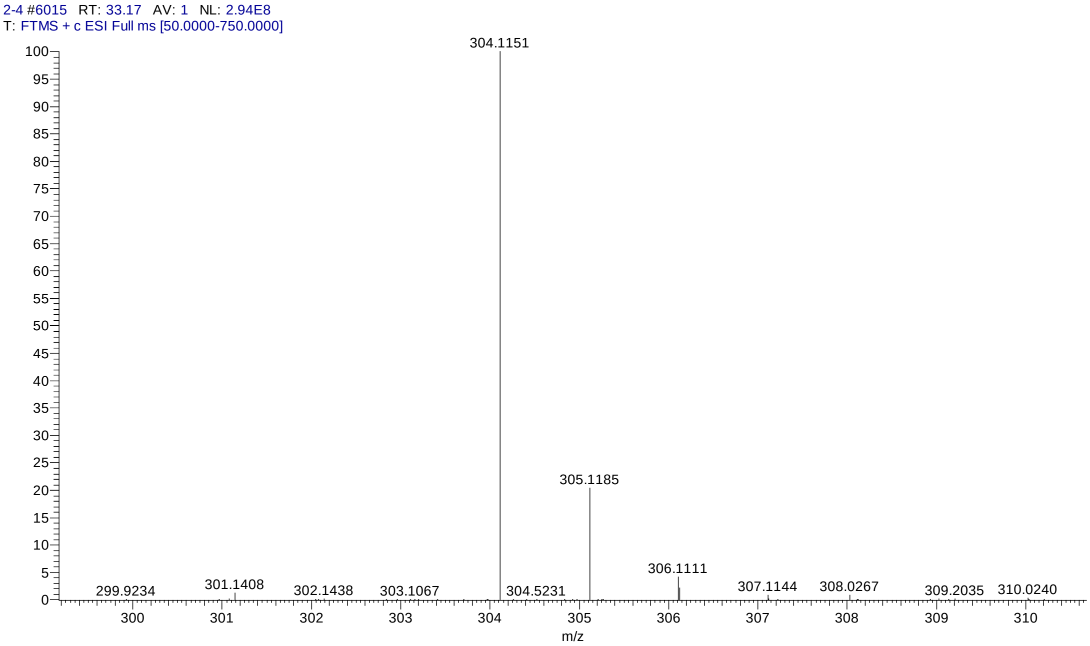
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

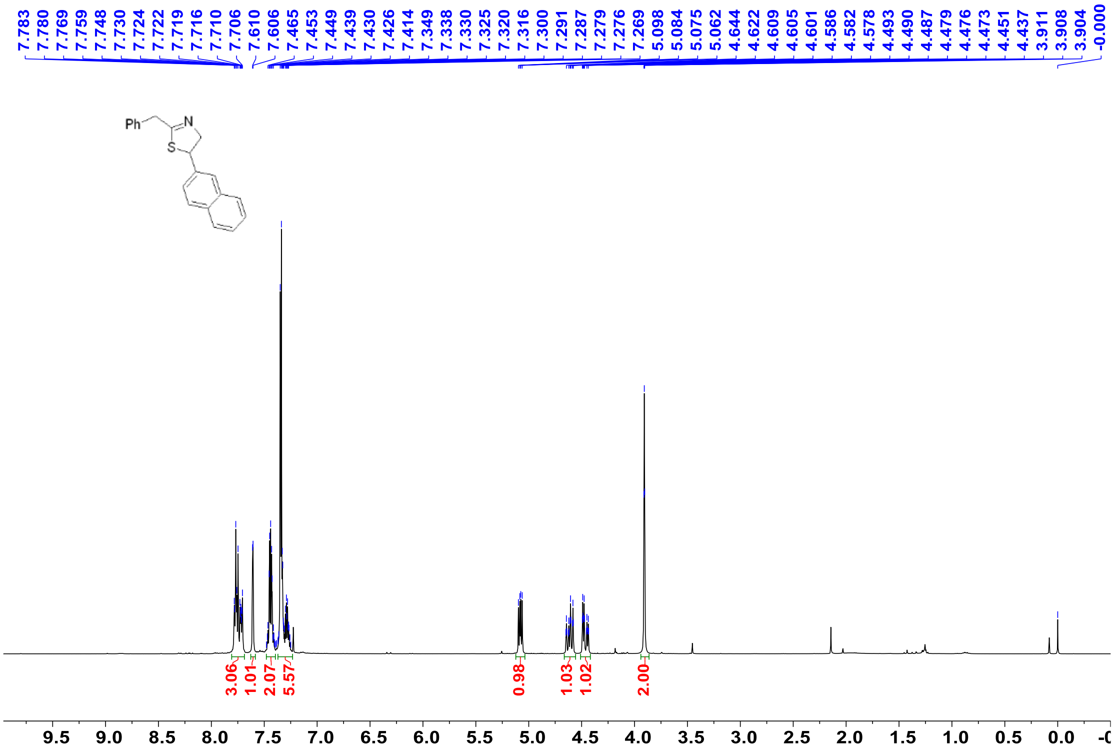


HRMS [M+H]+

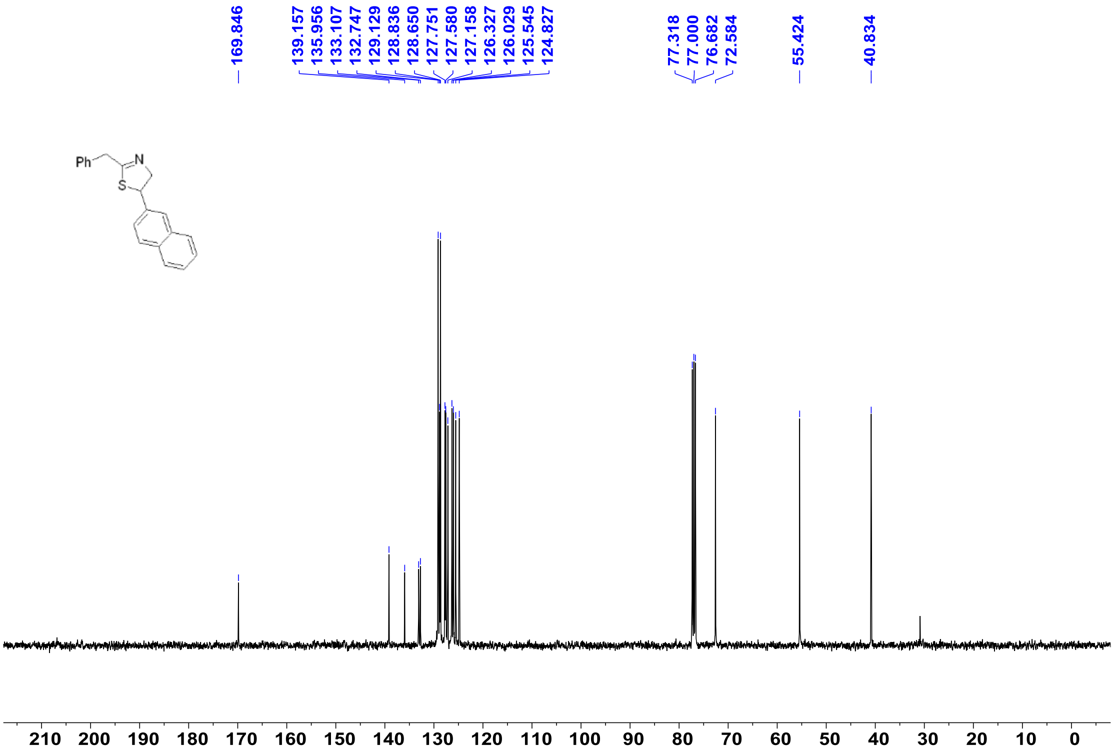


2-Benzyl-5-(naphthalen-2-yl)-4,5-dihydrothiazole (3ag)

[1]H MNR (400 MHz, $CDCl_3$)



[13]C NMR{[1]H} (101 MHz, $CDCl_3$)



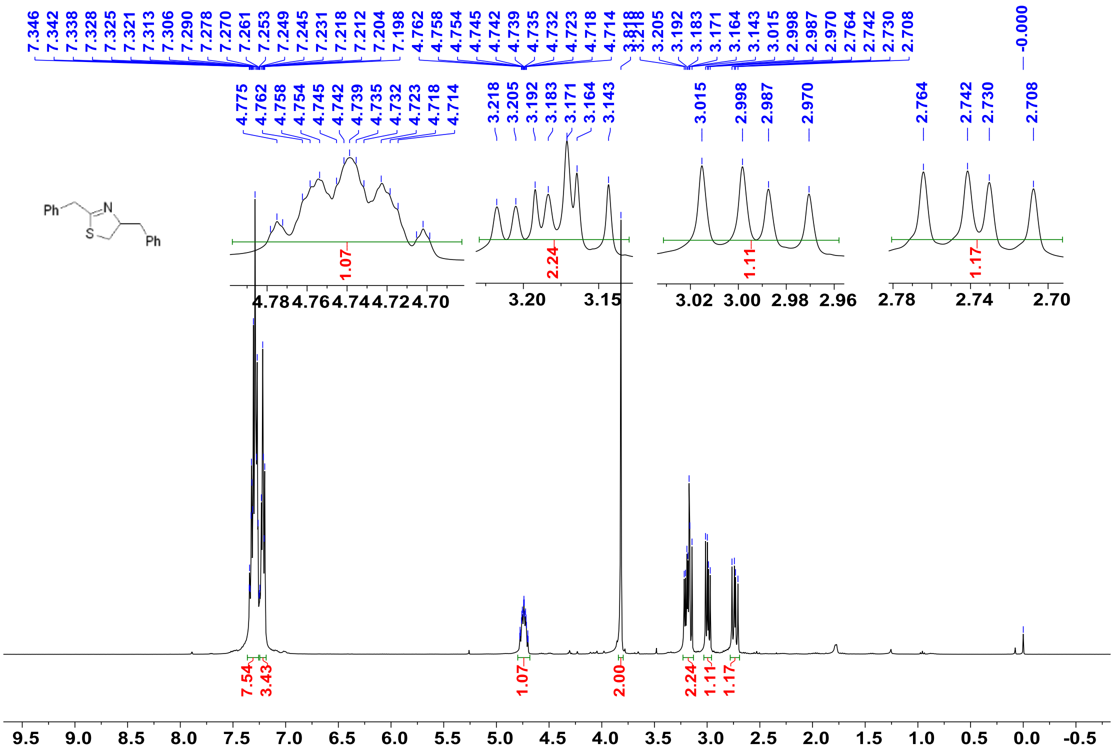
HRMS [M+H]$^+$

2 #6021 RT: 33.20 AV: 1 SB: 211 32.37-33.15 , 33.25-33.58 NL: 4.19E8
T: FTMS + c ESI Full ms [50.0000-750.0000]
304.1149
305.1183
306.1109
307.1142
301.0748
302.0782
303.1061
303.7133
304.8300
m/z

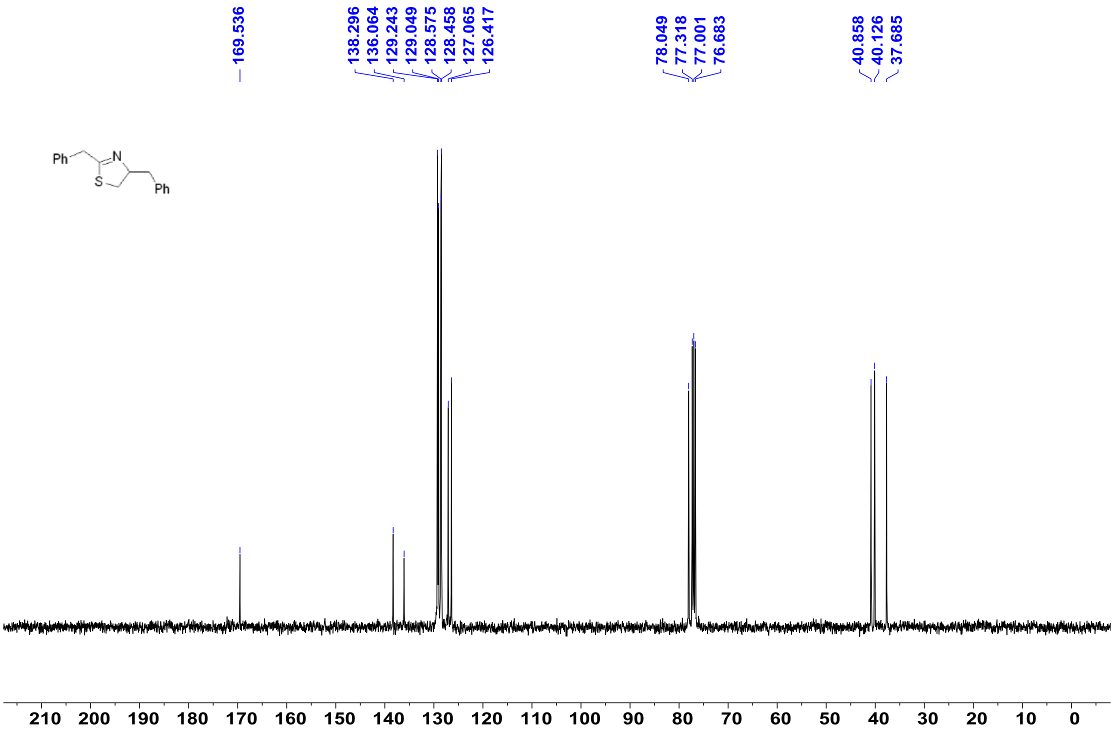
Copies of NMR and HRMS spectra of thiazolines 4

2,4-Dibenzyl-4,5-dihydrothiazole (4ah)

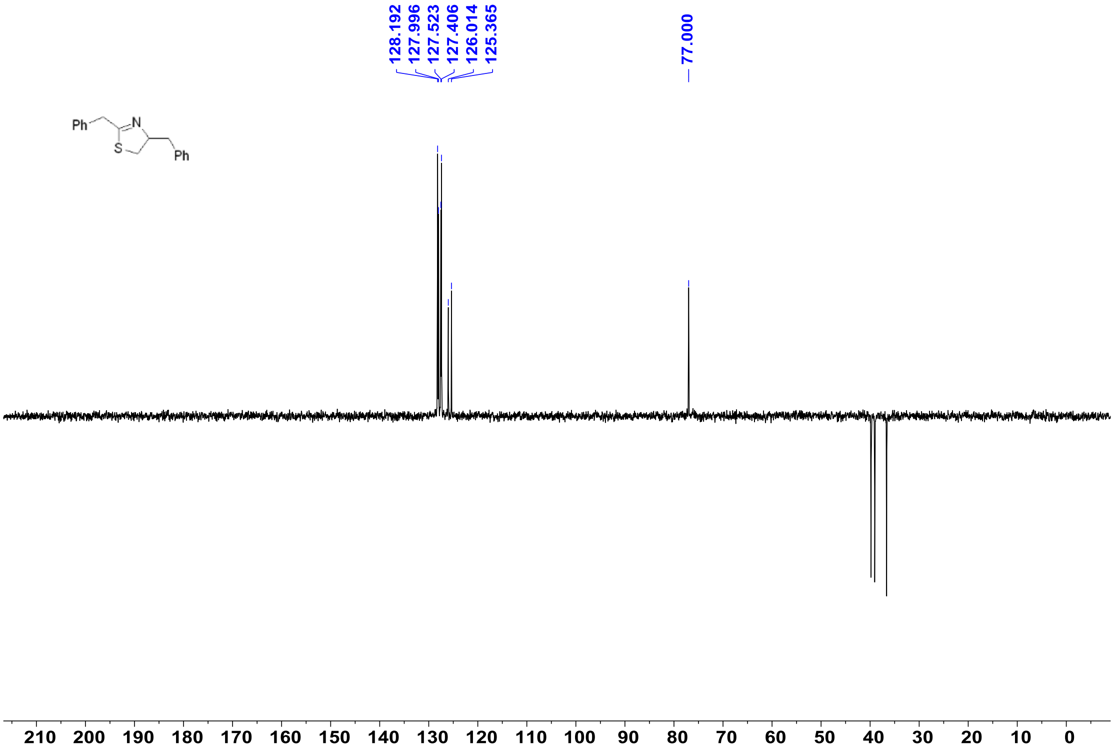
^{1}H MNR (400 MHz, $CDCl_3$)



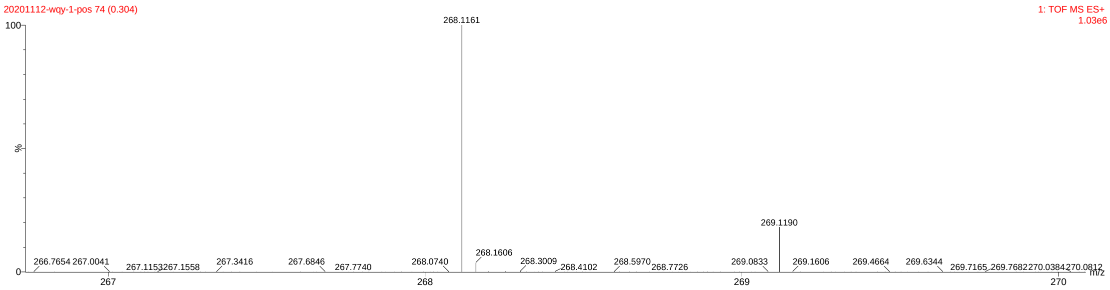
^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)



DEPT 135 ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

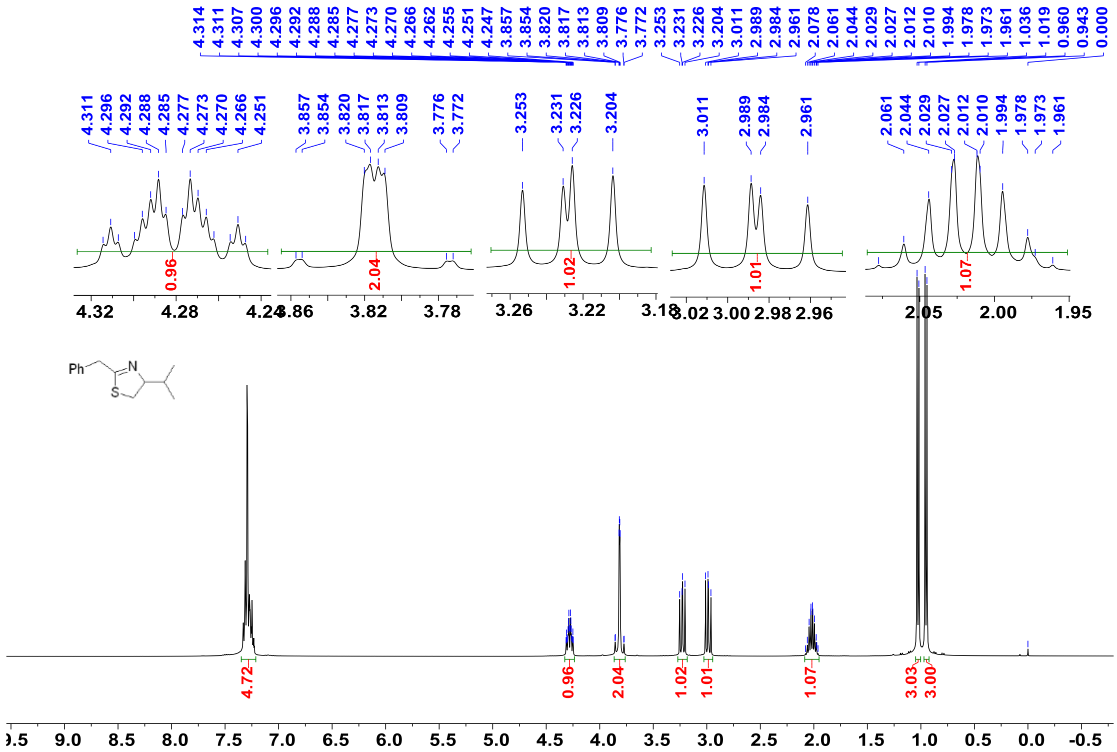


HRMS [M+H]$^{+}$

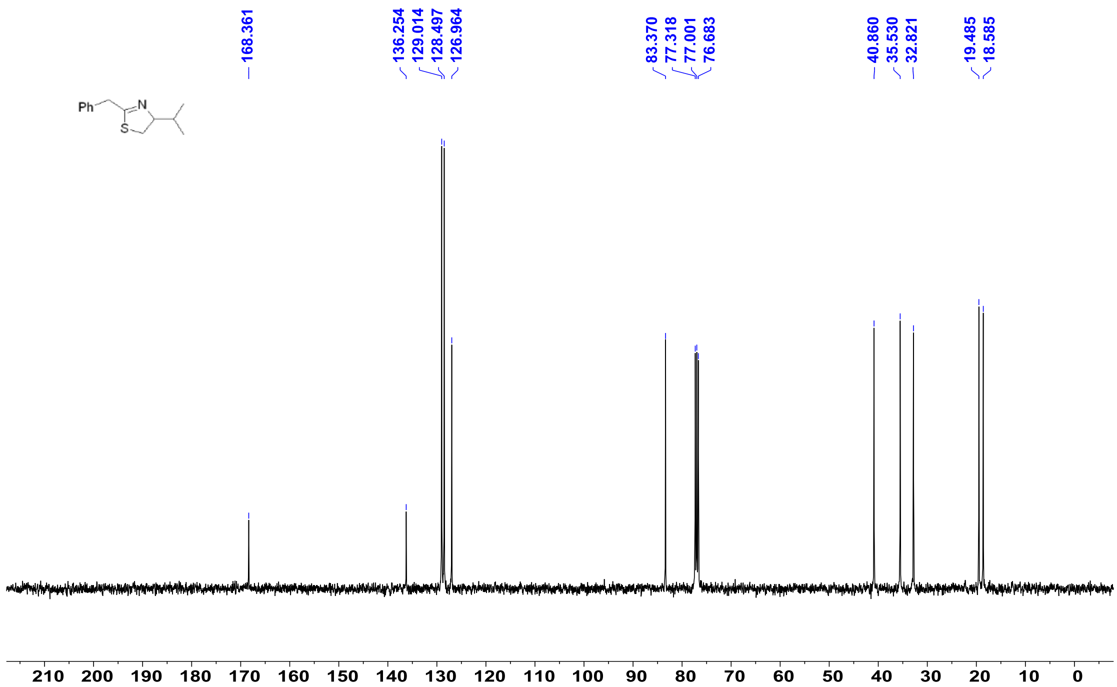


2-Benzyl-4-isopropyl-4,5-dihydrothiazole (4ai)

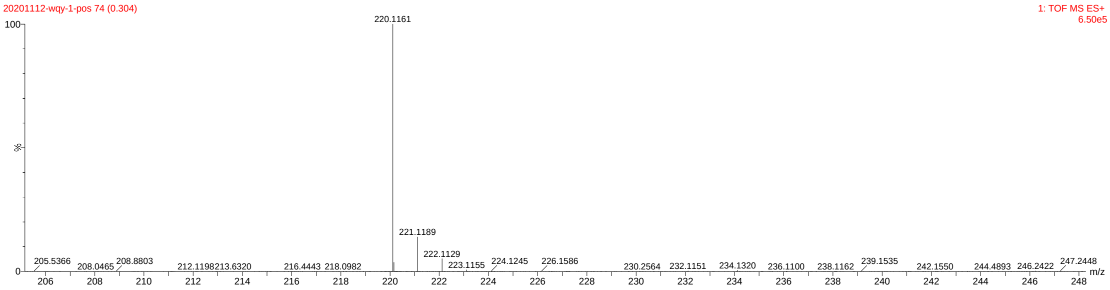
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

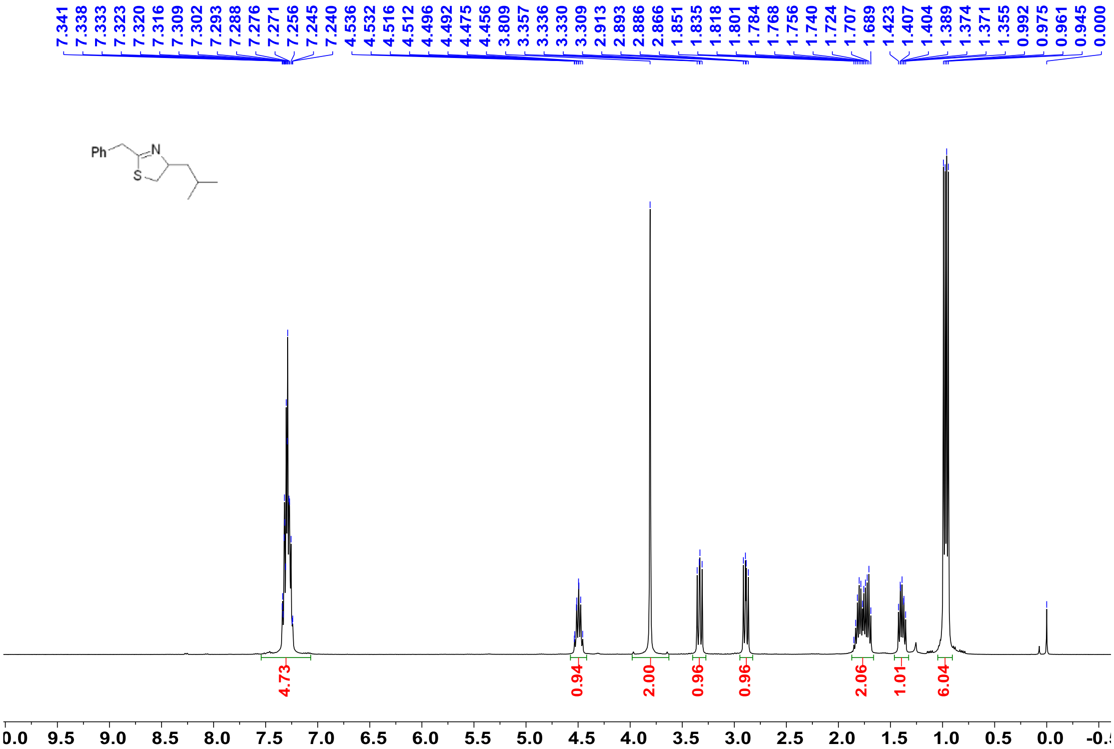


HRMS $[M+H]^+$

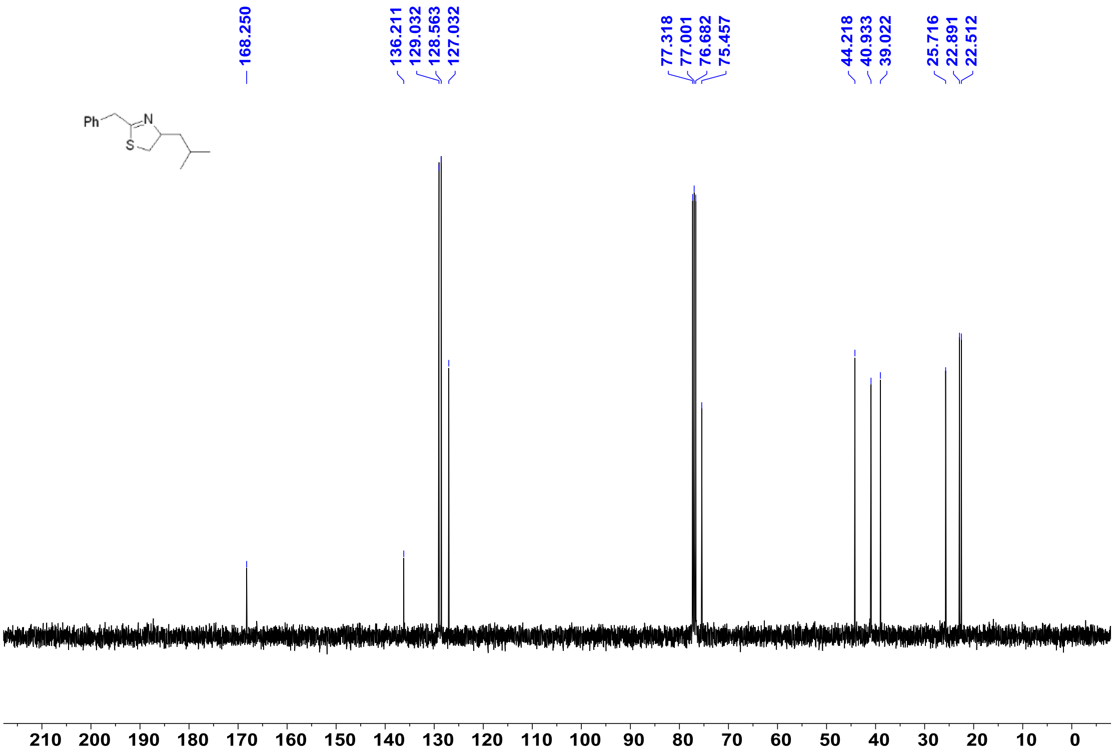


2-Benzyl-4-isobutyl-4,5-dihydrothiazole (4aj)

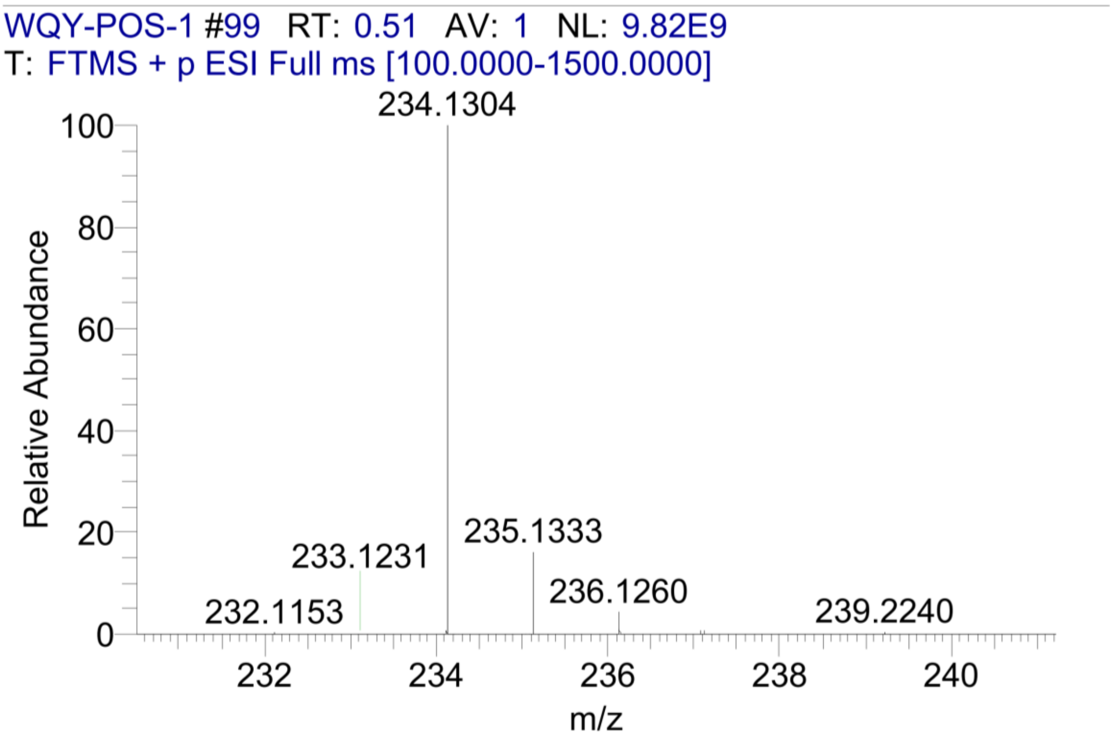
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

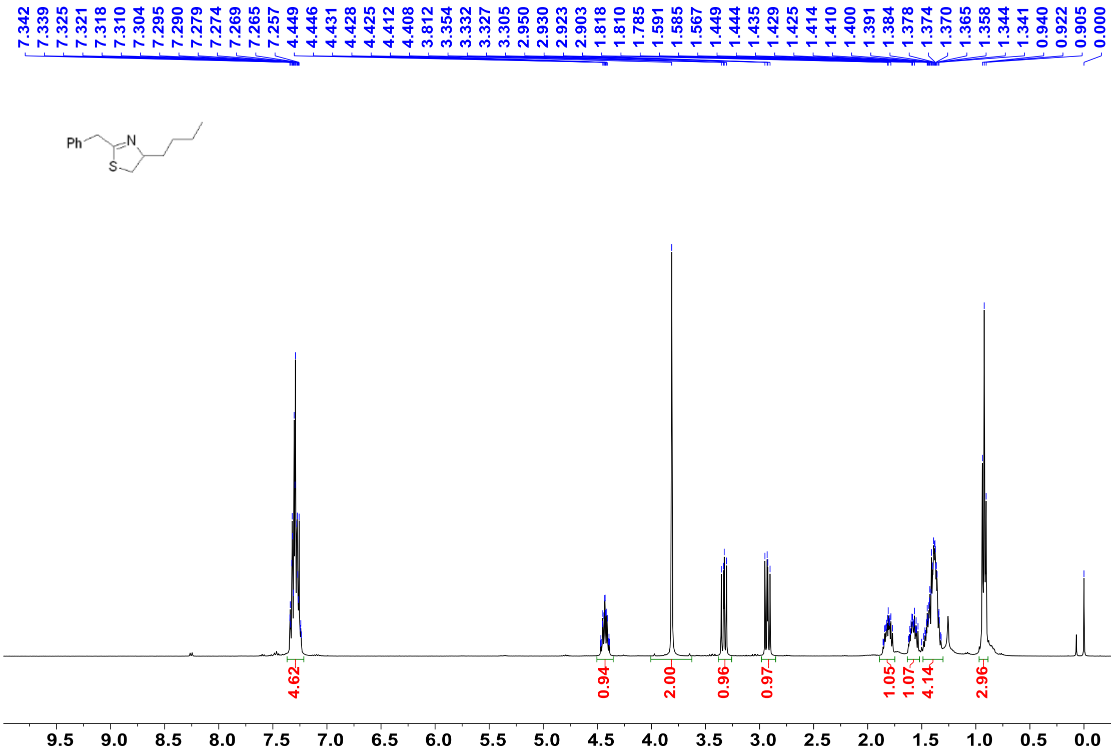


HRMS [M+H]+

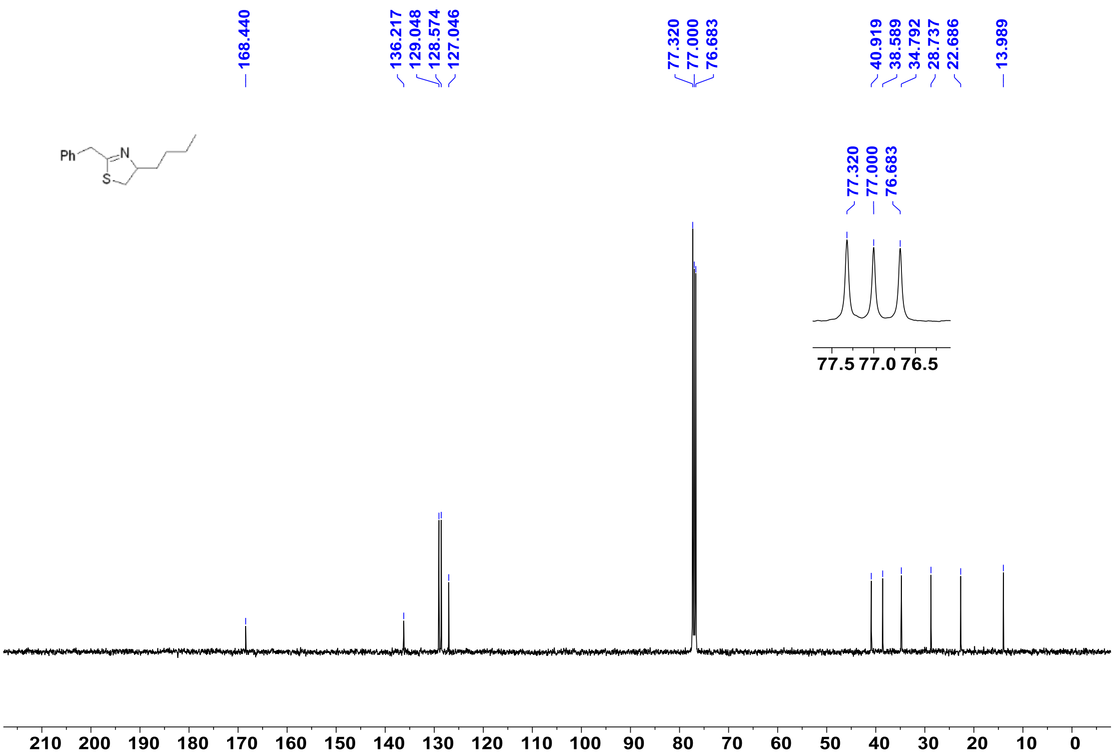


2-Benzyl-4-butyl-4,5-dihydrothiazole (4ak)

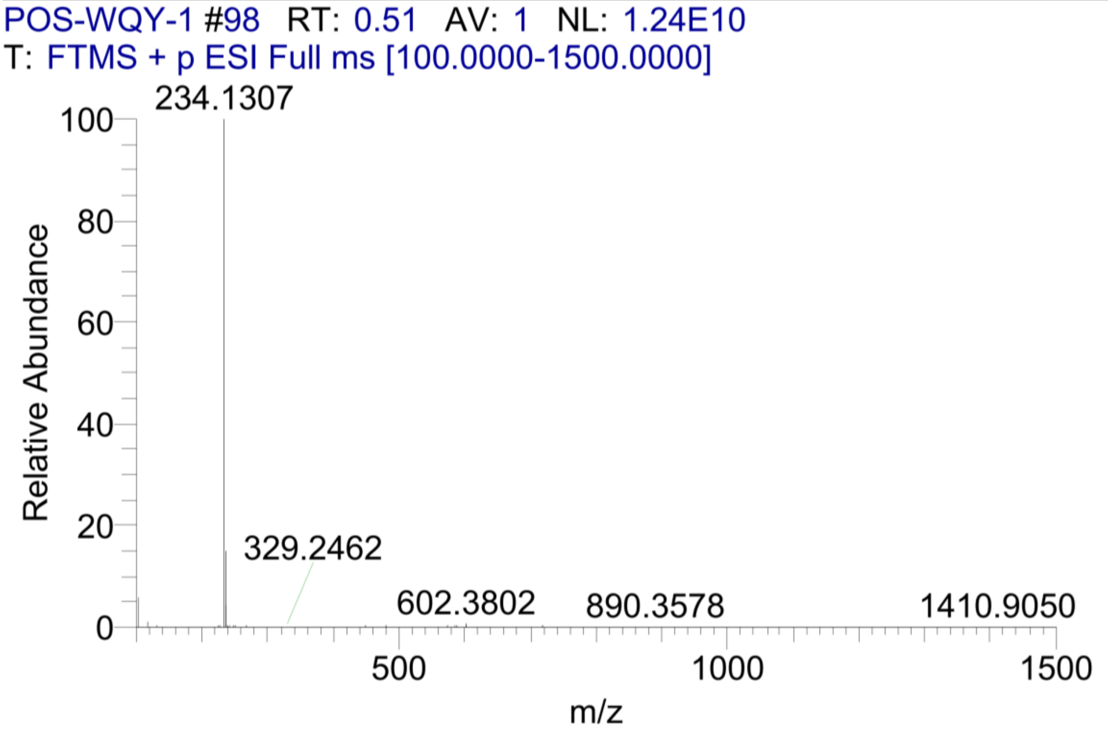
[1]H MNR (400 MHz, $CDCl_3$)



[13]C NMR{[1]H} (101 MHz, $CDCl_3$)

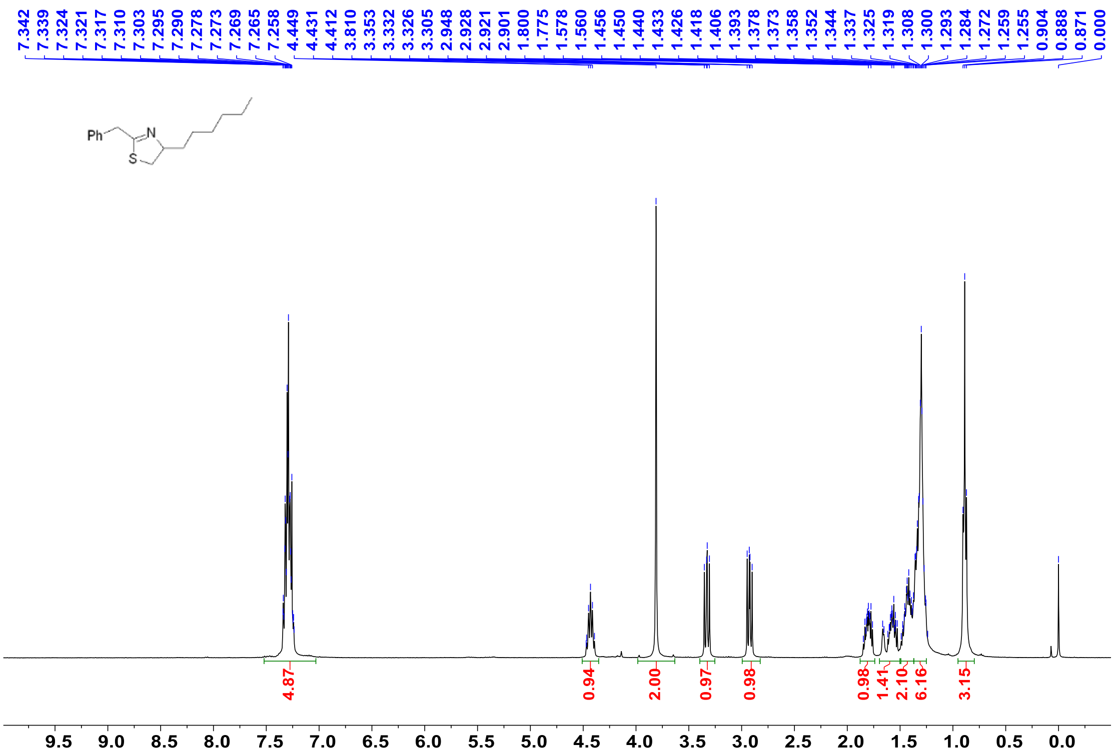


HRMS [M+H]+

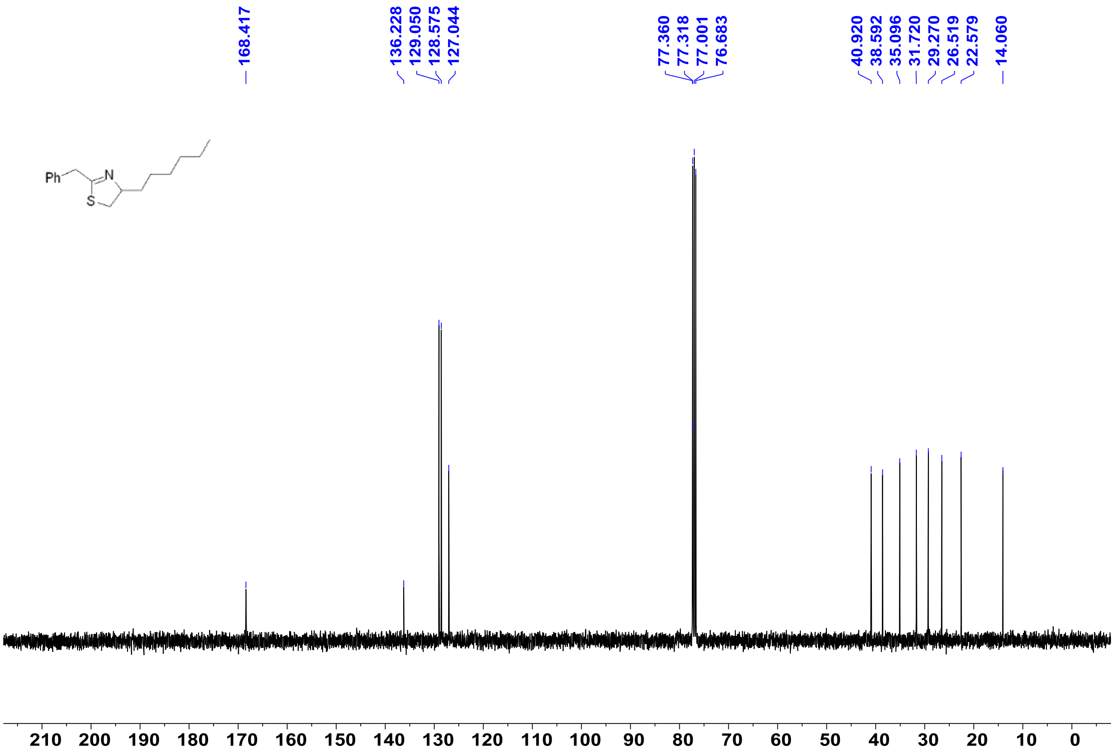


2-Benzyl-4-hexyl-4,5-dihydrothiazole (4al)

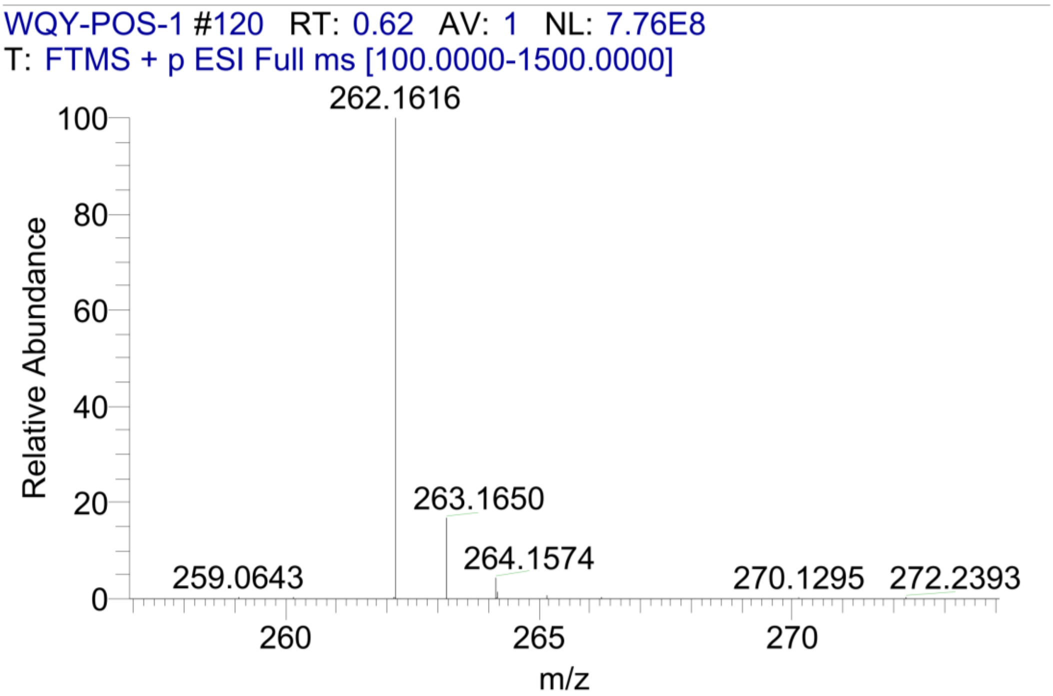
^{1}H MNR (400 MHz, CDCl$_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

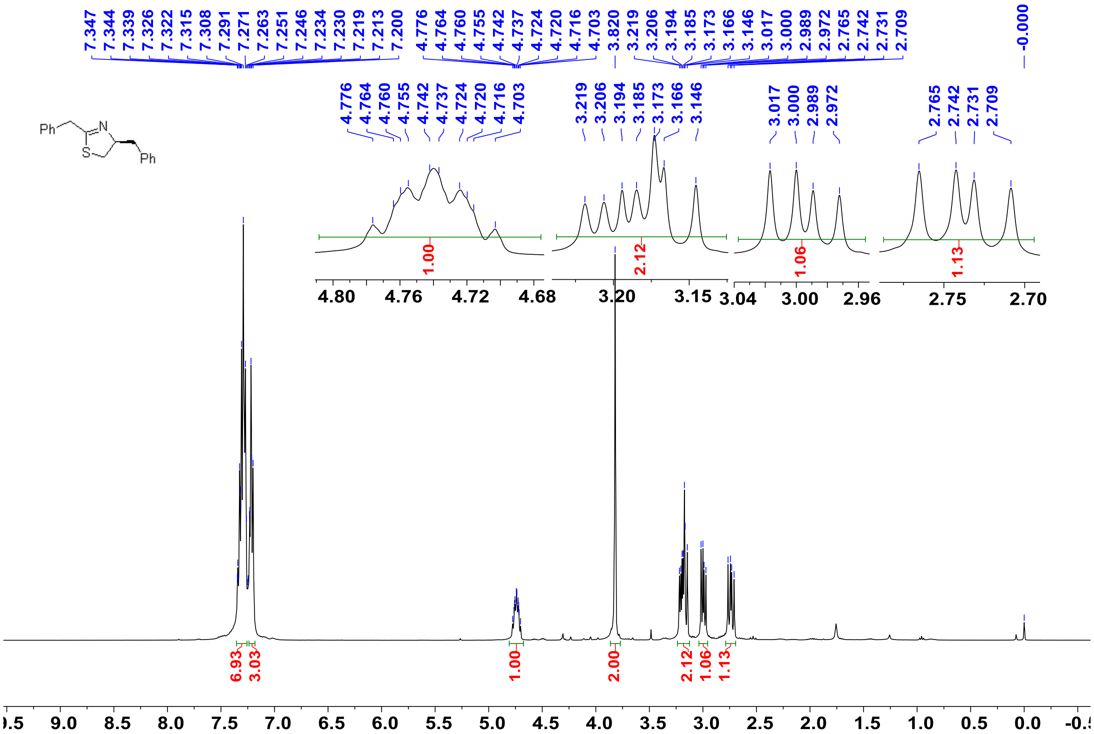


HRMS [M+H]$^{+}$

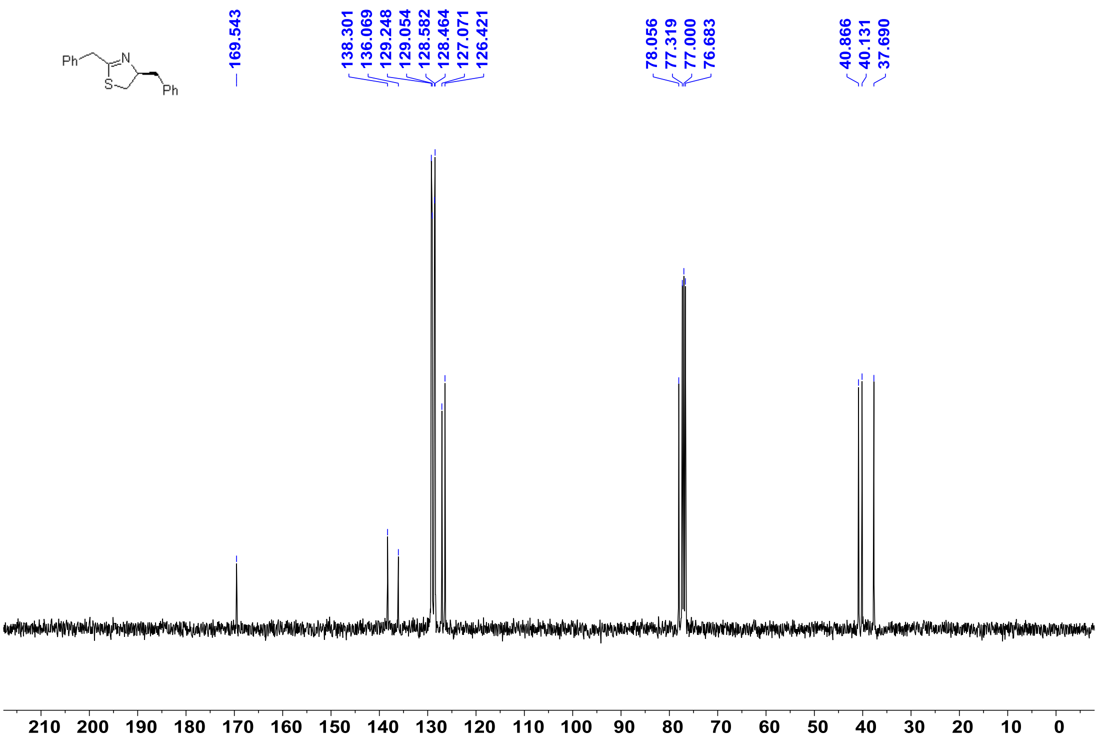


(*S*)-2,4-Dibenzyl-4,5-dihydrothiazole ((*S*)-4ah)

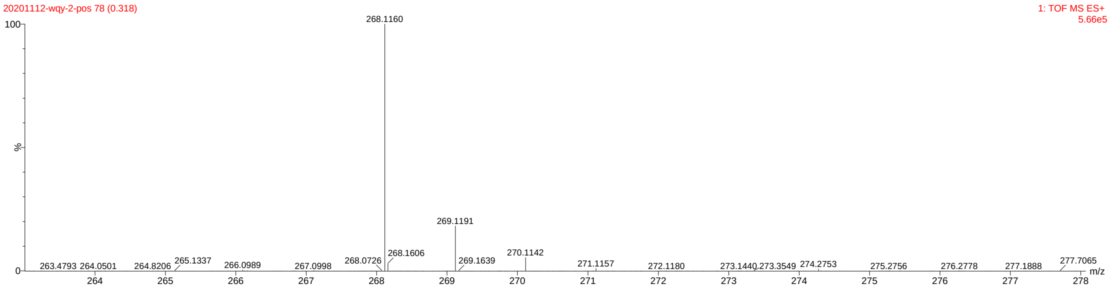
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

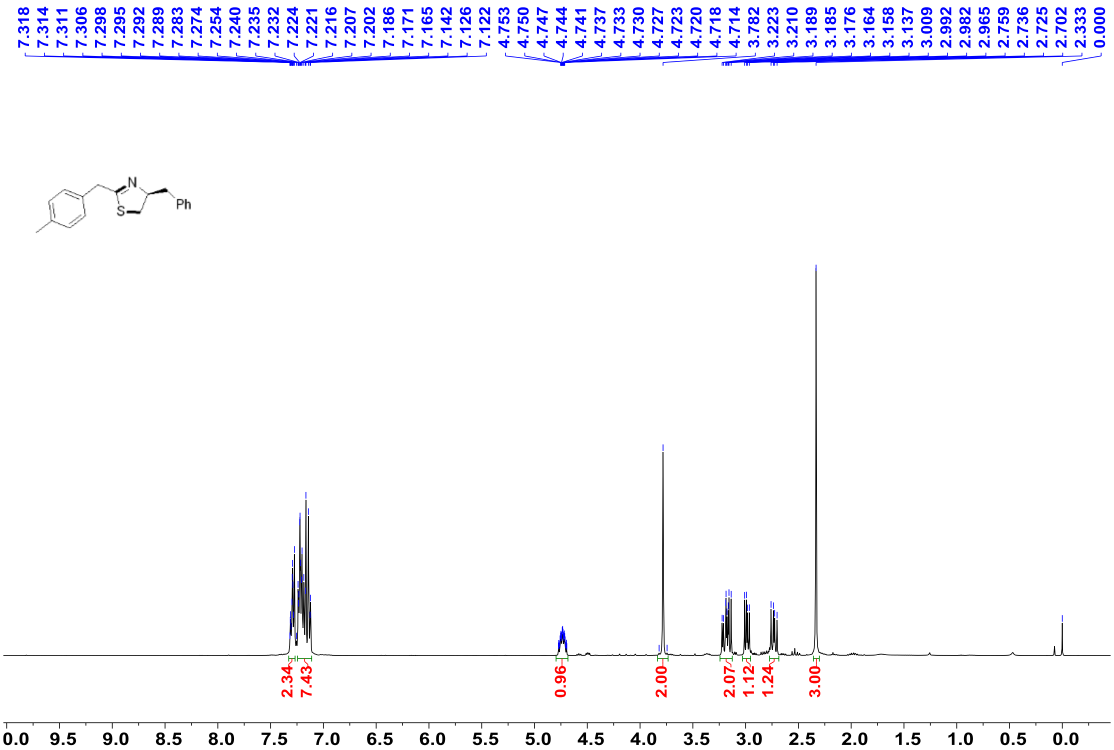


HRMS $[M+H]^+$

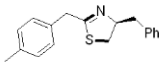


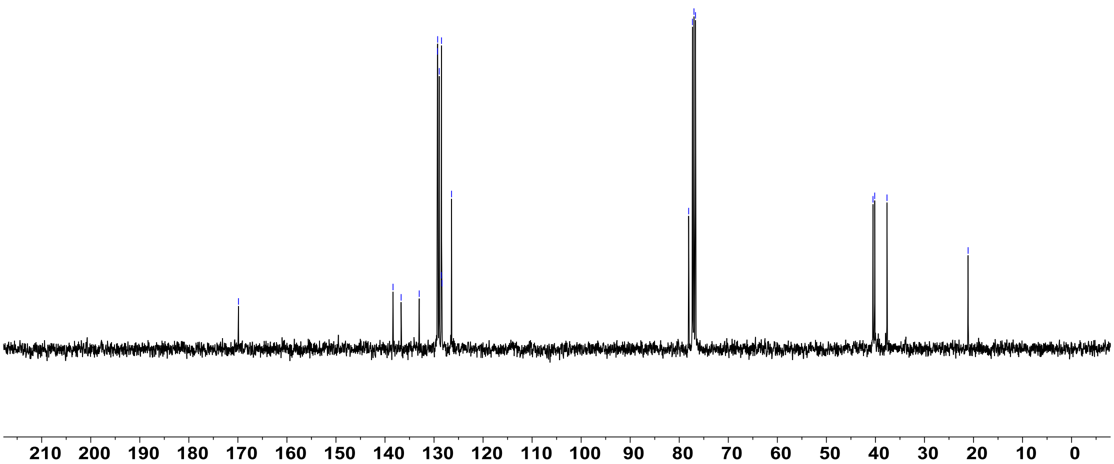
(*S*)-4-Benzyl-2-(4-methylbenzyl)-4,5-dihydrothiazole ((*S*)-4bh)

^{1}H MNR (400 MHz, $CDCl_3$)

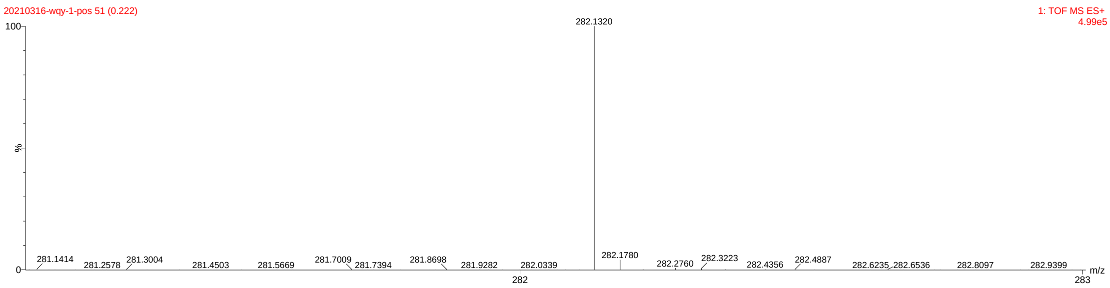


^{13}C NMR{^1H} (101 MHz, $CDCl_3$)



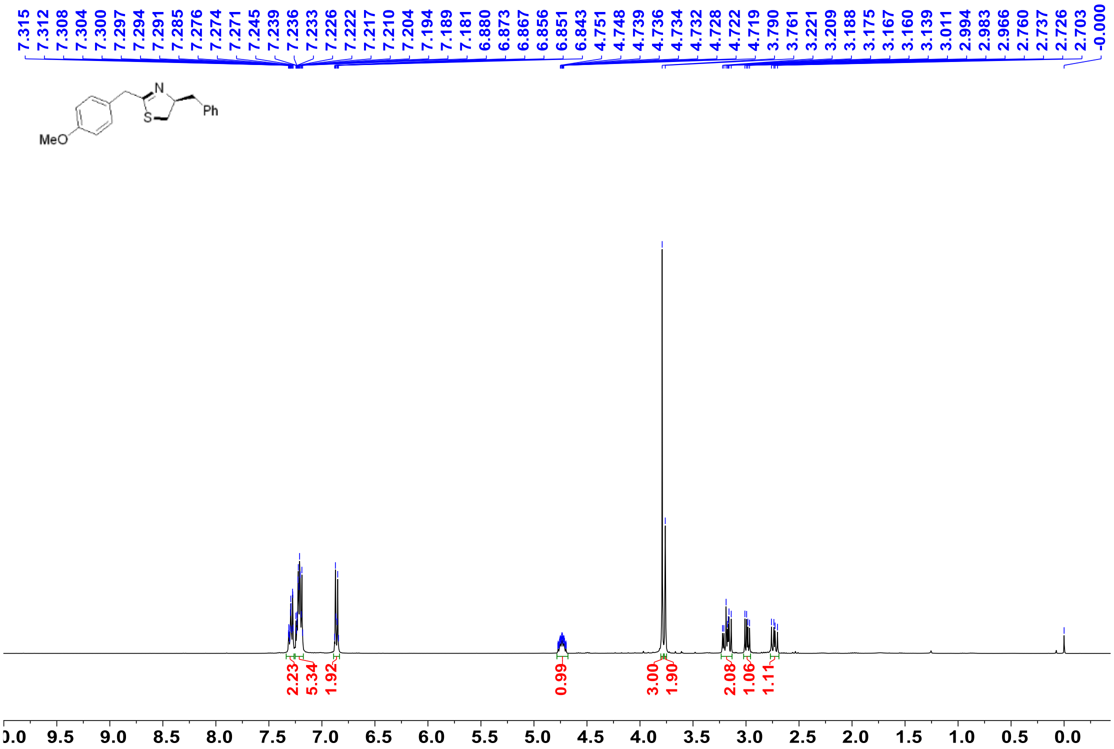


HRMS [M+H]$^+$

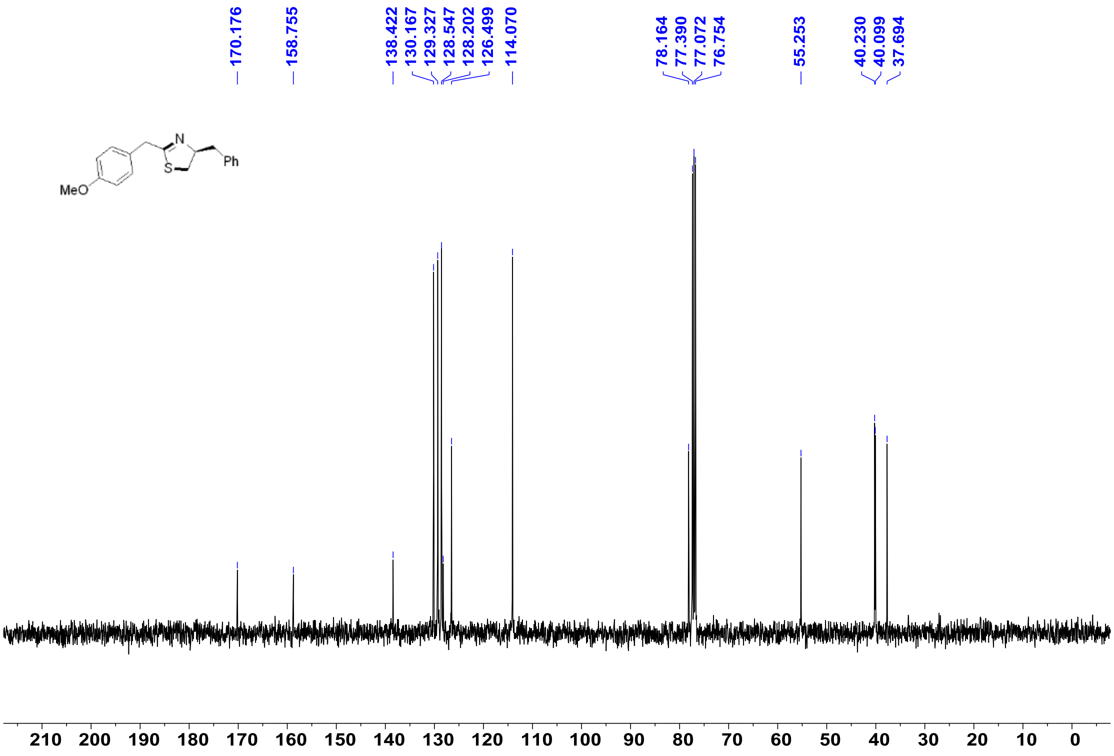


(*S*)-4-Benzyl-2-(4-methoxybenzyl)-4,5-dihydrothiazole ((*S*)-4eh)

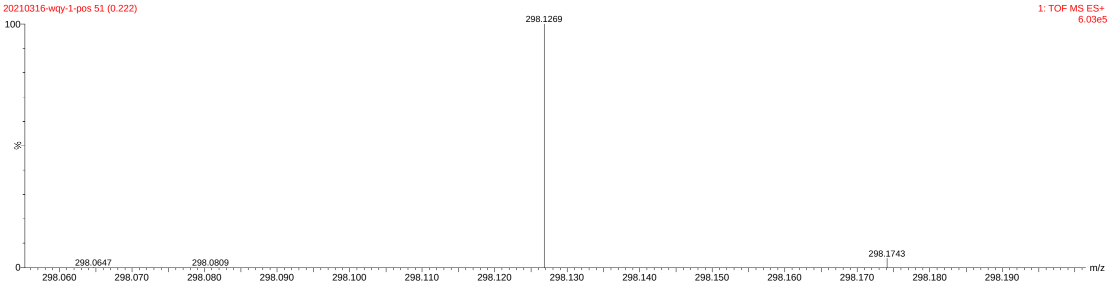
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

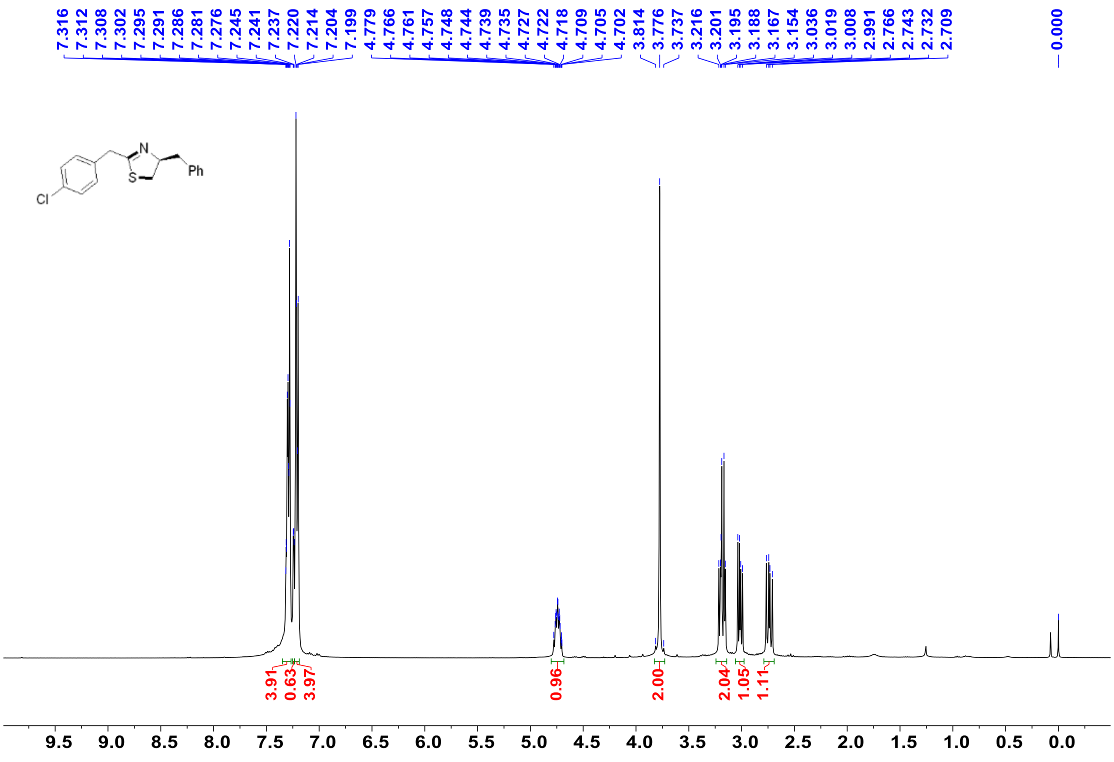


HRMS $[M+H]^+$

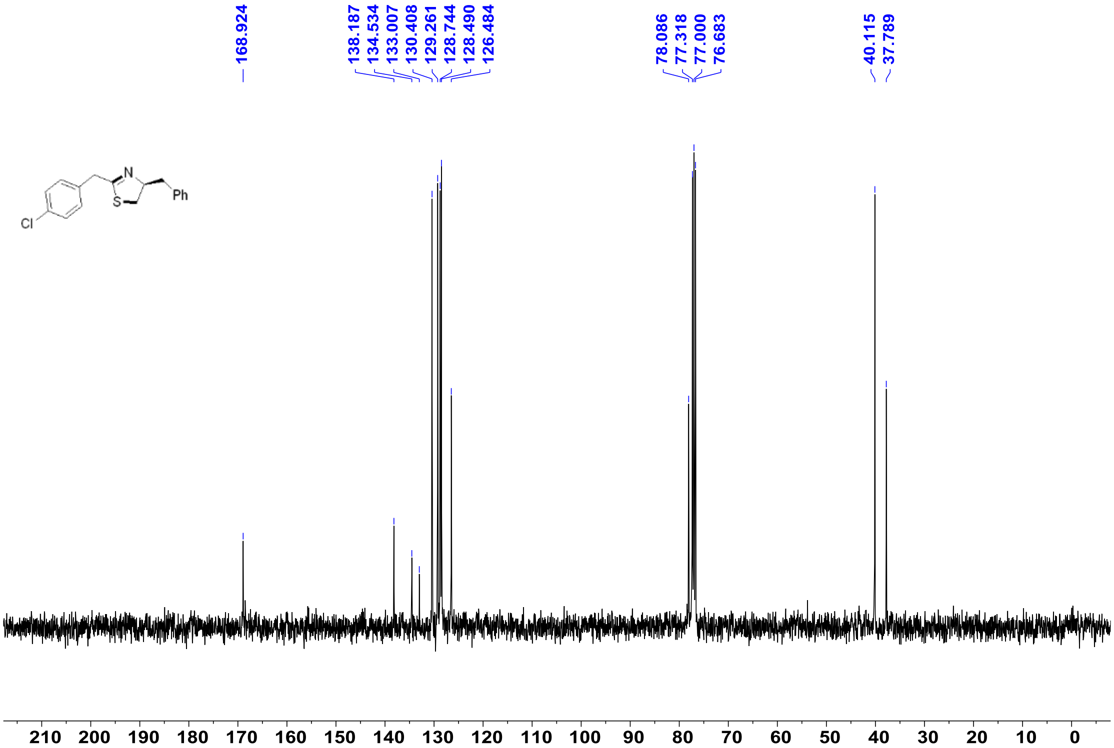


(*S*)-4-Benzyl-2-(4-chlorobenzyl)-4,5-dihydrothiazole ((*S*)-4jh)

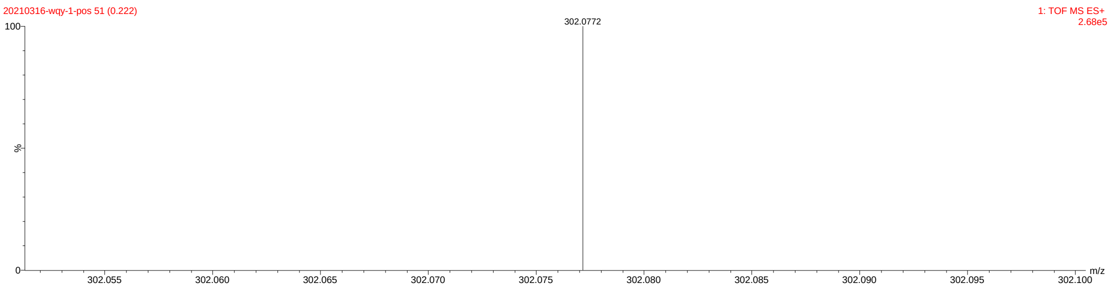
^1H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

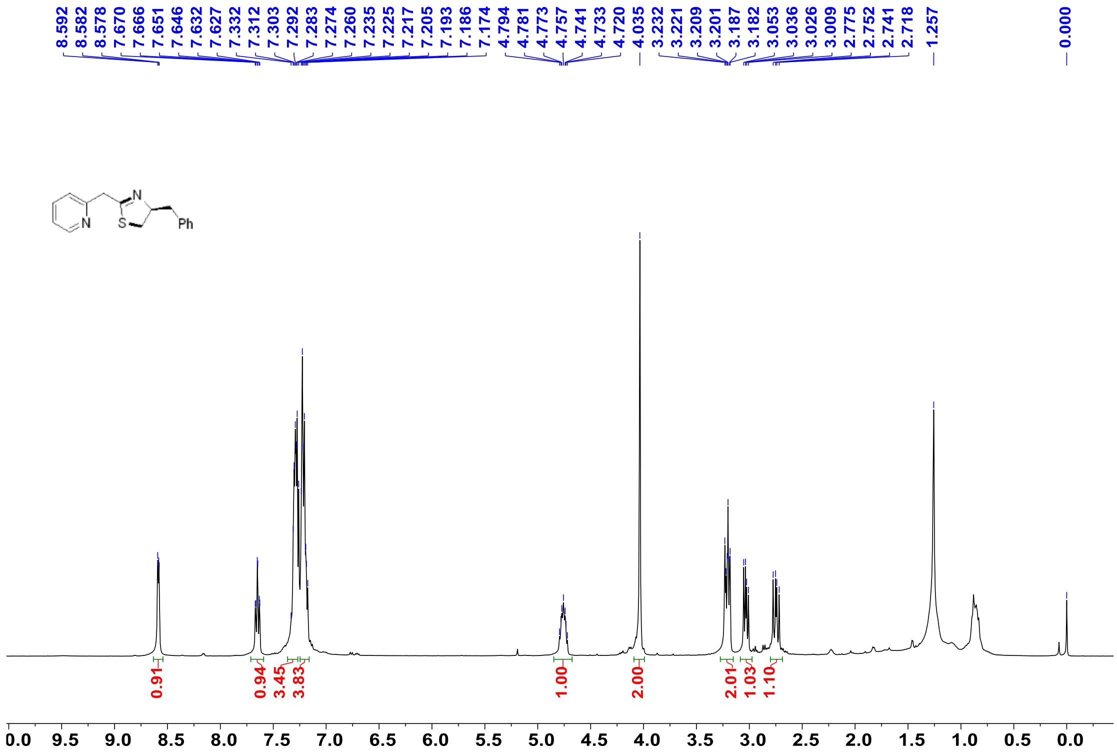


HRMS [M+H]+

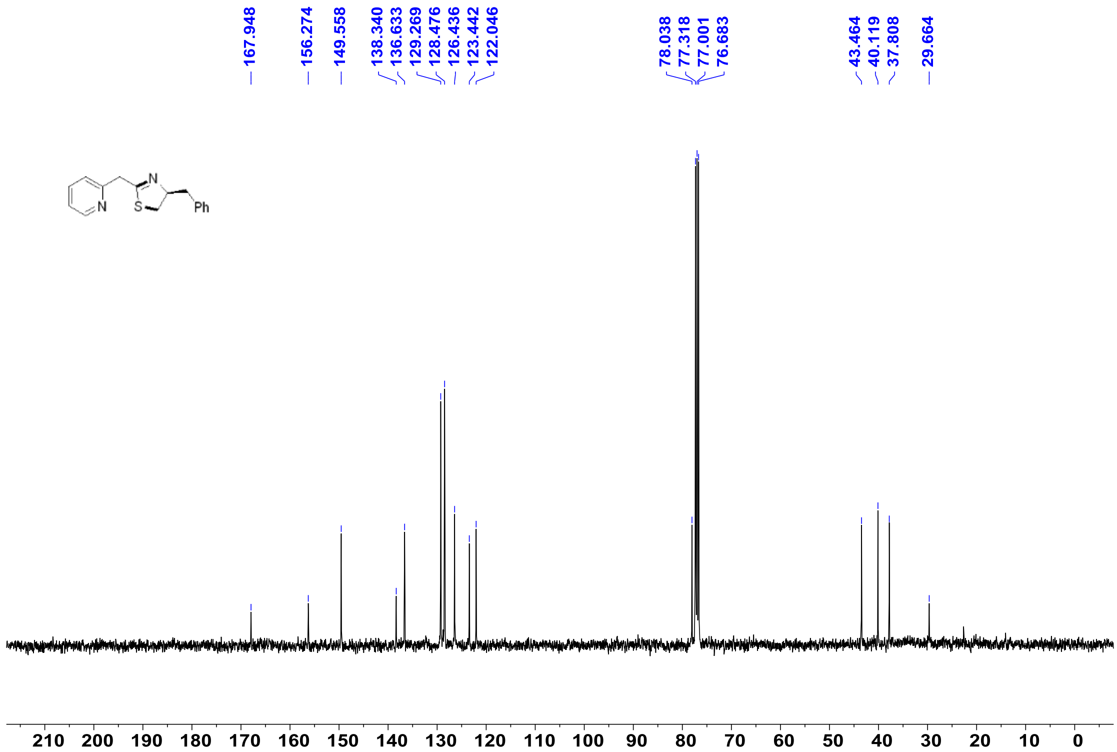


(*S*)-4-Benzyl-2-(pyridin-2-ylmethyl)-4,5-dihydrothiazole ((*S*)-4rh)

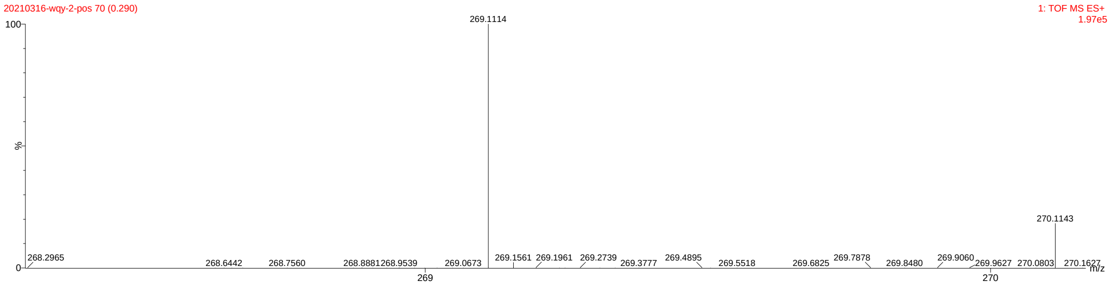
[1]H MNR (400 MHz, $CDCl_3$)



[13]C NMR{[1]H} (101 MHz, $CDCl_3$)

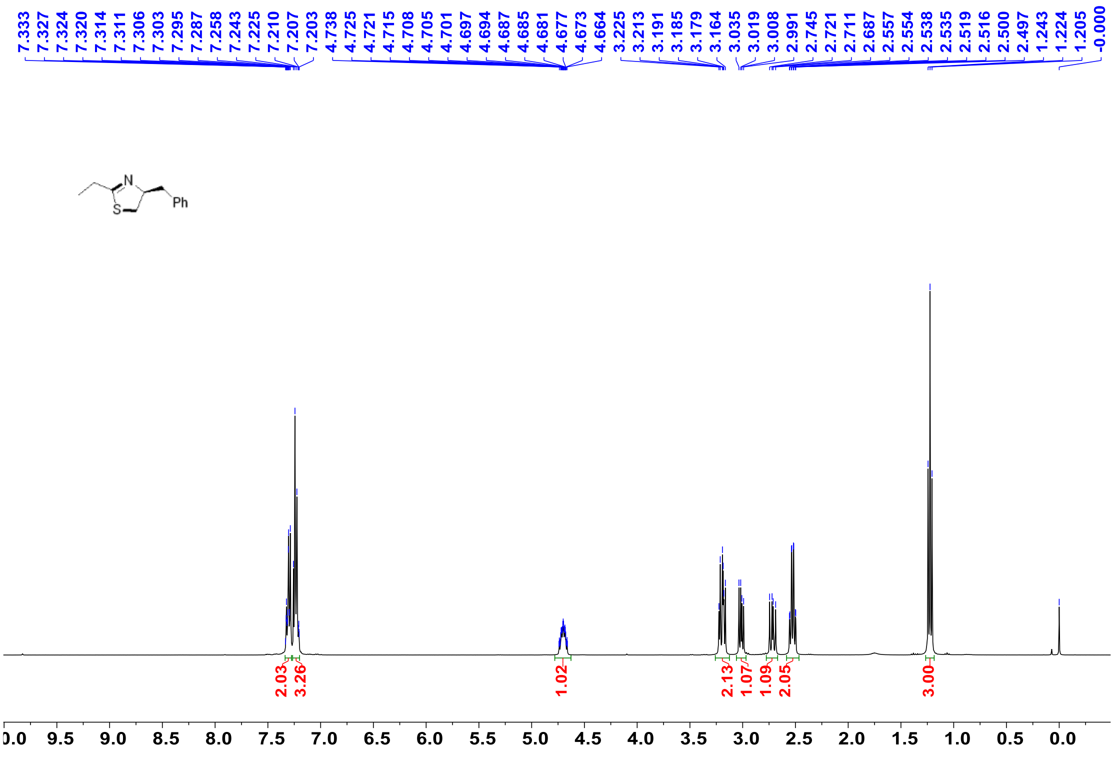


HRMS [M+H]+

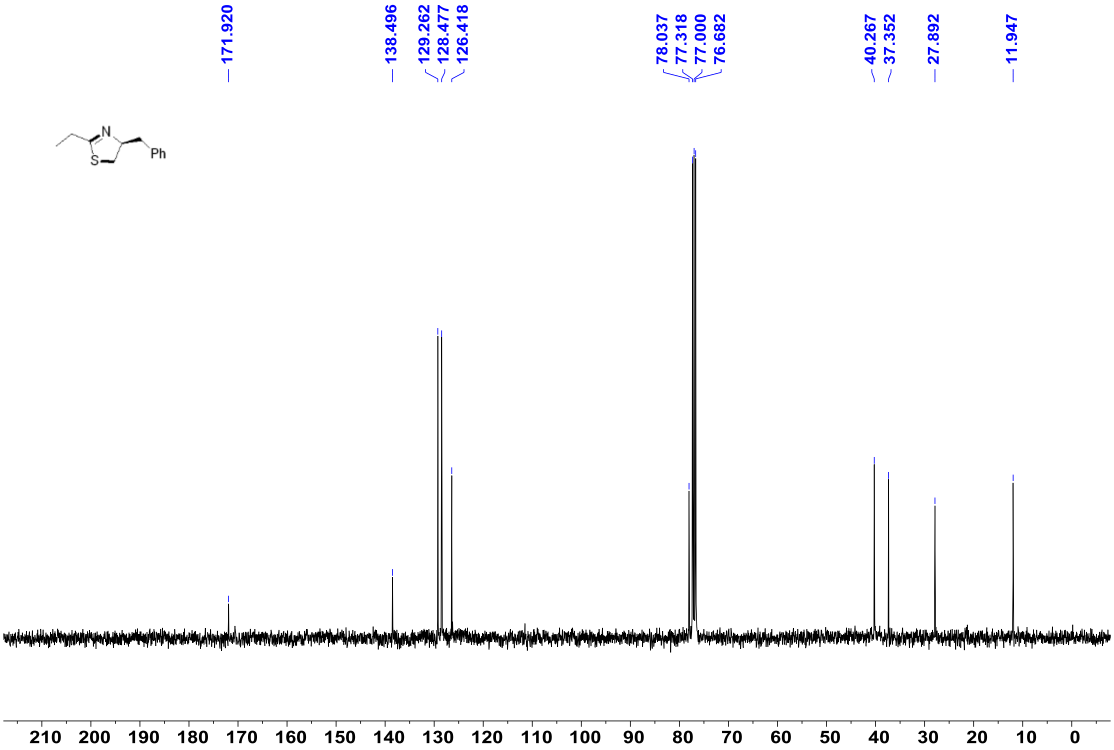


(*S*)-4-Benzyl-2-ethyl-4,5-dihydrothiazole ((*S*)-4sh)

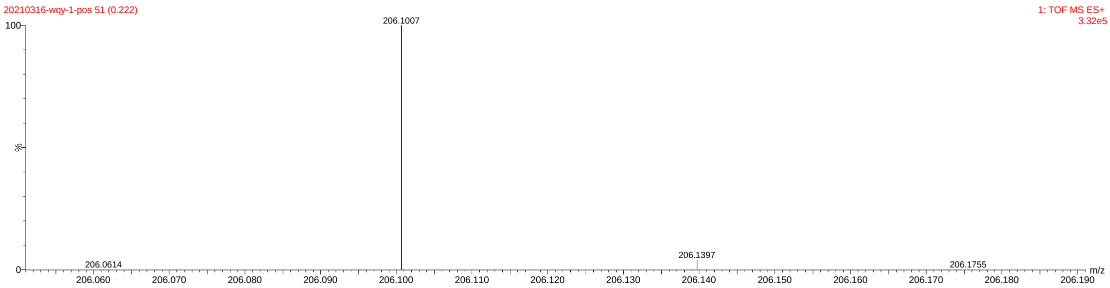
[1]H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

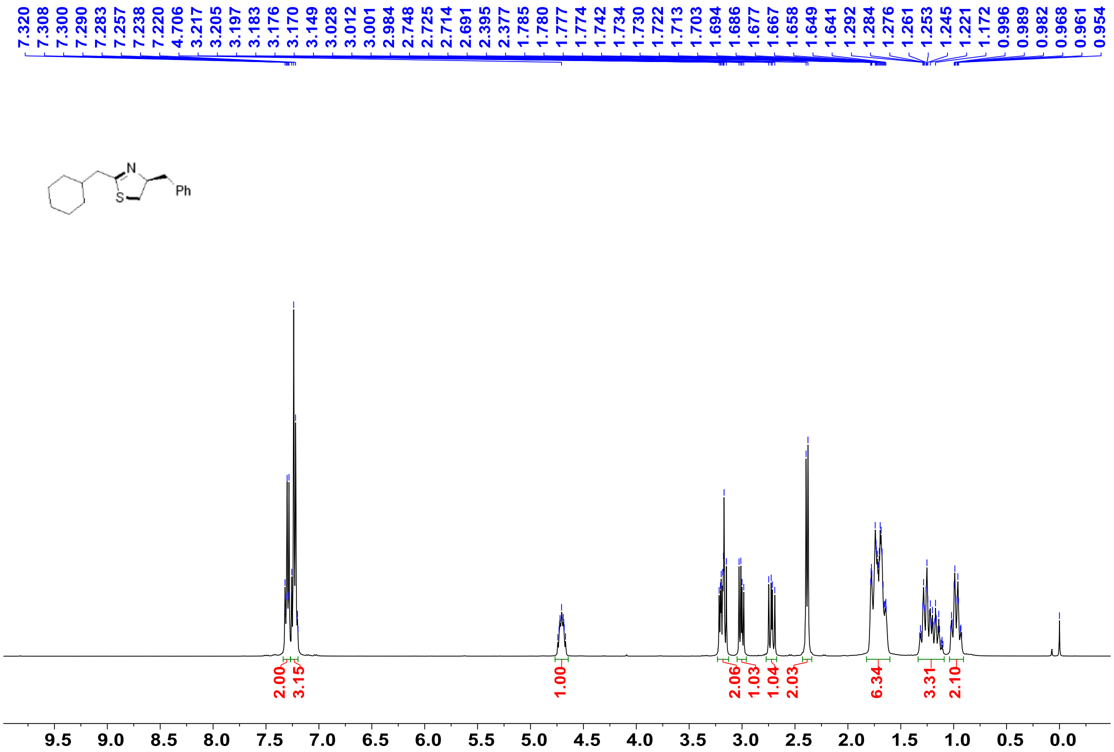


HRMS $[M+H]^+$

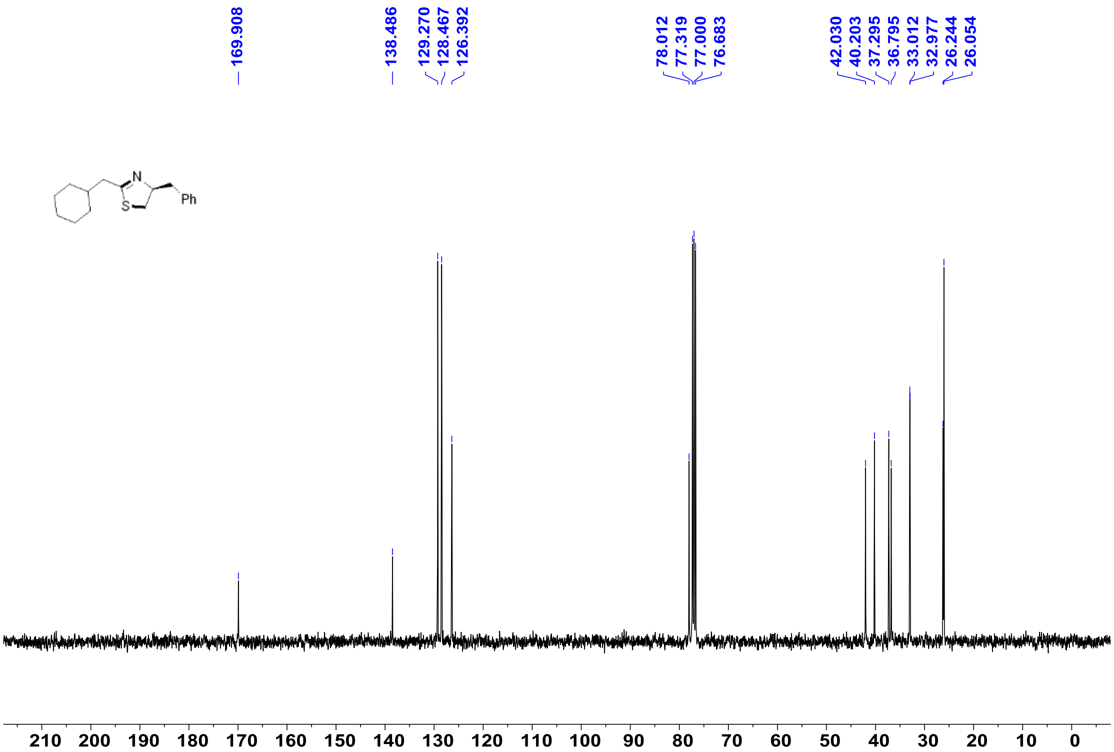


(*S*)-4-Benzyl-2-(cyclohexylmethyl)-4,5-dihydrothiazole ((*S*)-4uh)

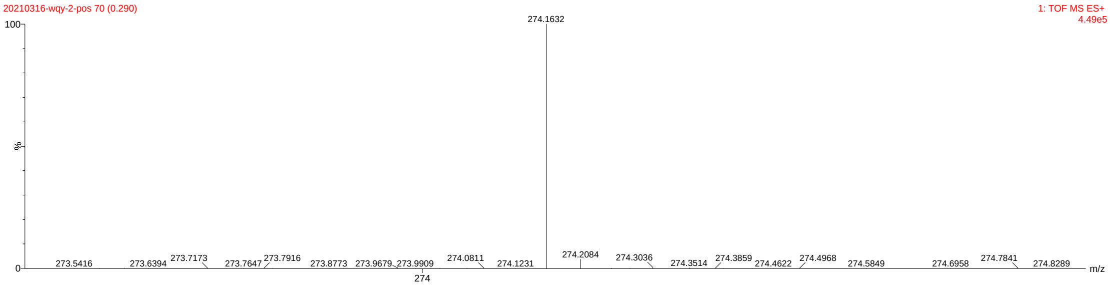
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

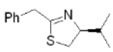


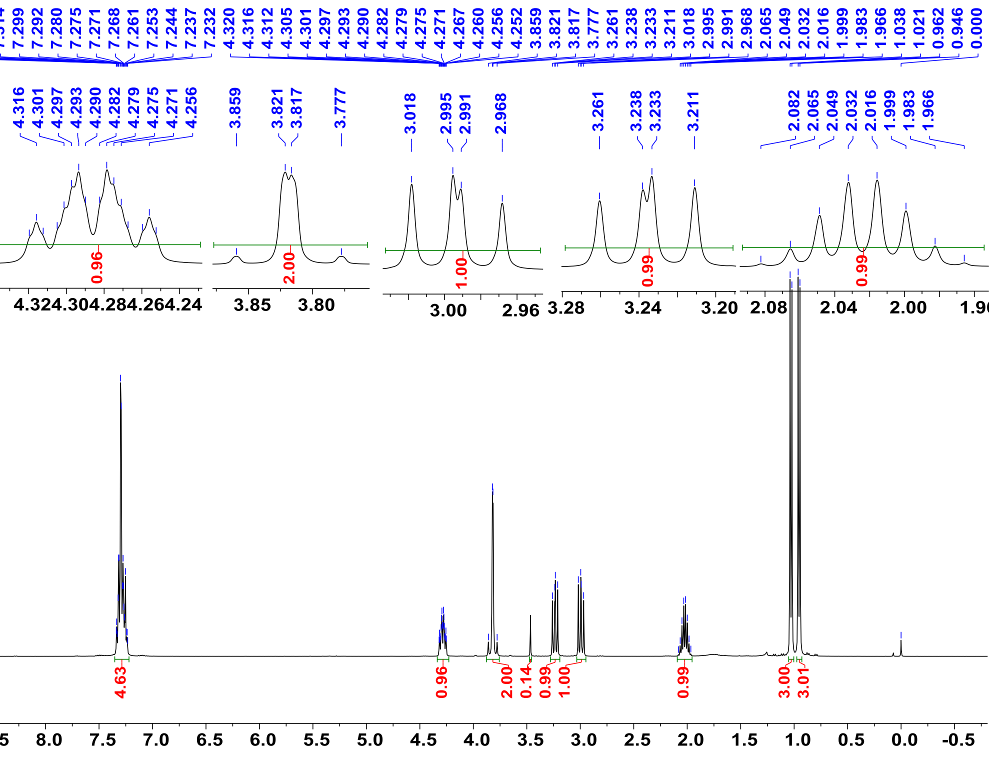
HRMS [M+H]+



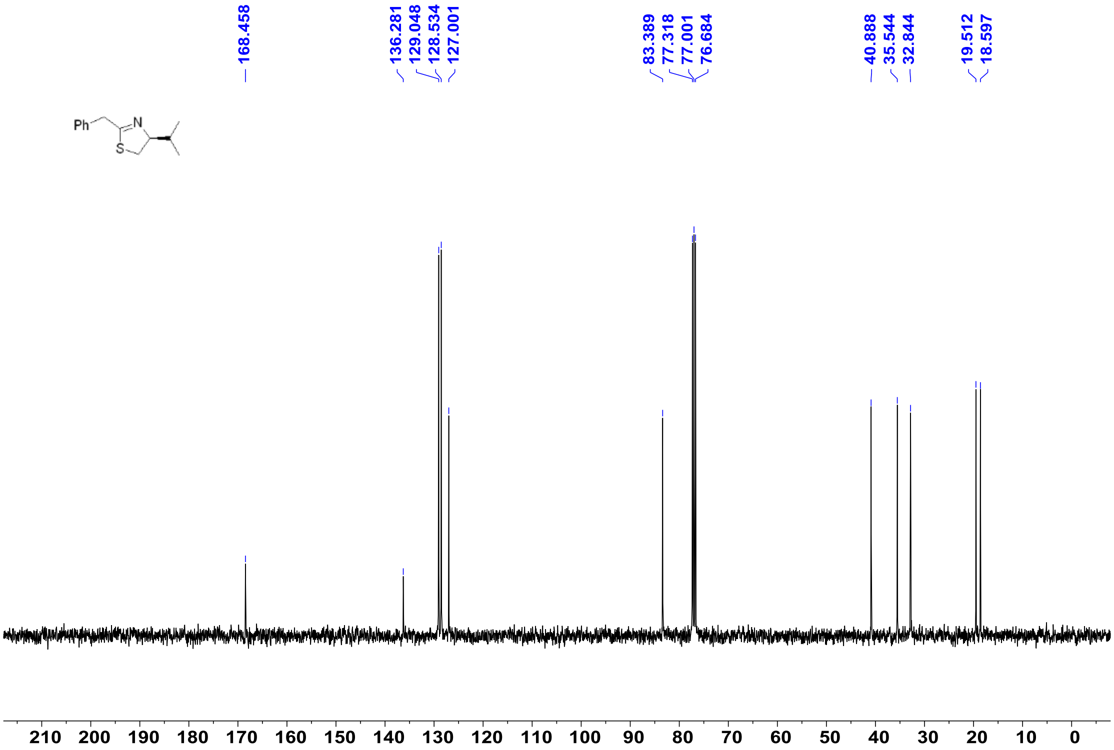
(*S*)-2-Benzyl-4-isopropyl-4,5-dihydrothiazole ((*S*)-4ai)

1H MNR (400 MHz, $CDCl_3$)

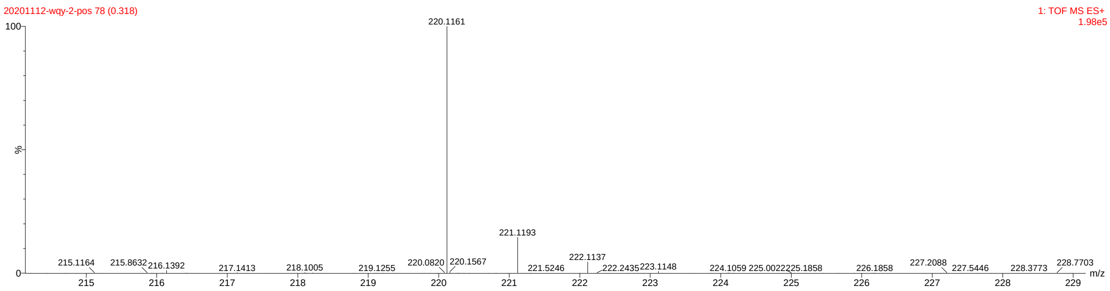




^{13}C NMR{^1H} (101 MHz, $CDCl_3$)

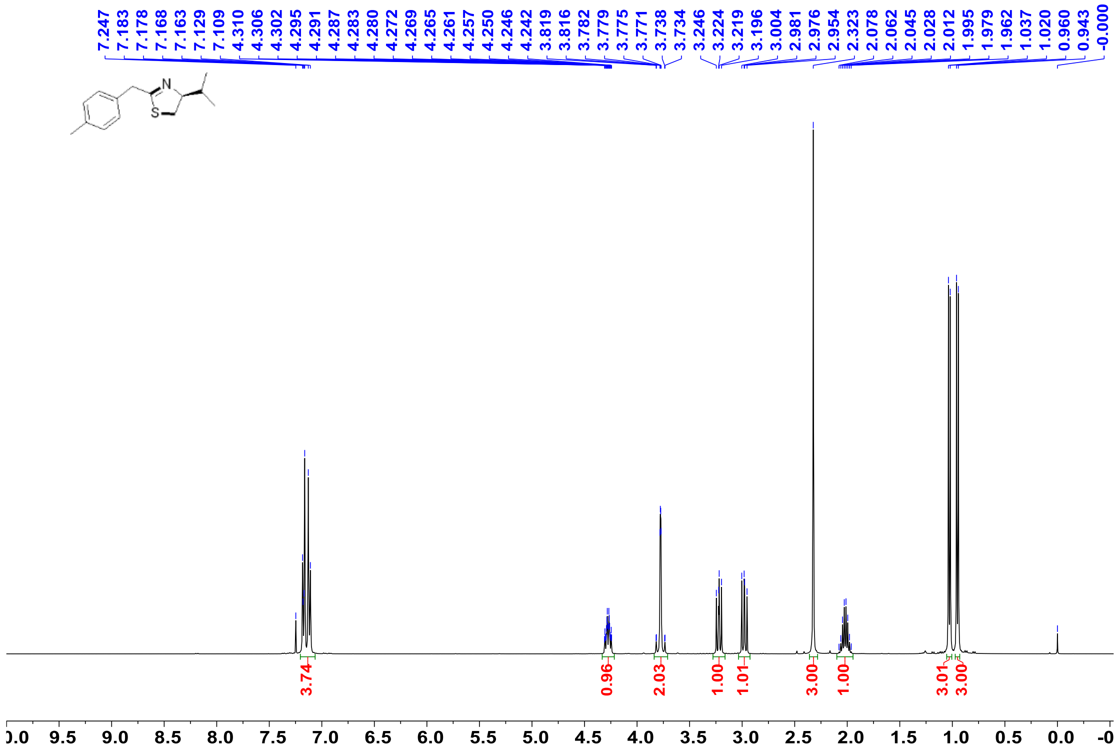


HRMS [M+H]$^+$

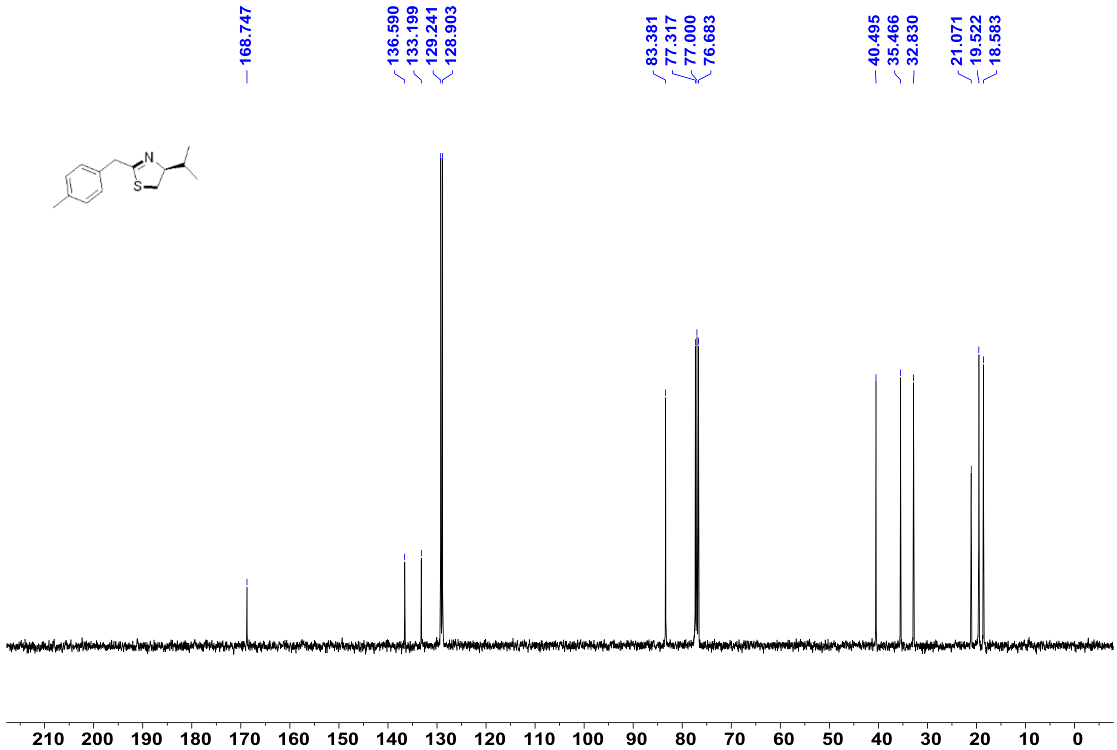


(*S*)-4-Isopropyl-2-(4-methylbenzyl)-4,5-dihydrothiazole ((*S*)-4bi)

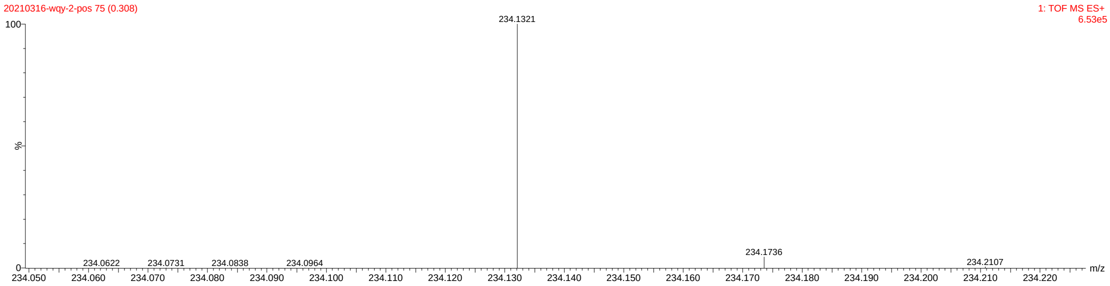
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

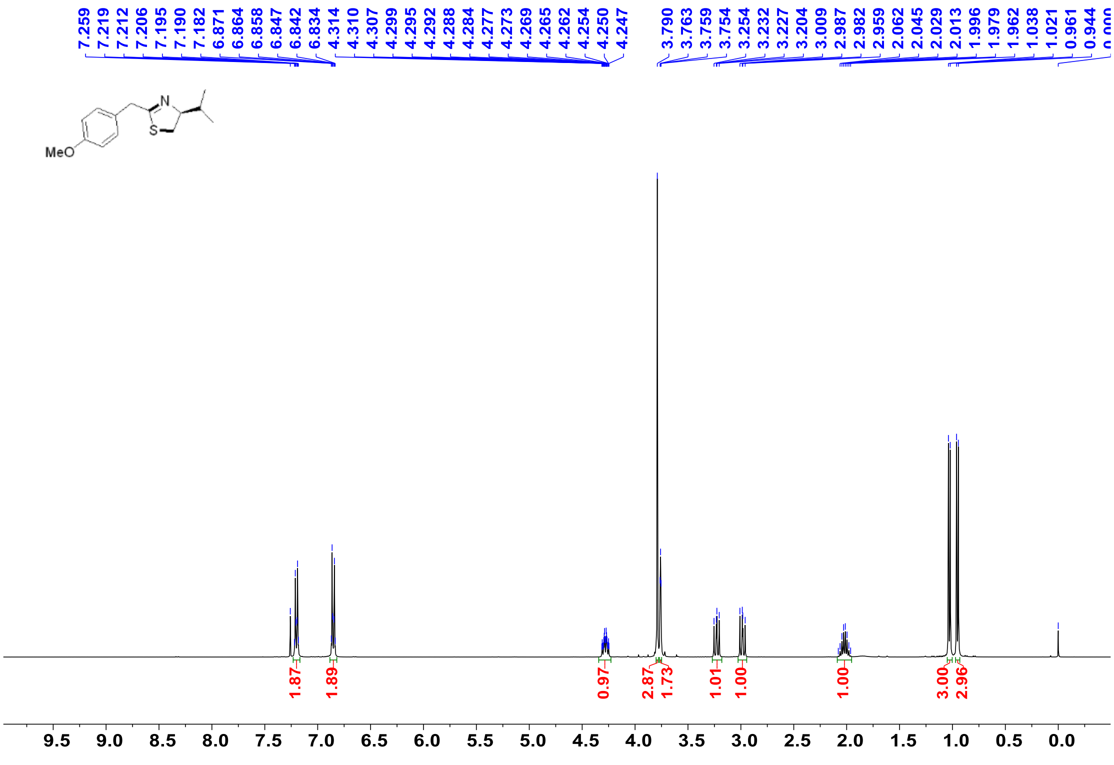


HRMS [M+H]+

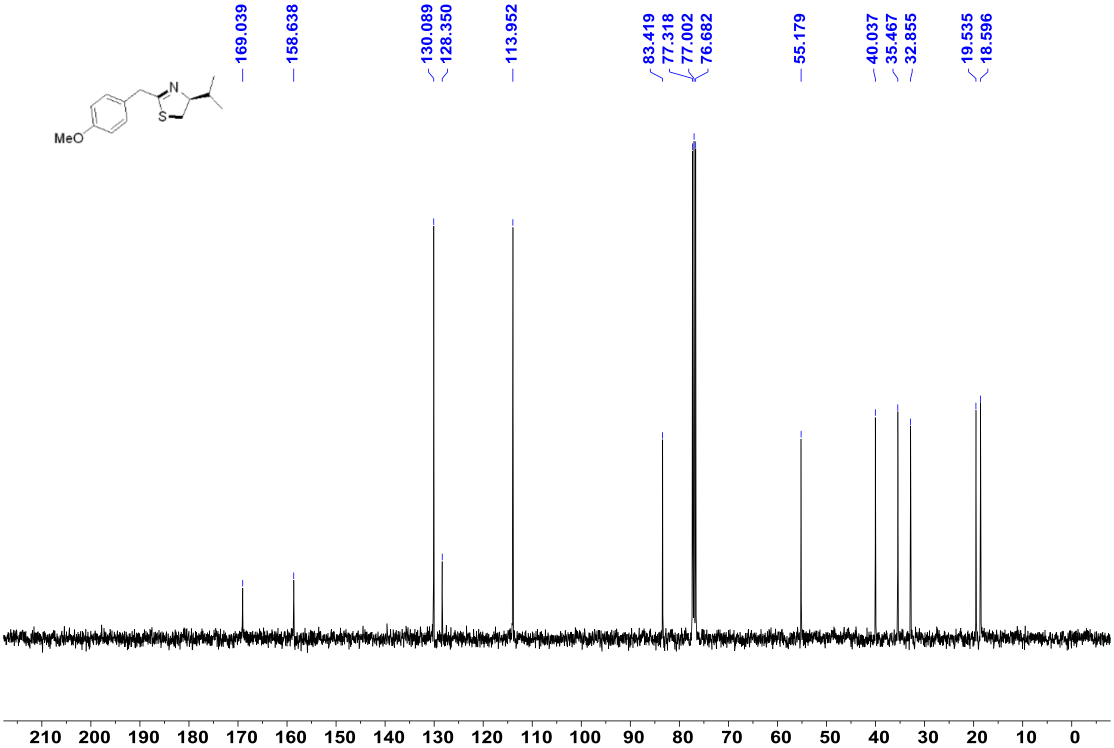


(*S*)-4-Isopropyl-2-(4-methoxybenzyl)-4,5-dihydrothiazole ((*S*)-4ei)

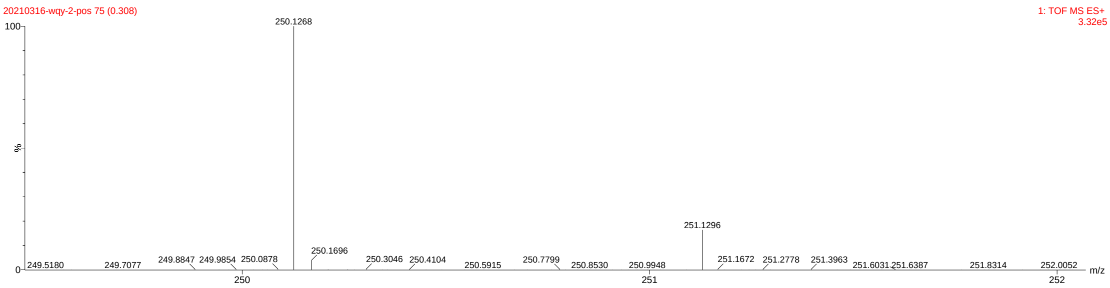
¹H MNR (400 MHz, CDCl₃)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

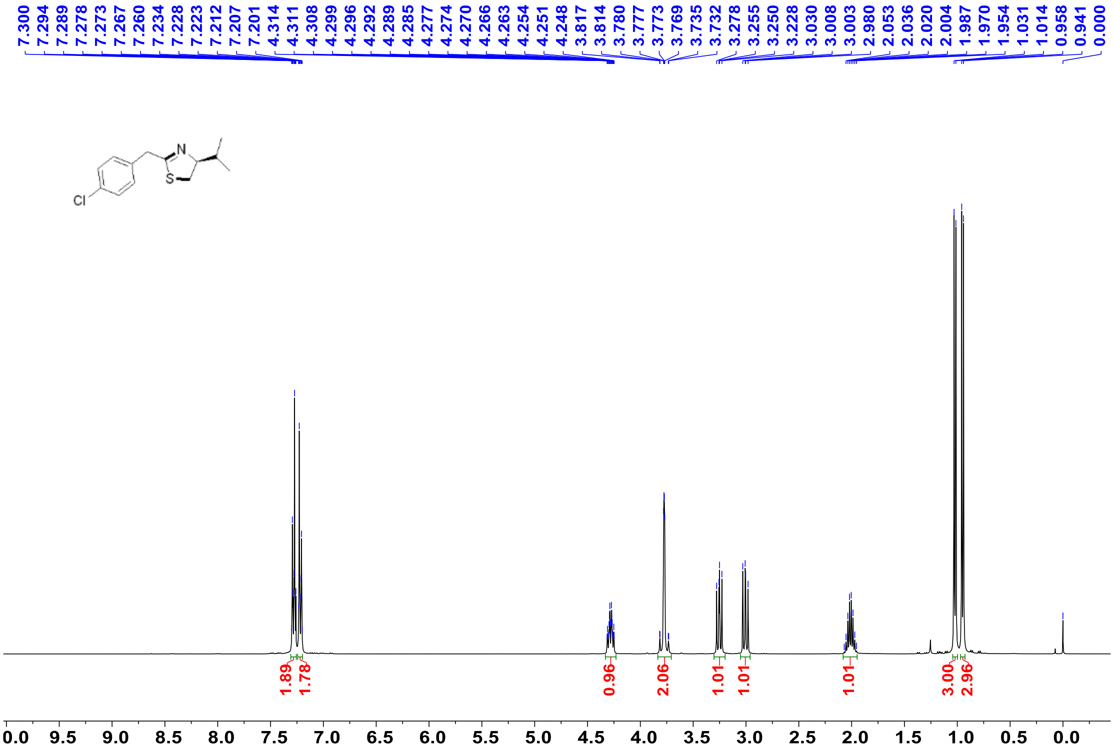


HRMS [M+H]$^{+}$

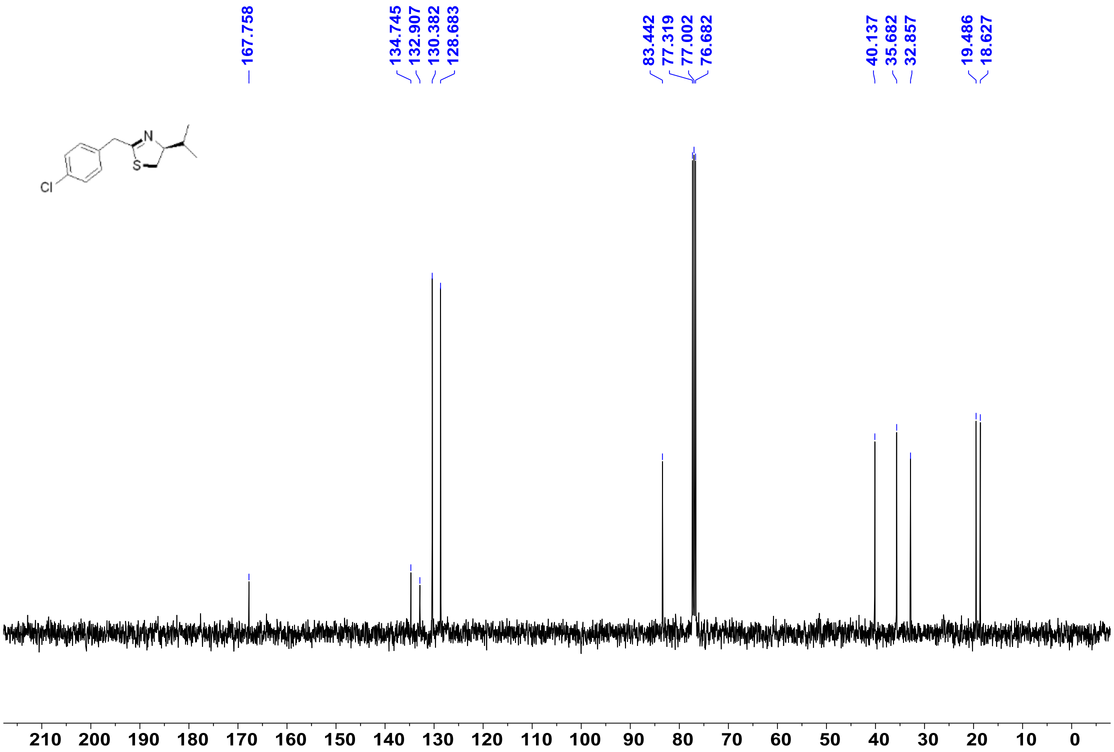


(S)-2-(4-Chlorobenzyl)-4-isopropyl-4,5-dihydrothiazole ((S)-4ji)

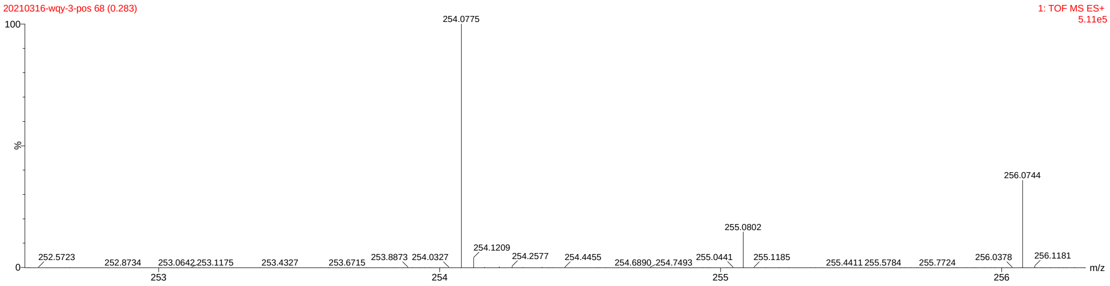
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

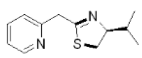


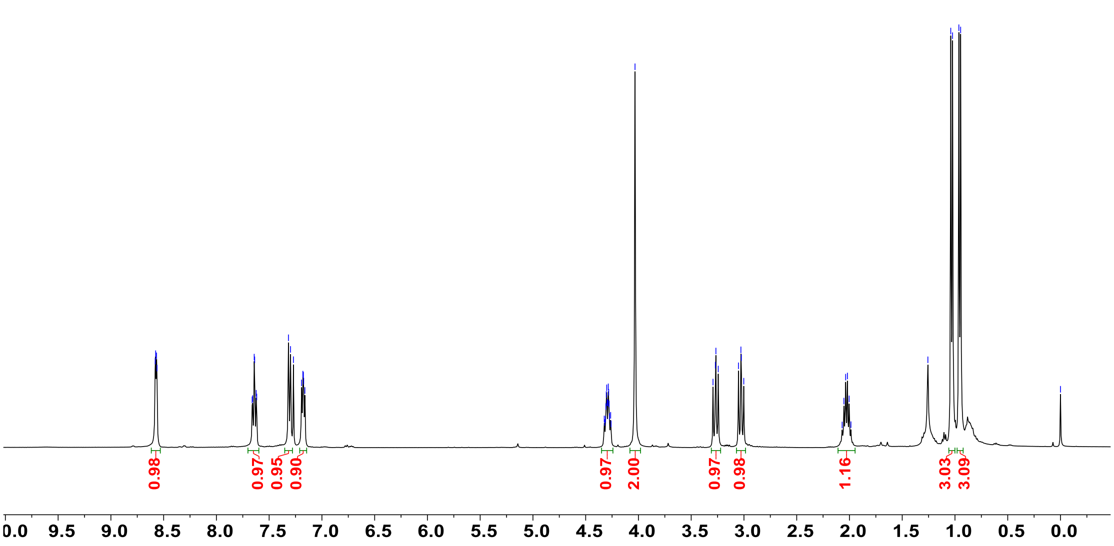
HRMS [M+H]$^+$



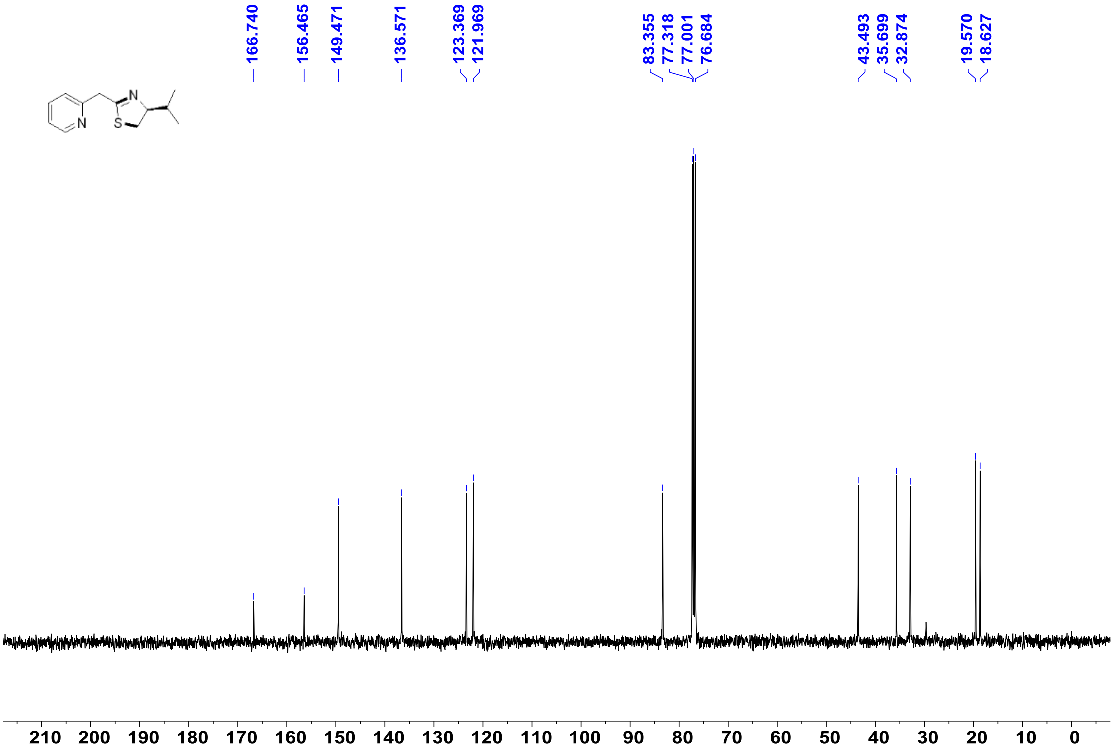
(*S*)-4-Isopropyl-2-(pyridin-2-ylmethyl)-4,5-dihydrothiazole ((*S*)-4ri)

^{1}H MNR (400 MHz, $CDCl_3$)

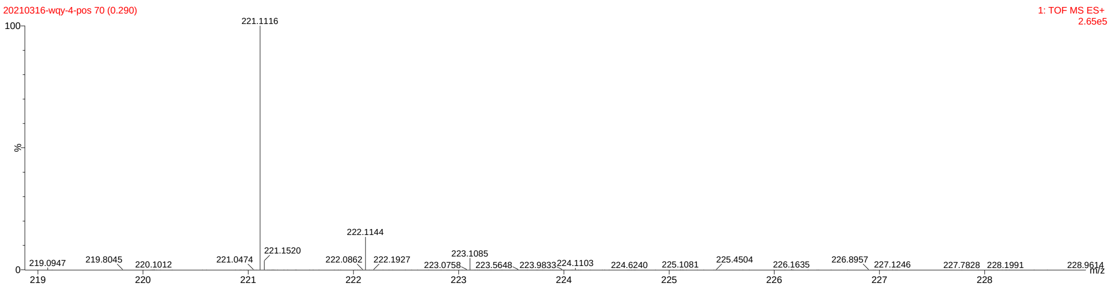




^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

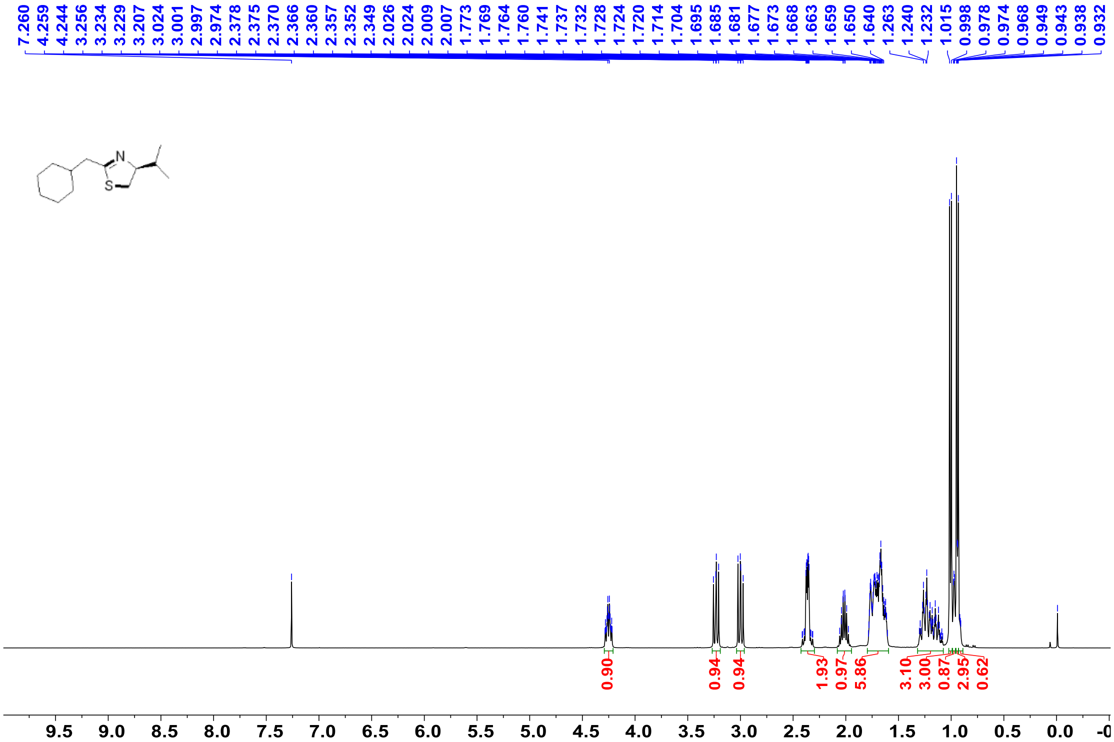


HRMS [M+H]$^{+}$

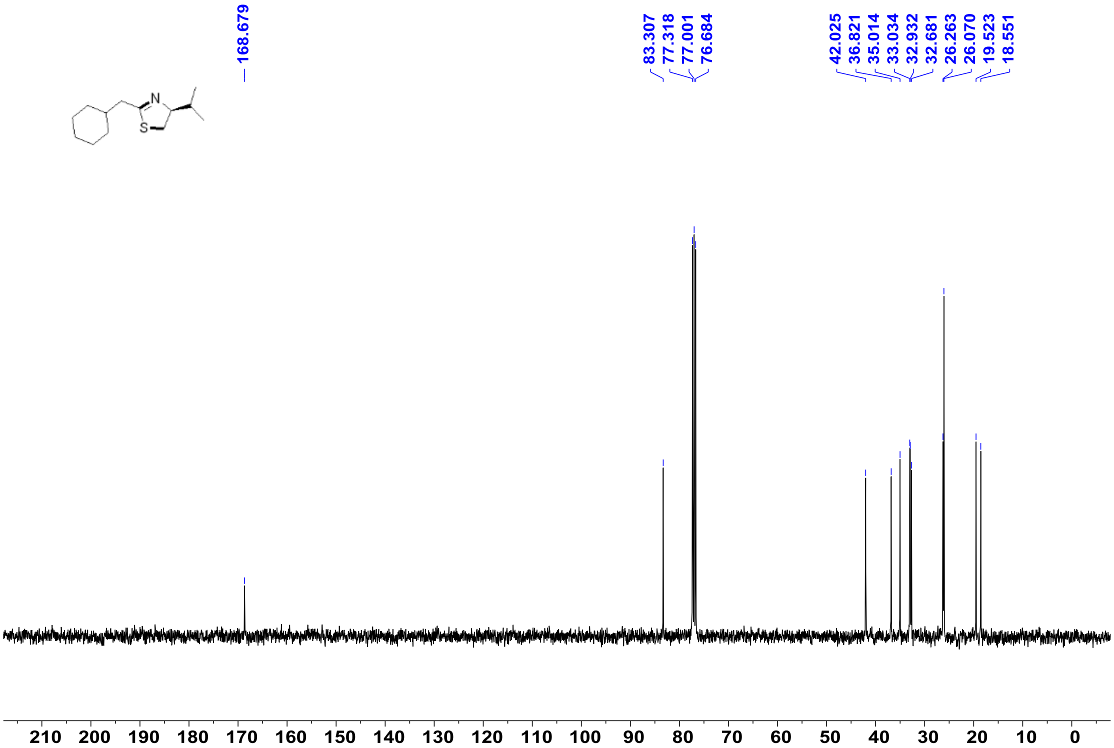


(*S*)-2-(Cyclohexylmethyl)-4-isopropyl-4,5-dihydrothiazole ((*S*)-4ui)

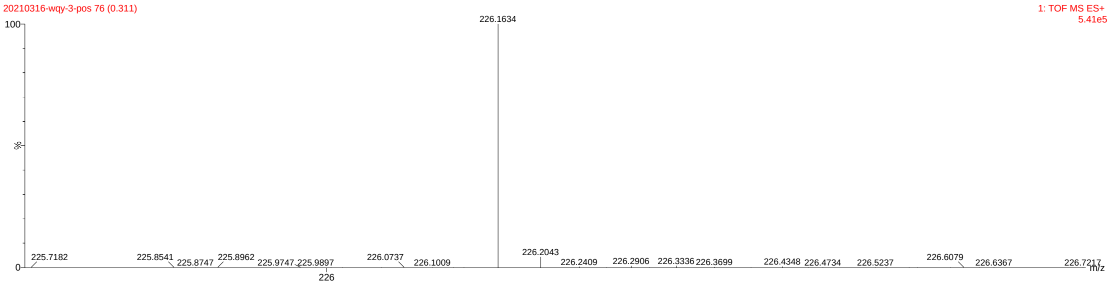
^{1}H MNR (400 MHz, CDCl$_3$)



^{13}C NMR{^{1}H} (101 MHz, CDCl$_3$)

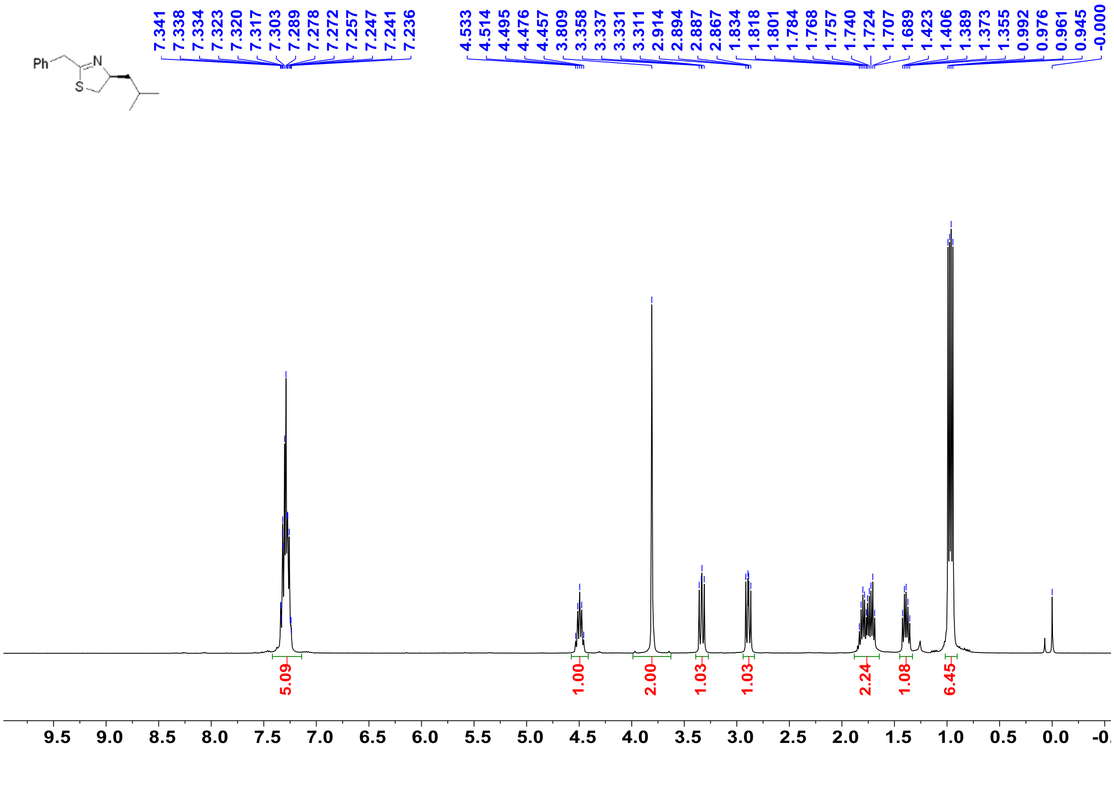


HRMS [M+H]$^+$

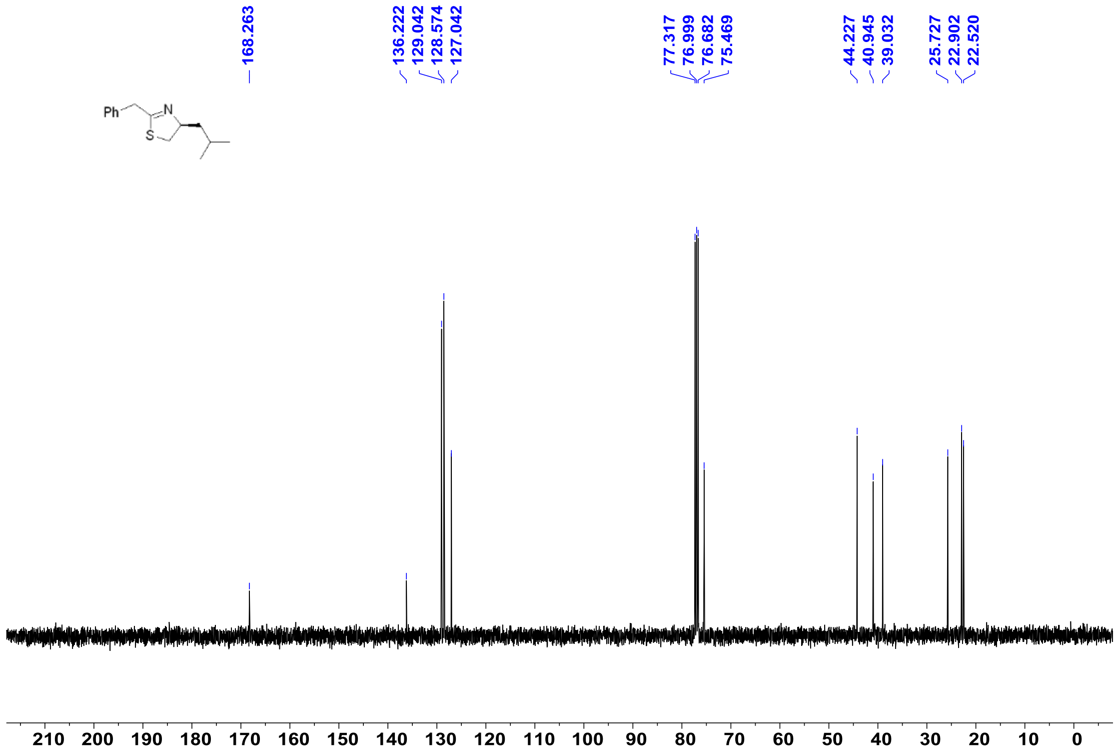


(*S*)-2-Benzyl-4-butyl-4,5-dihydrothiazole ((*S*)-4aj)

^{1}H MNR (400 MHz, $CDCl_3$)

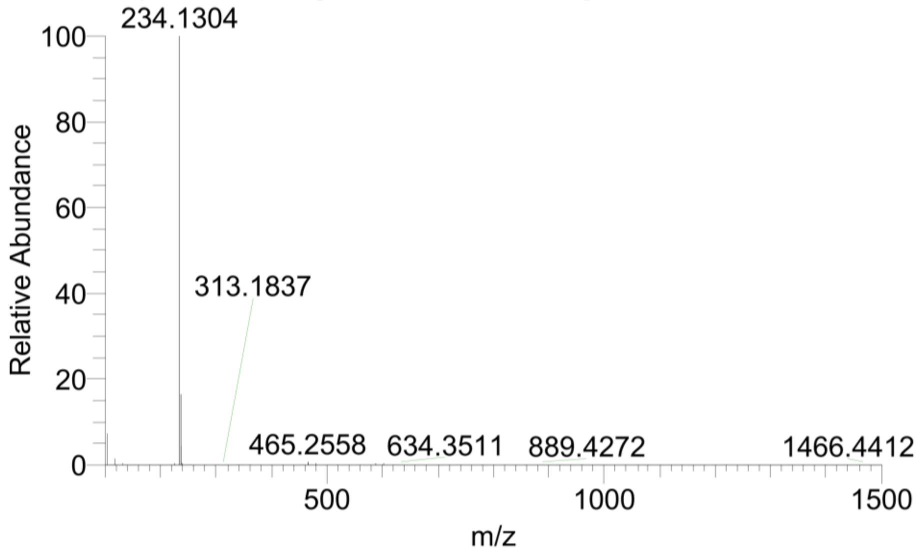


^{13}C NMR{^1H} (101 MHz, $CDCl_3$)



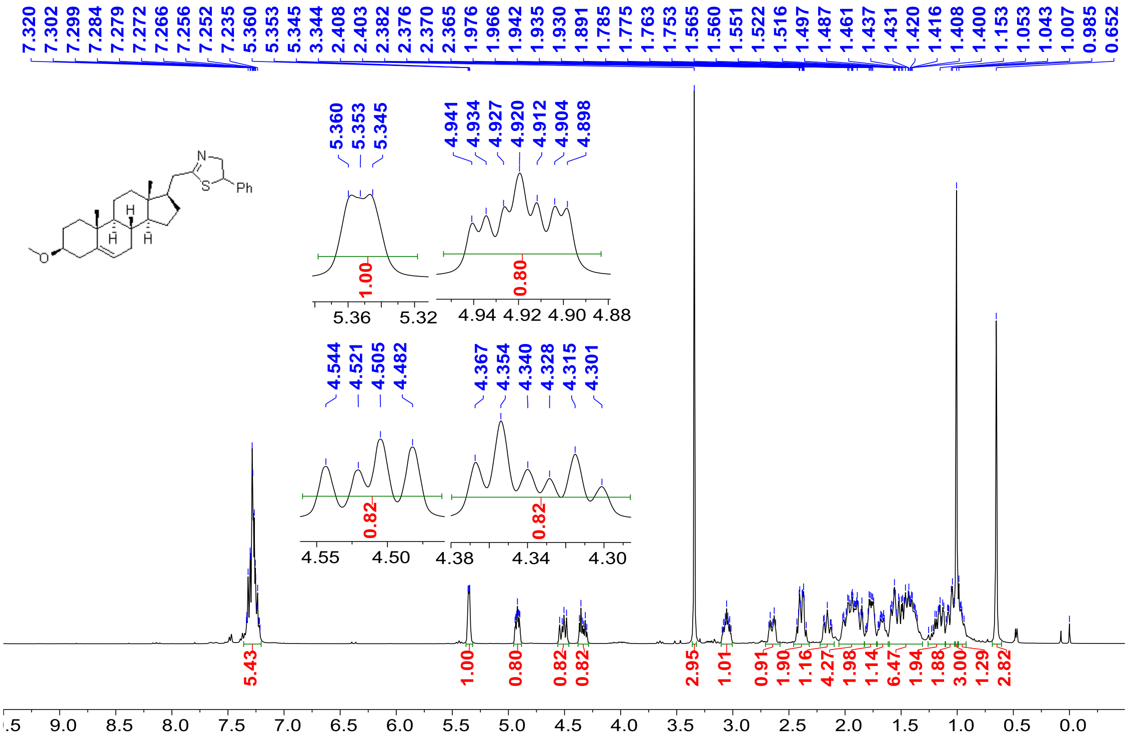
HRMS [M+H]$^+$

WQY-POS-2 #98 RT: 0.51 AV: 1 NL: 1.06E10
T: FTMS + p ESI Full ms [100.0000-1500.0000]

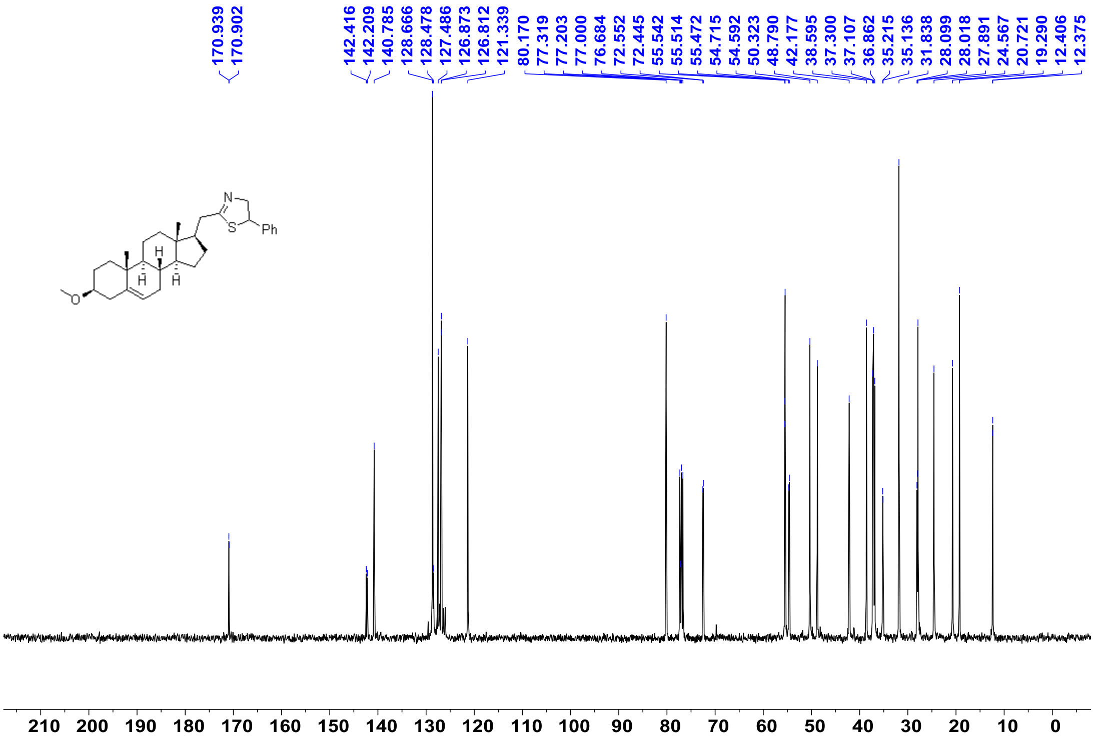


2-(((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-Methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)methyl)-5-phenyl-4,5-dihydrothiazole (3va)

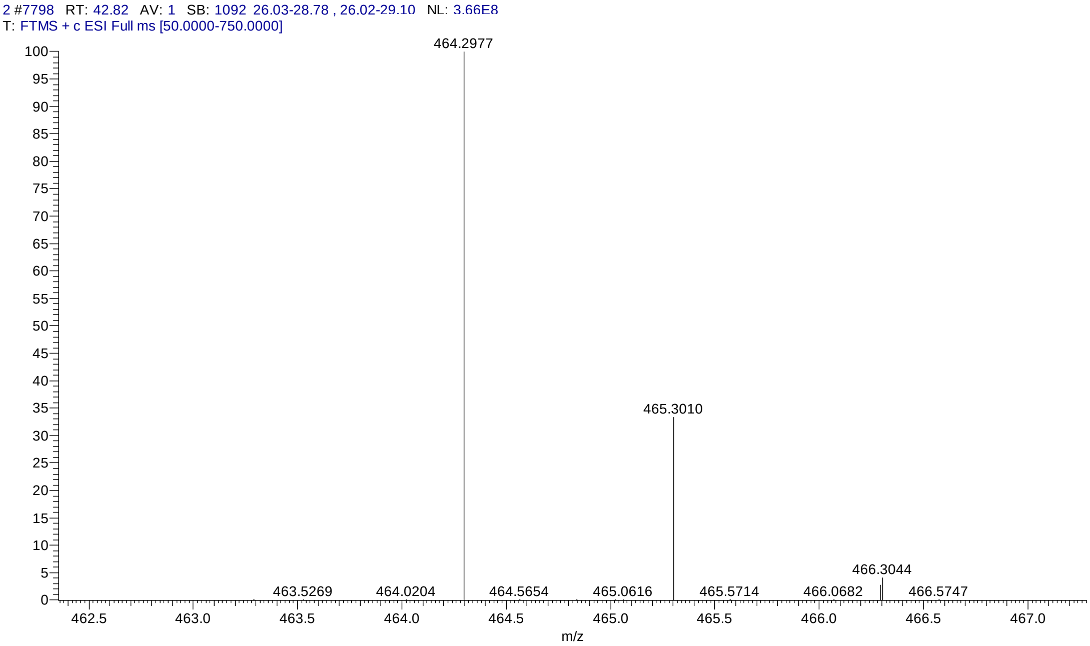
[1]H MNR (400 MHz, $CDCl_3$)



[13]C NMR{[1]H} (101 MHz, $CDCl_3$)

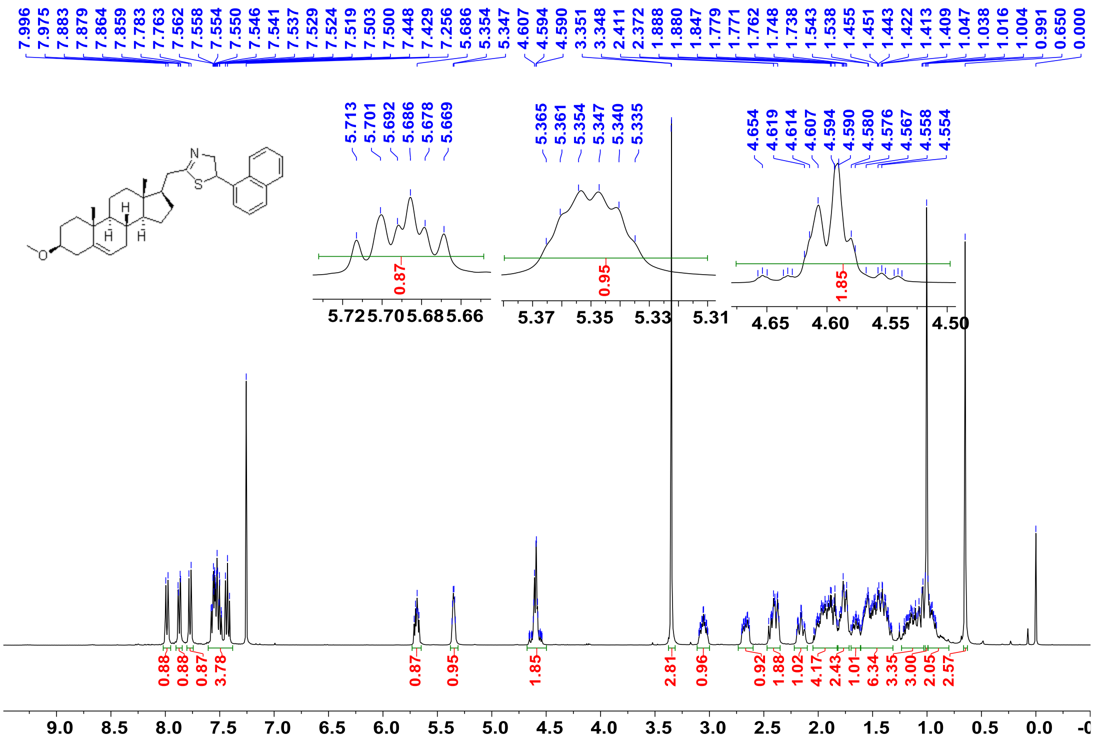


HRMS [M+H]⁺

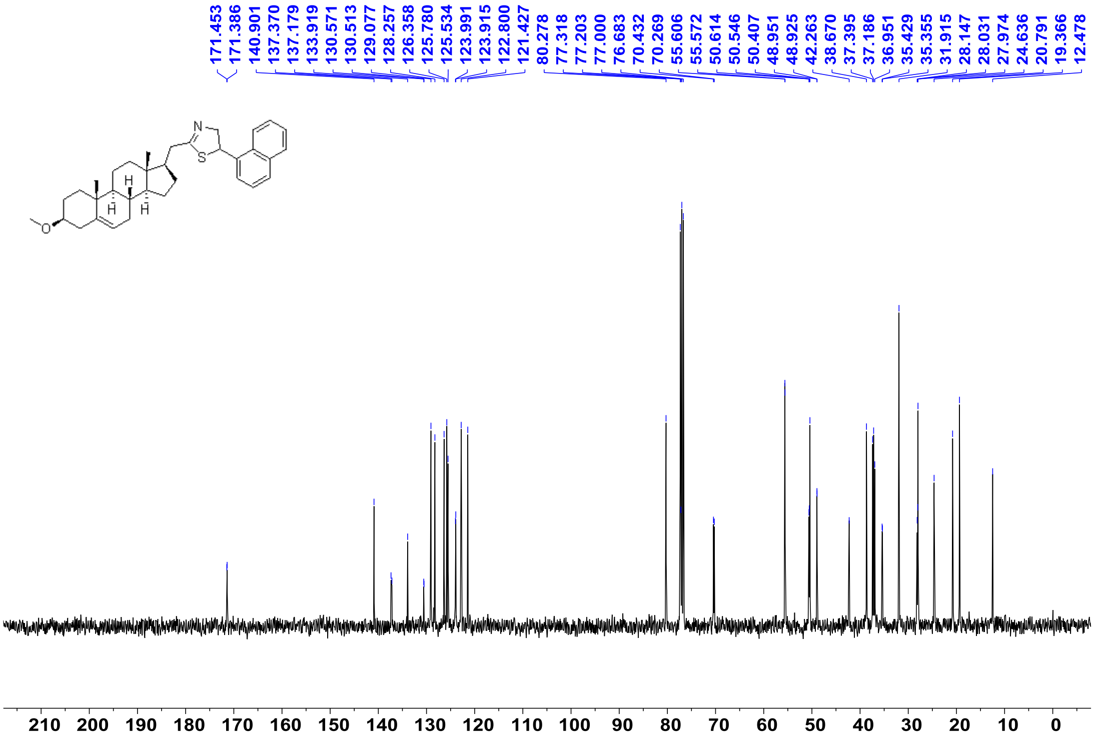


2-(((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-Methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)methyl)-5-(naphthalen-1-yl)-4,5-dihydrothiazole (3vf)

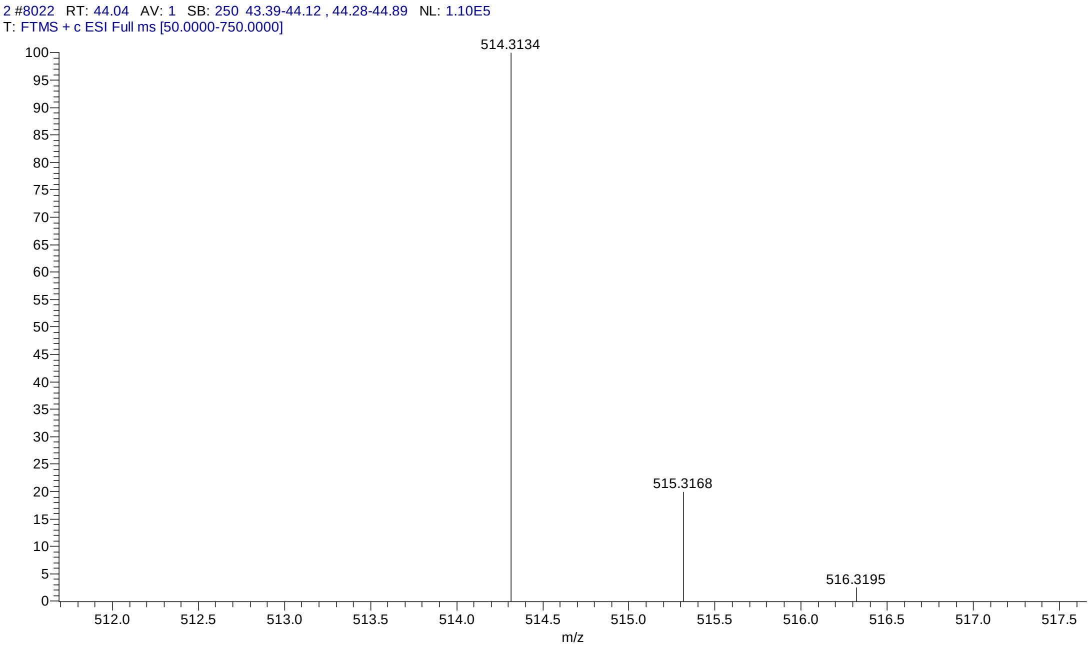
¹H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, CDCl$_3$)

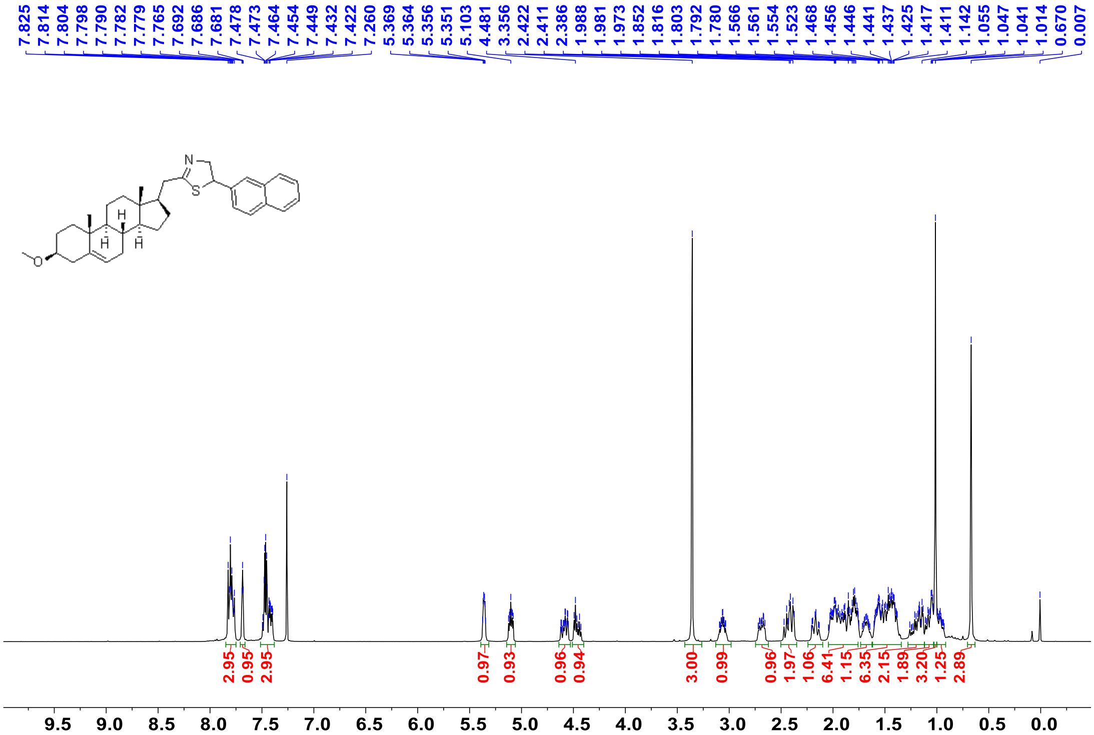


HRMS [M+H]+

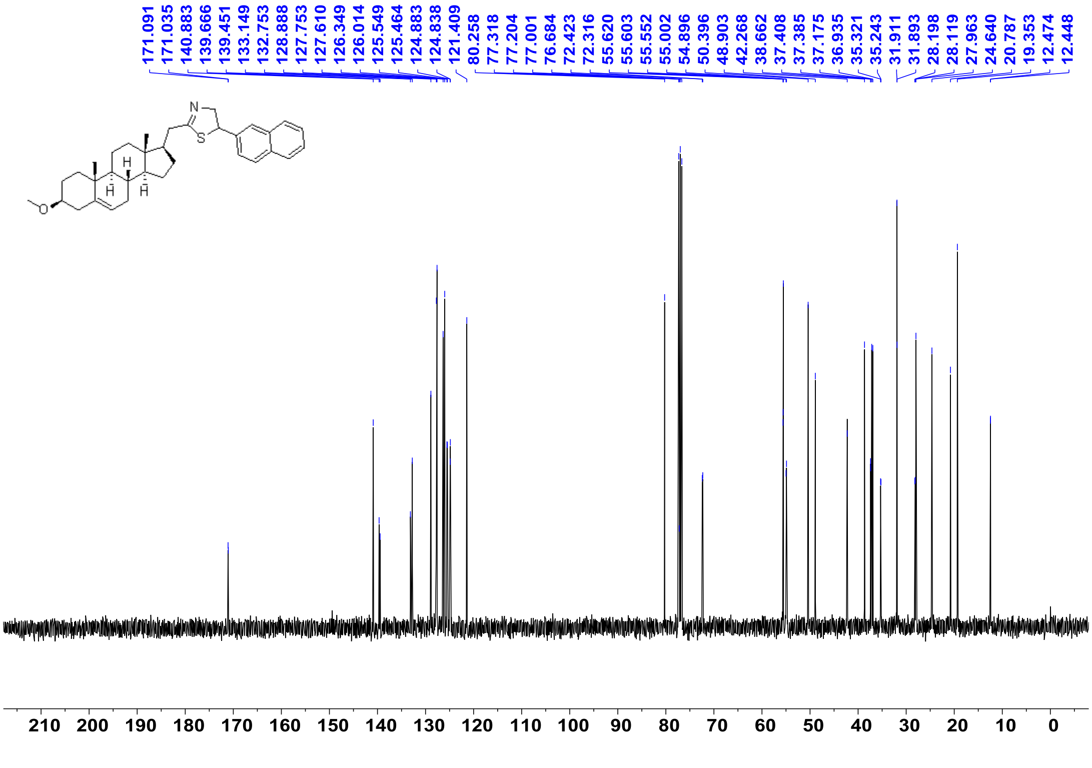


2-(((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-Methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)methyl)-5-(naphthalen-2-yl)-4,5-dihydrothiazole (3vg)

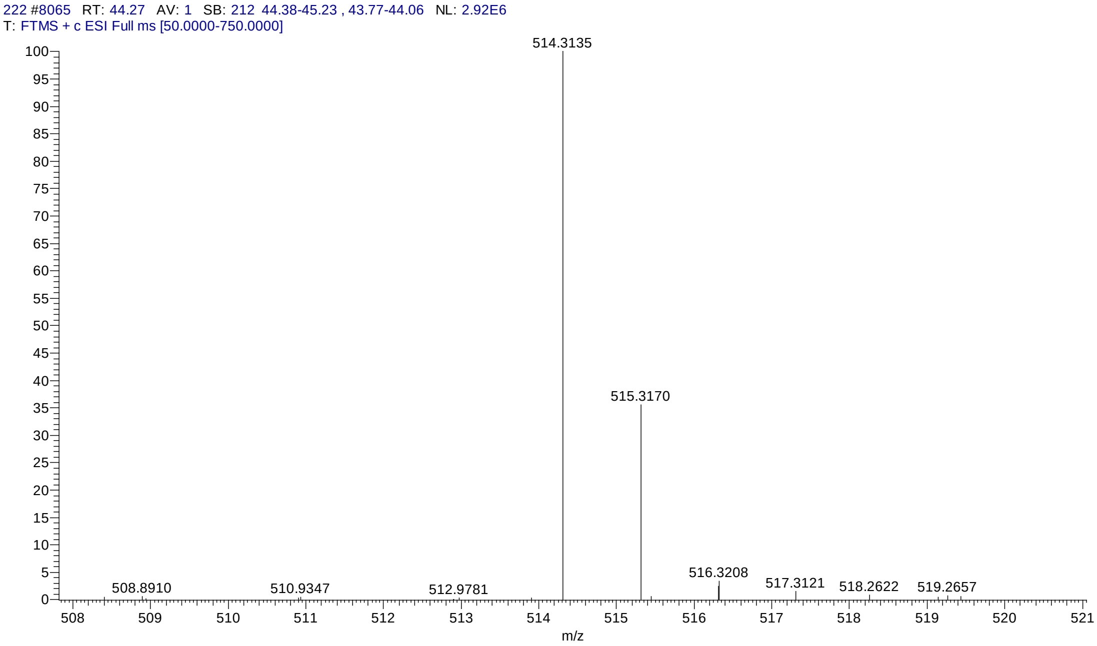
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

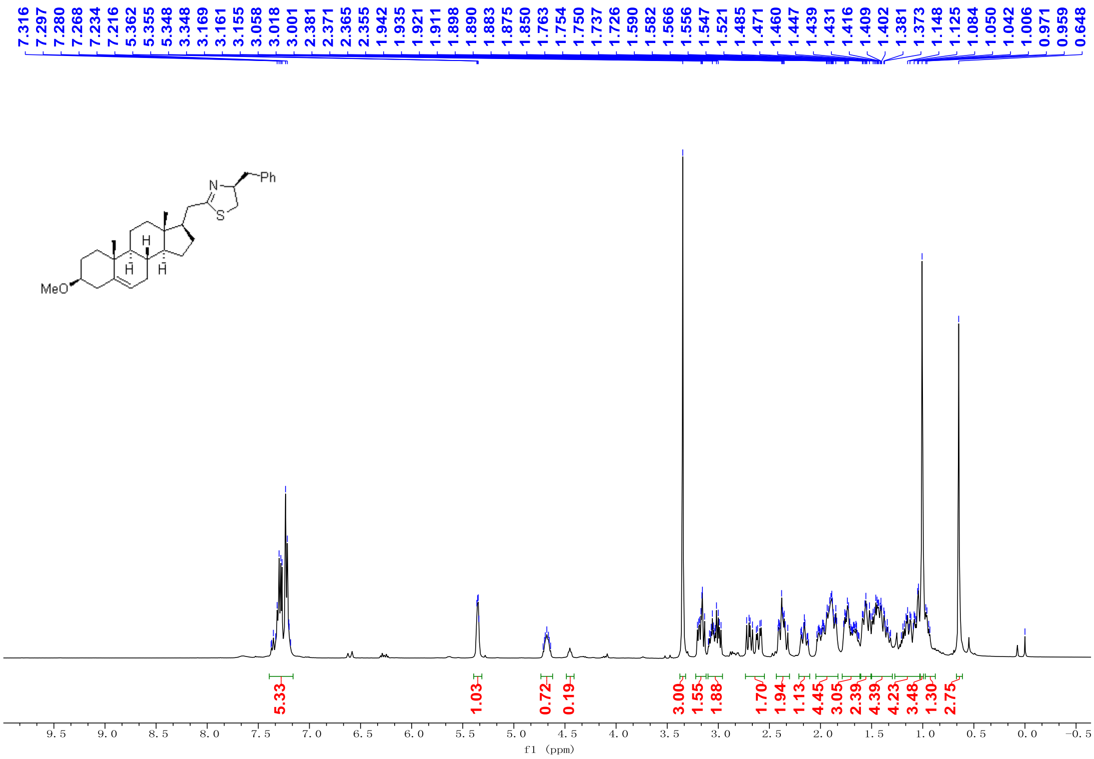


HRMS [M+H]+

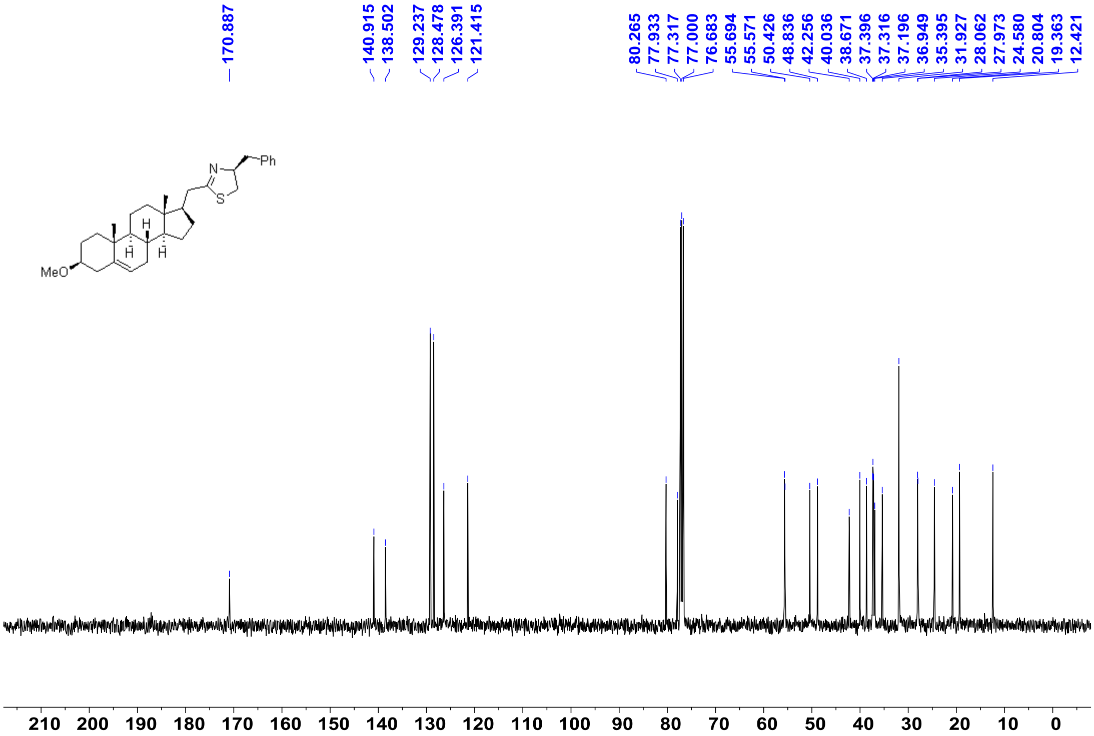


(4*S*)-4-Benzyl-2-(((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[a]phenanthren-17-yl)methyl)-4,5-dihydrothiazole ((*S*)-4vh)

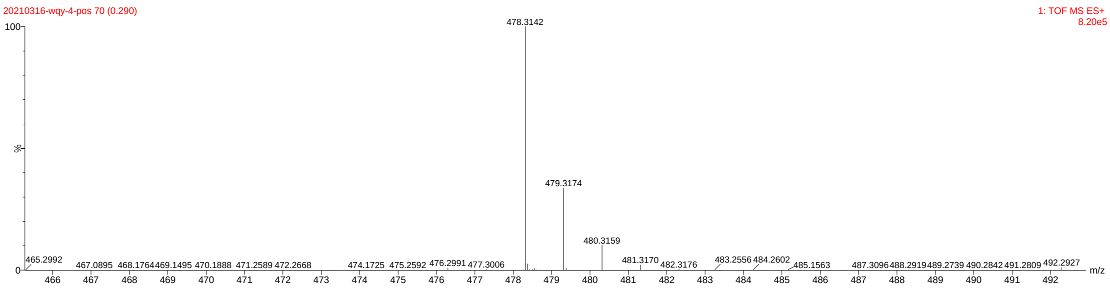
[1]H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)



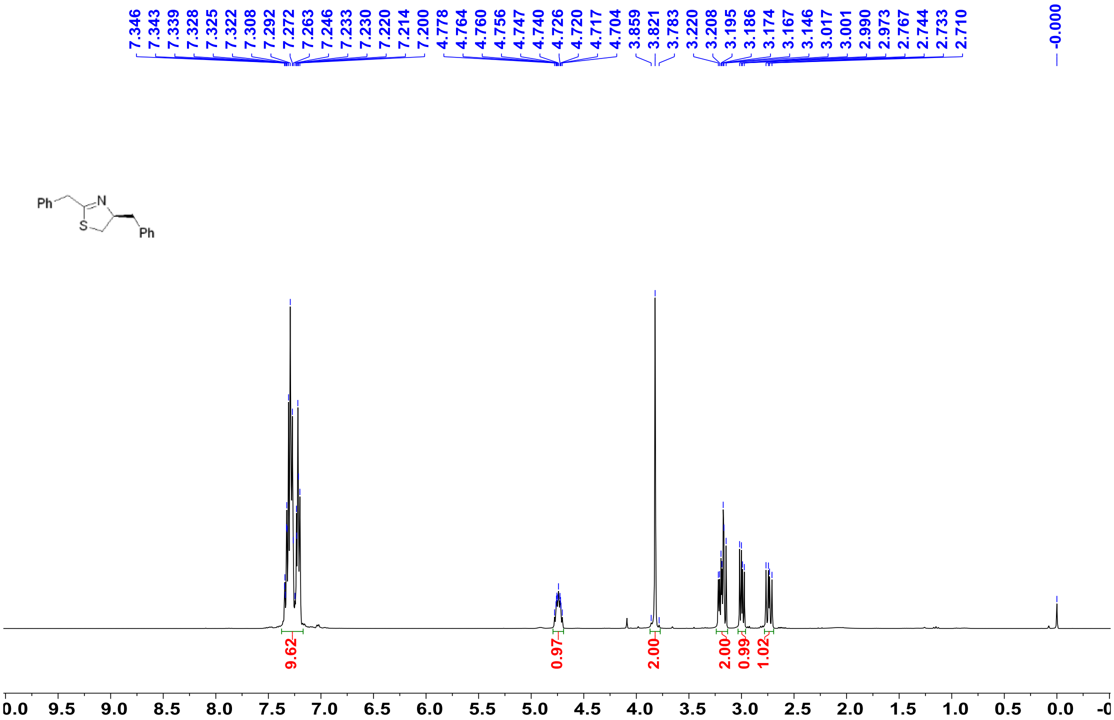
HRMS [M+H]+



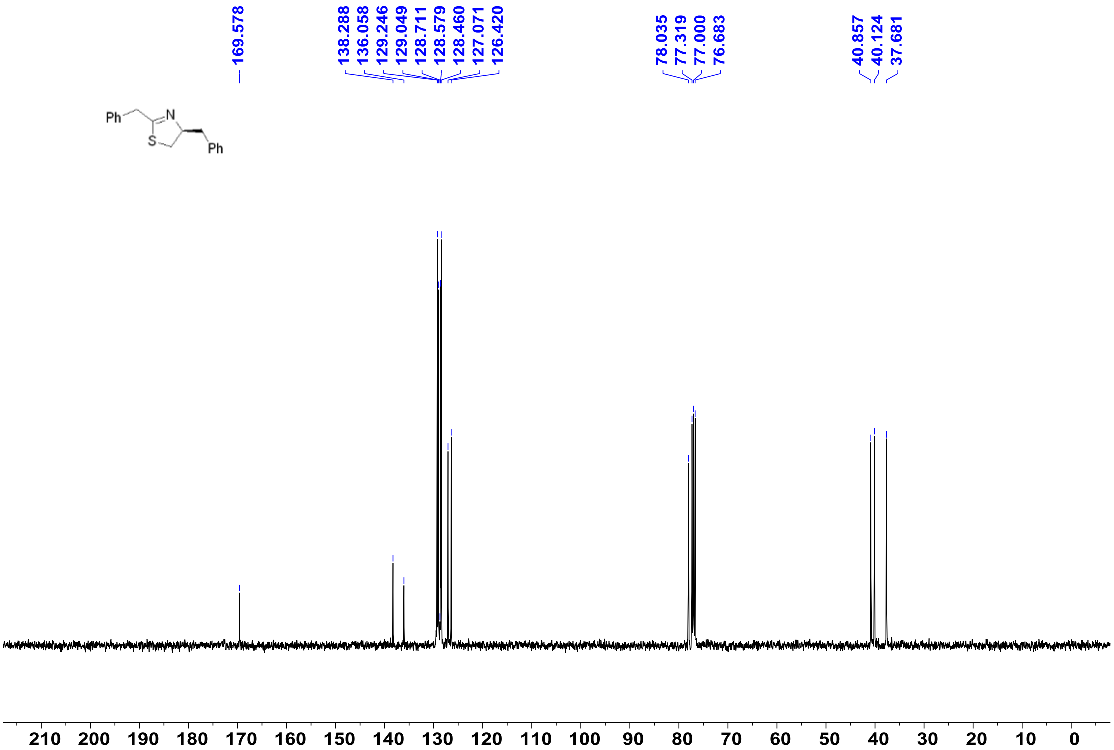
Copies of NMR spectra in mechanistic studies

(*S*)-2,4-Dibenzyl-4,5-dihydrothiazole ((*S*)-4ah)

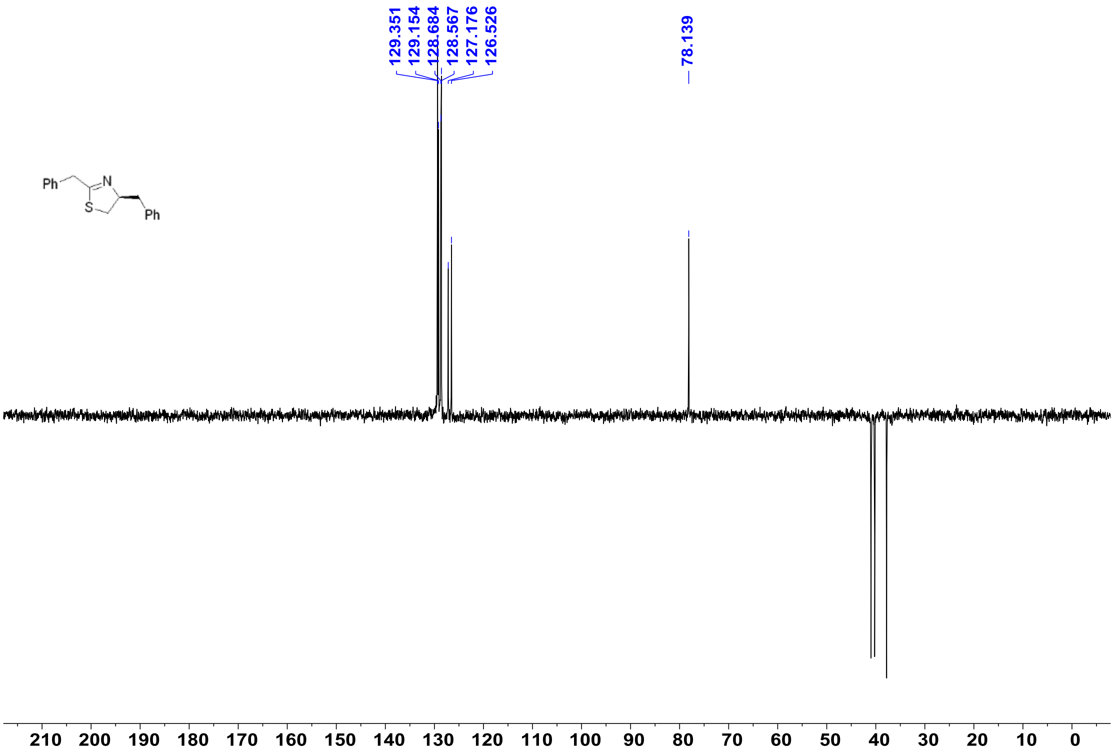
^{1}H MNR (400 MHz, $CDCl_3$)



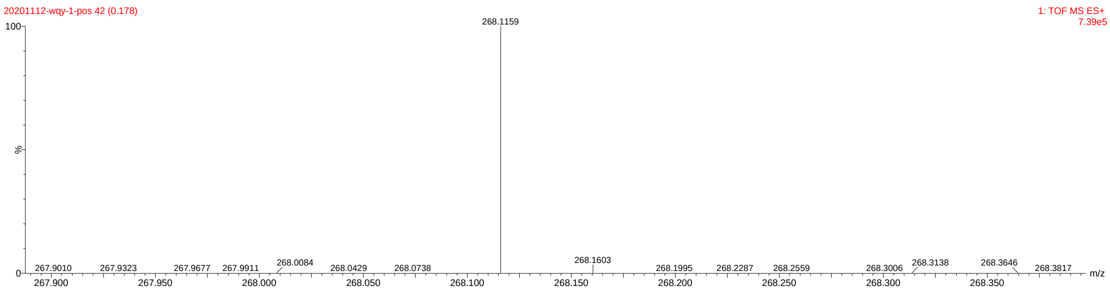
^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)



DEPT 135 ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

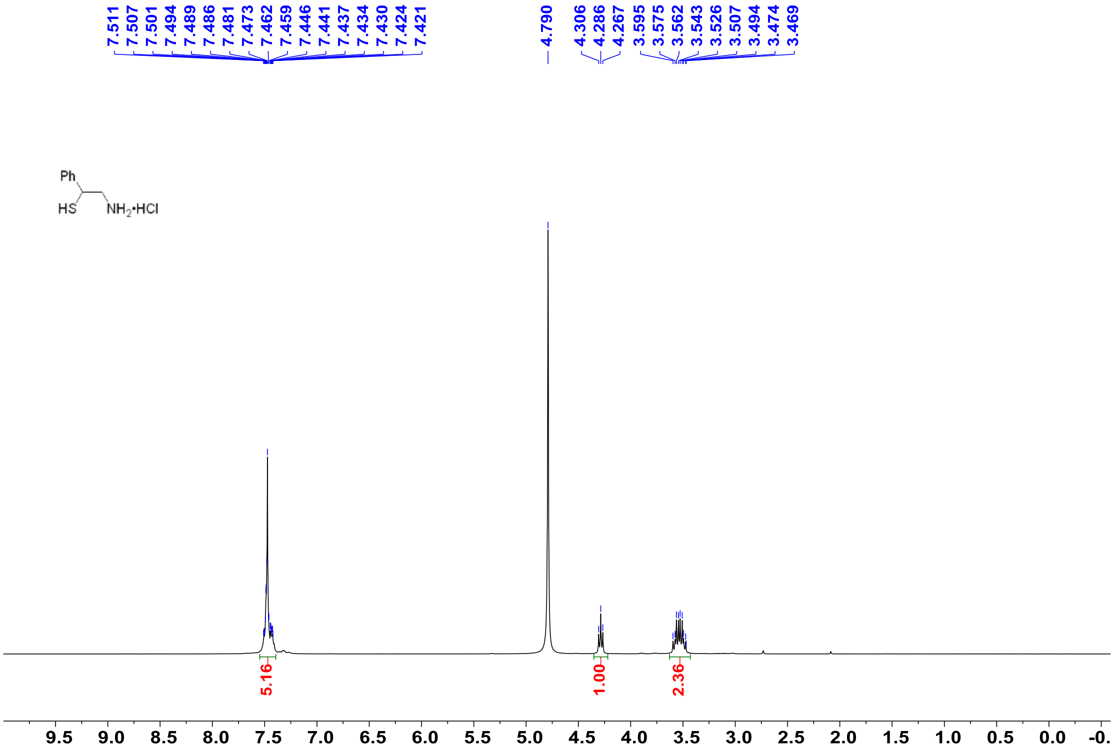


HRMS [M+H]+

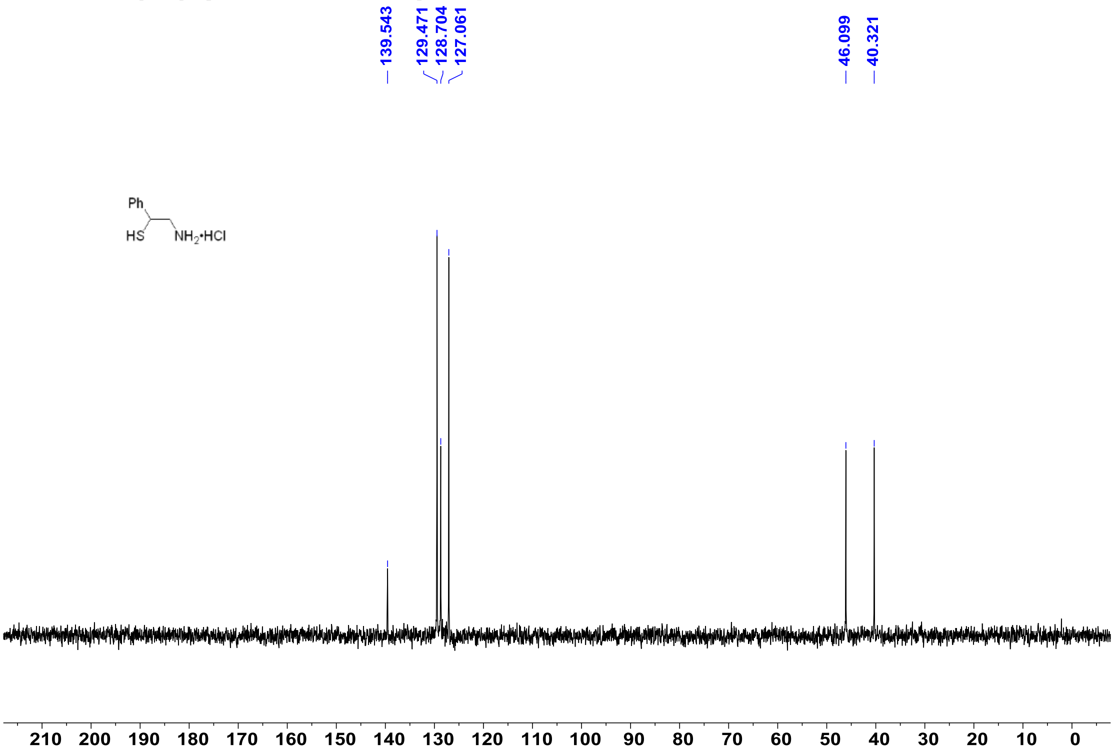


2-Amino-1-phenylethane-1-thiol hydrochloride (7·HCl)

^{1}H MNR (400 MHz, D_2O)

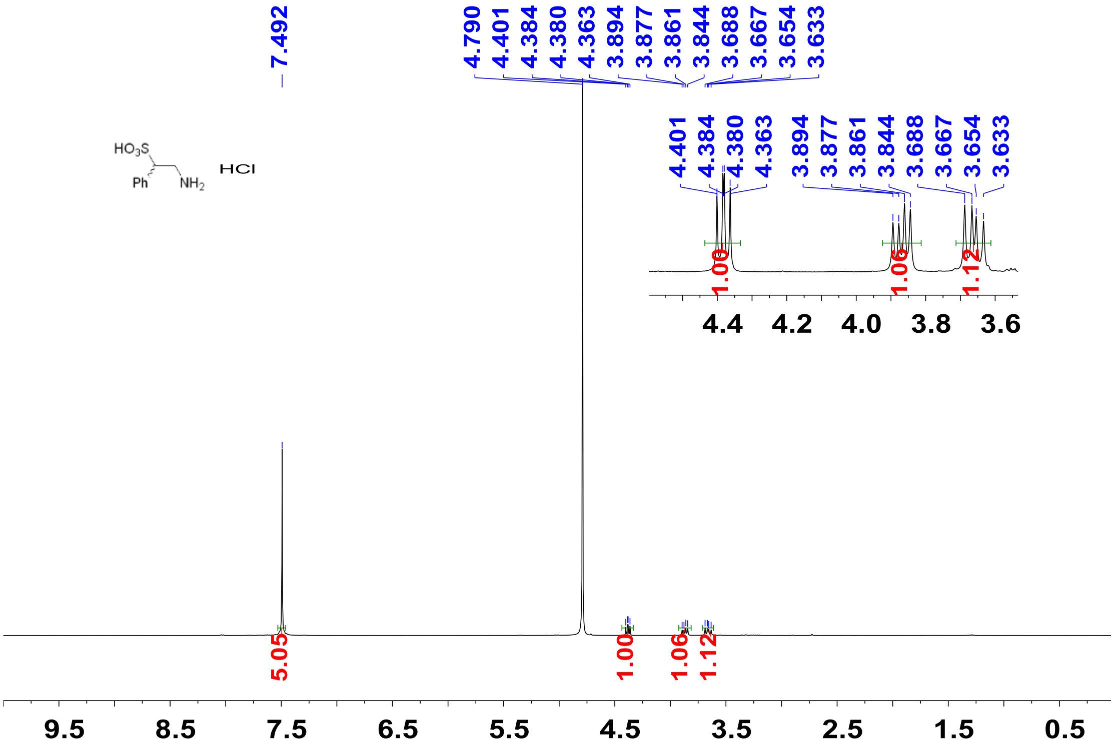


^{13}C NMR{^{1}H} (101 MHz, D_2O)

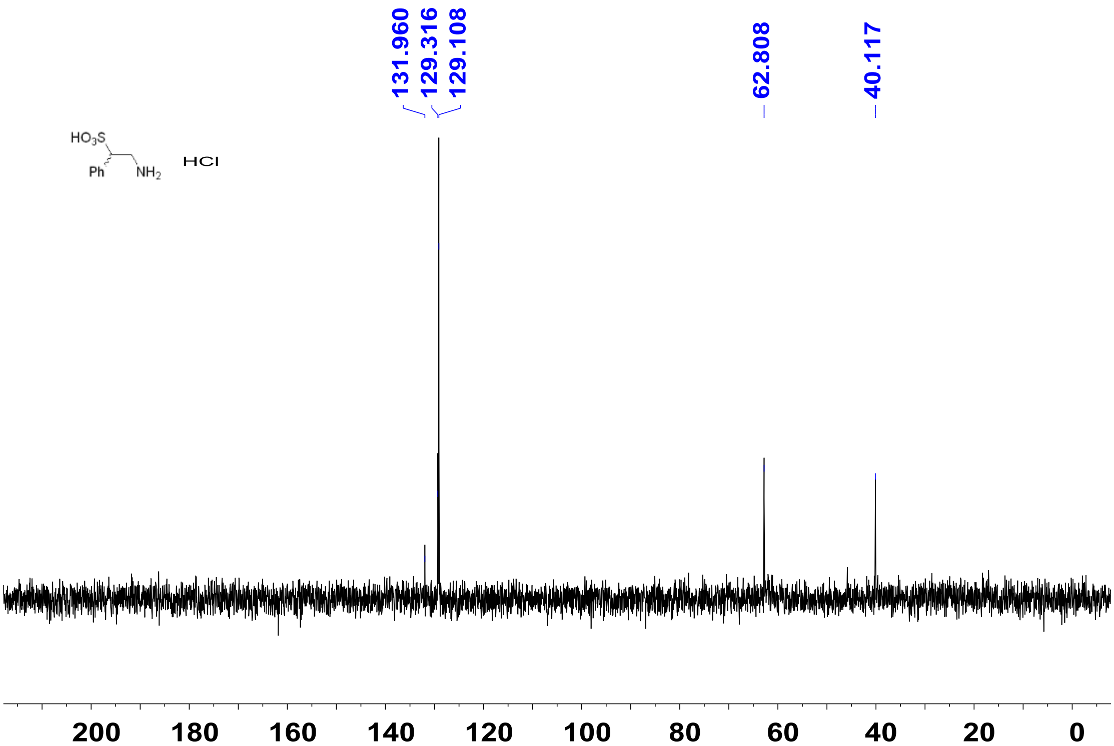


2-Amino-1-phenylethane-1-sulfonic acid hydrochloride (8·HCl)

^{1}H MNR (400 MHz, D_2O)

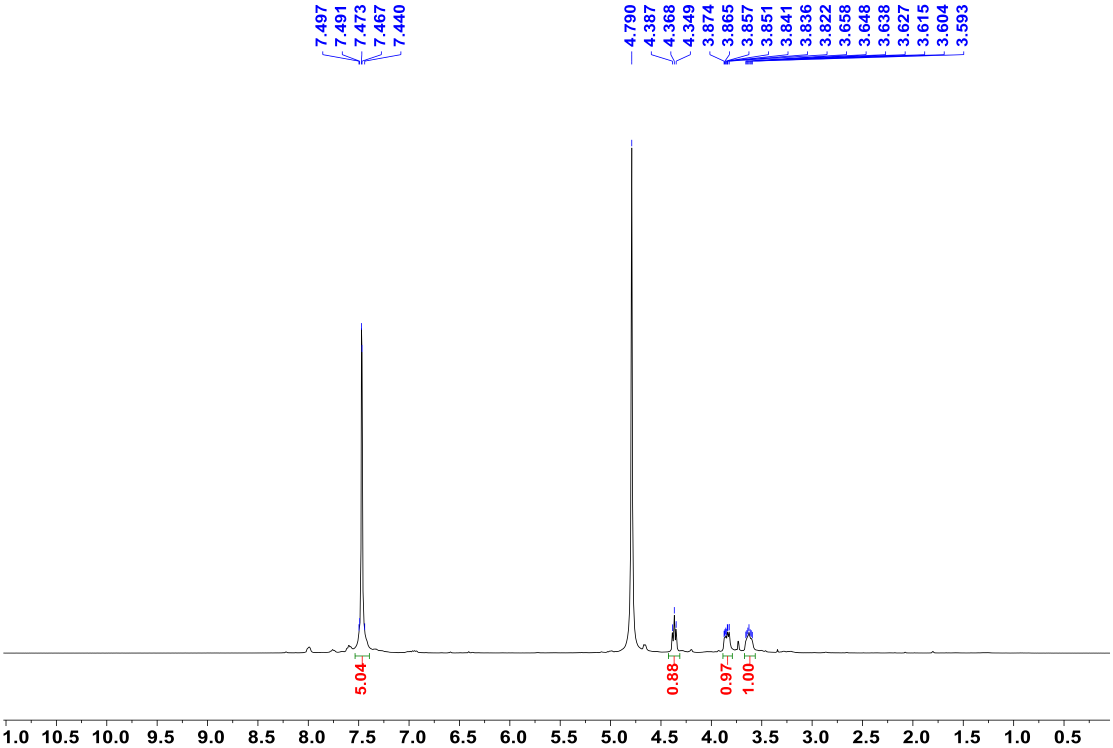


^{13}C NMR{^{1}H} (101 MHz, D_2O)

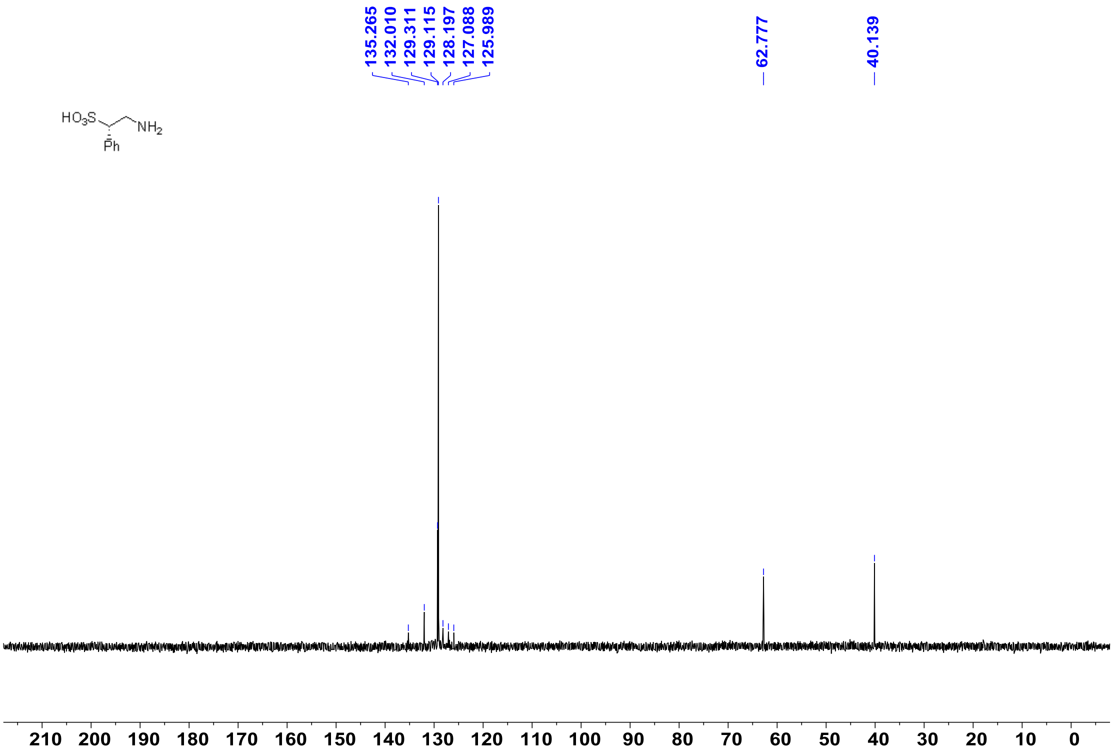


2-Amino-1-phenylethane-1-sulfonic acid (8)

^{1}H MNR (400 MHz, D_2O)

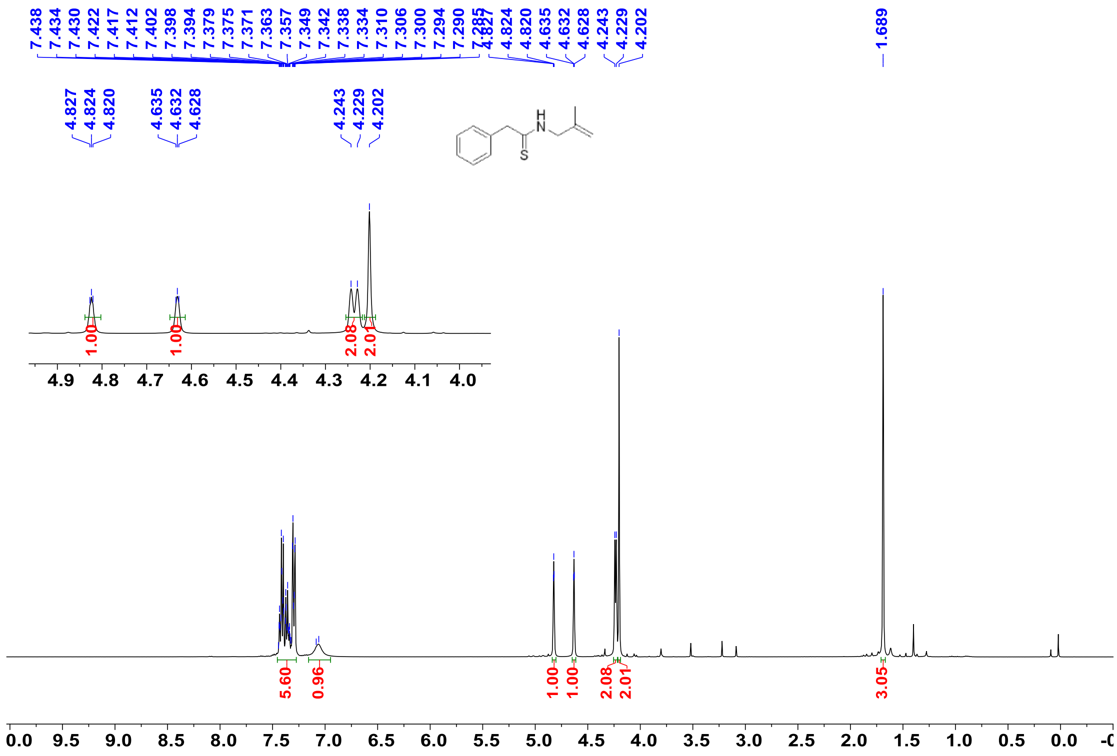


^{13}C NMR{^{1}H} (101 MHz, D_2O)

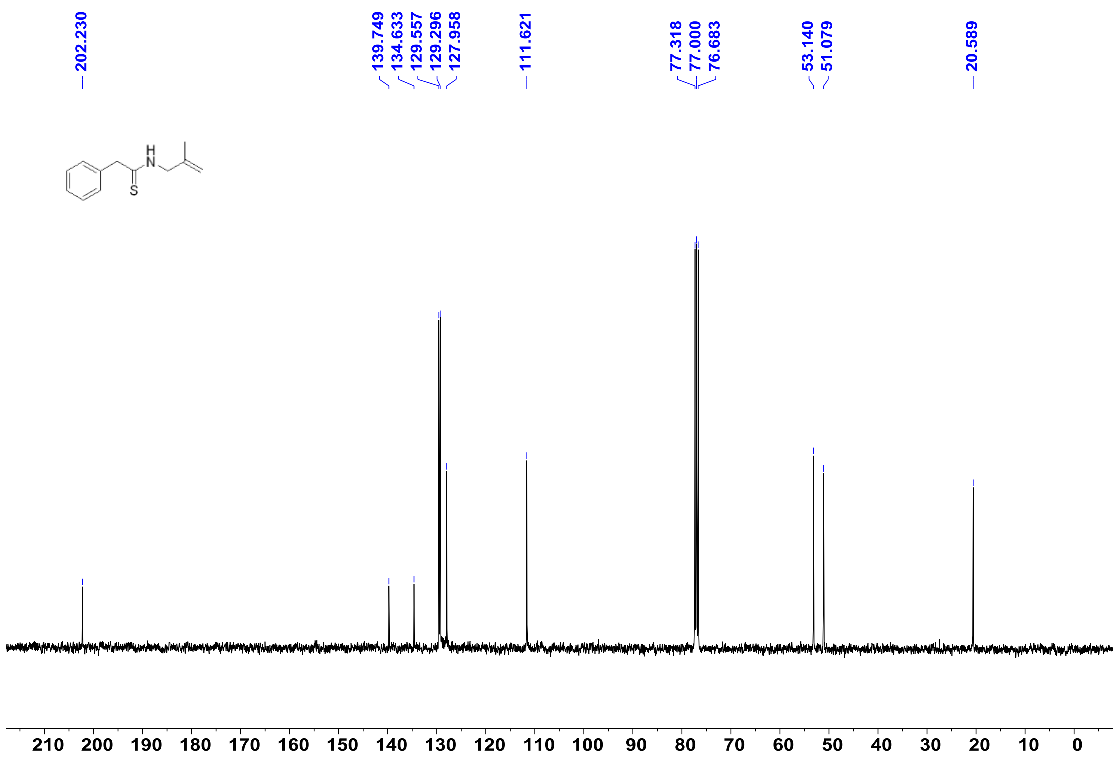


N-(2-Methylallyl)-2-phenylethanethioamide (9am)

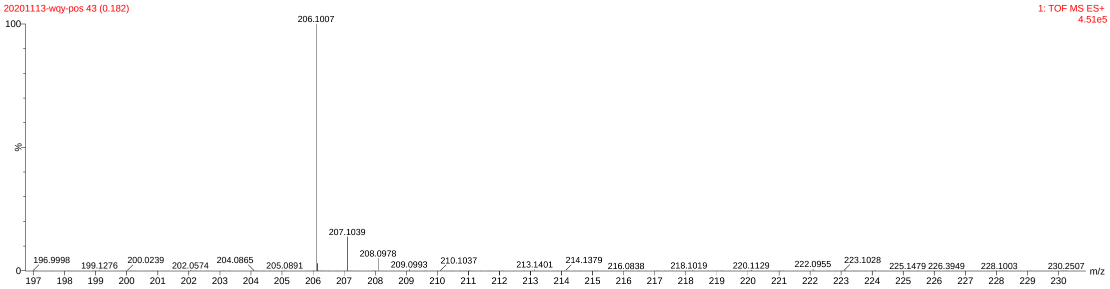
^{1}H NMR (400 MHz, $CDCl_3$):



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$):

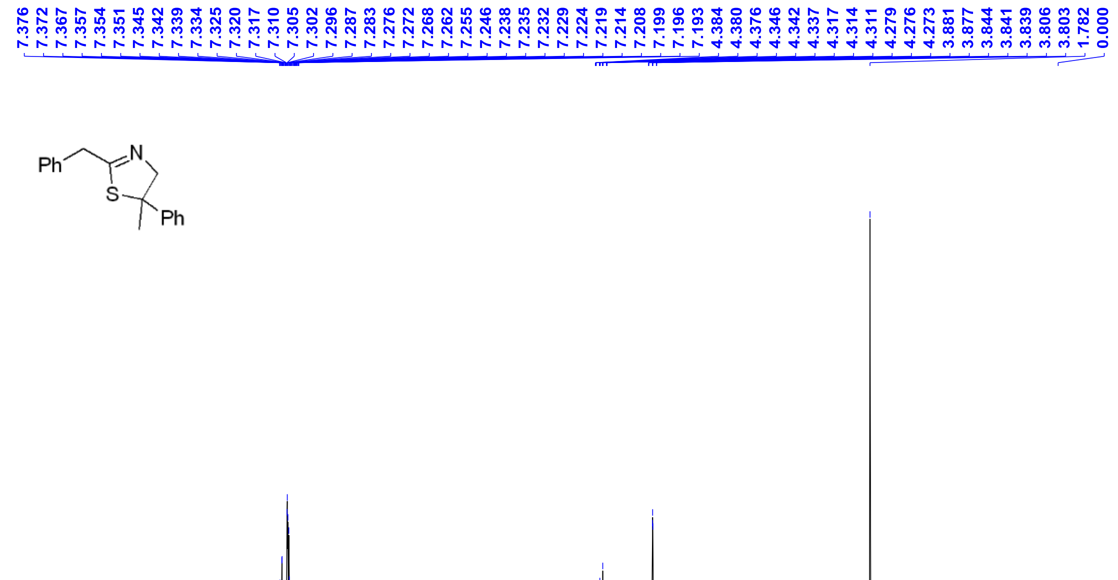


HRMS [M+H]$^+$

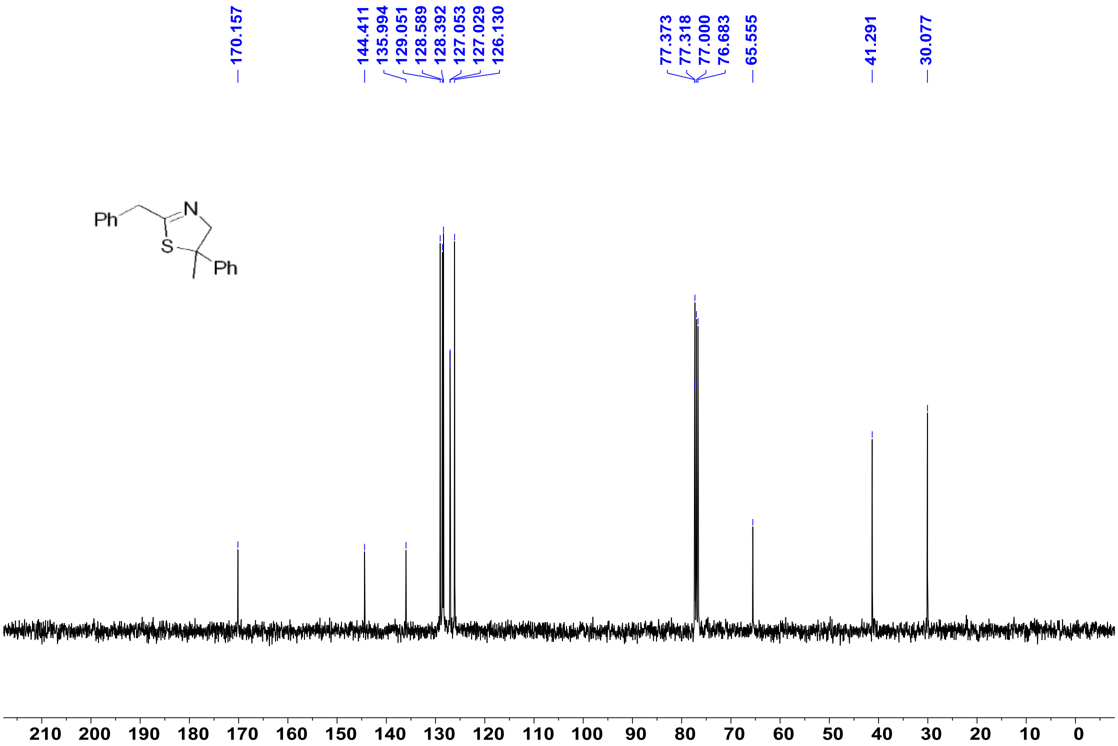


2-Benzyl-5-methyl-5-phenyl-4,5-dihydrothiazole (3an)

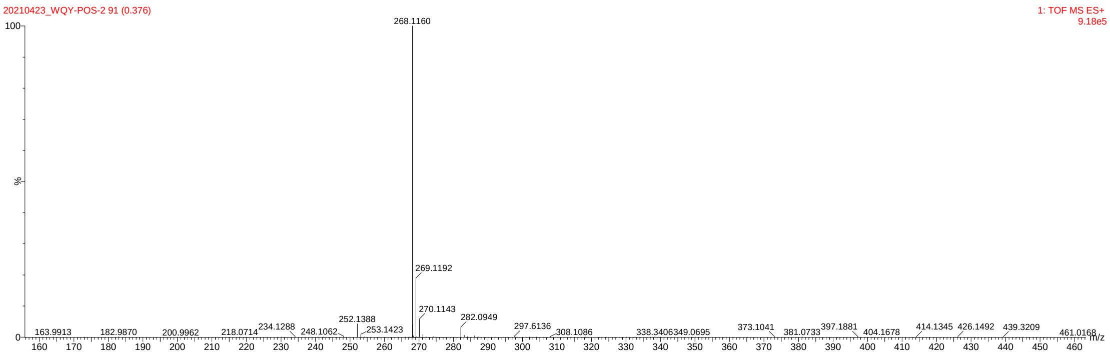
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^1H} (101 MHz, $CDCl_3$)

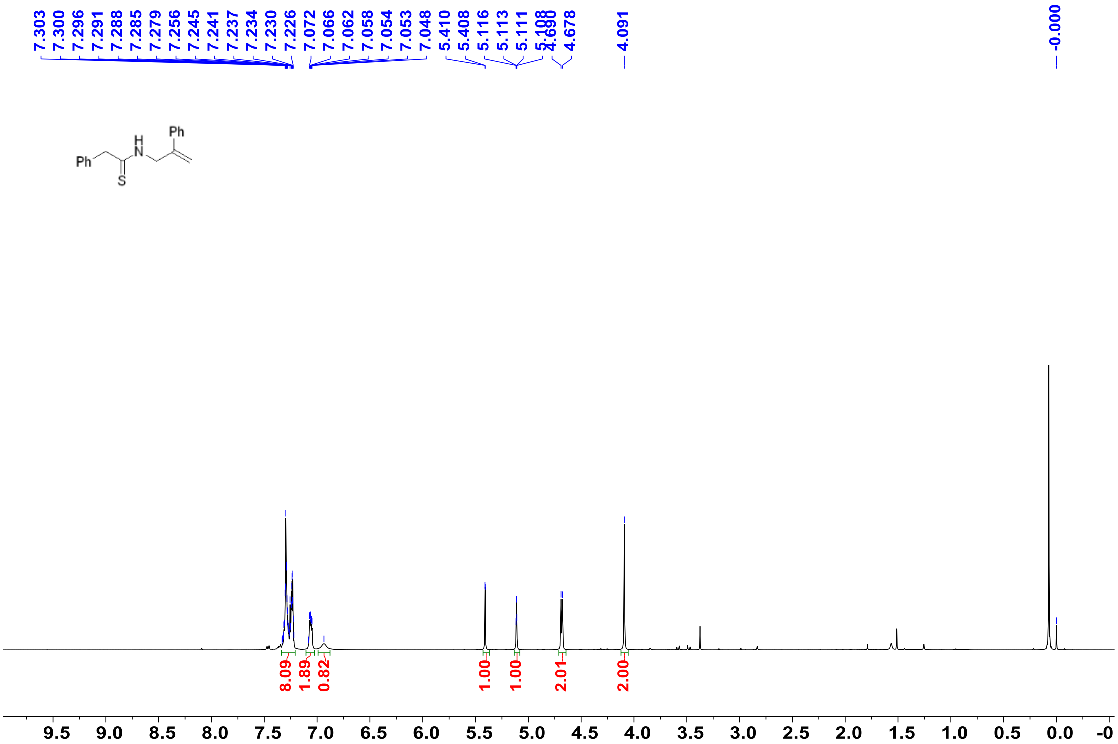


HRMS [M+H]$^+$

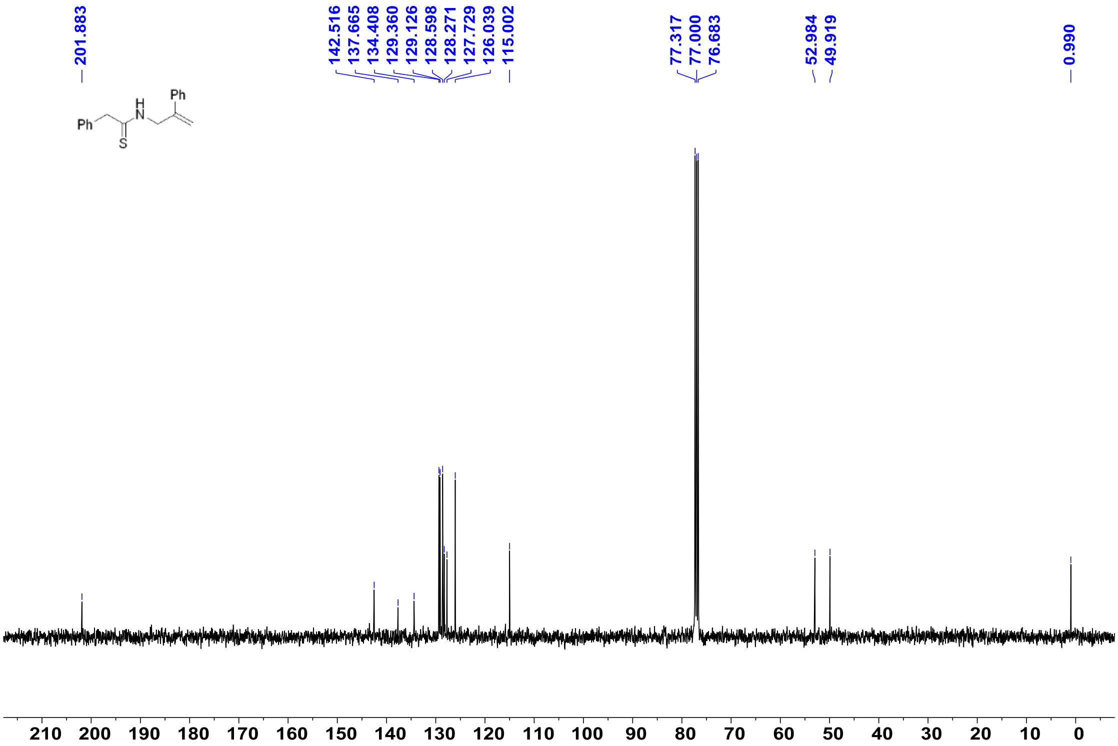


2-Phenyl-*N*-(2-phenylallyl)ethanethioamide (9an)

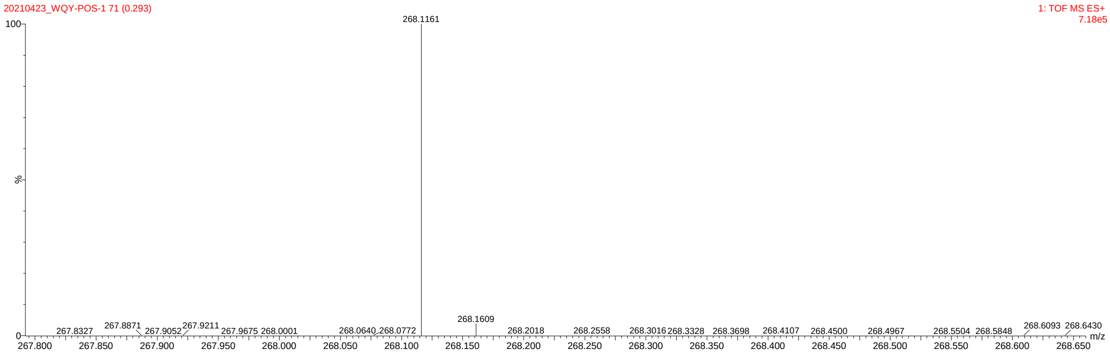
^{1}H MNR (400 MHz, $CDCl_3$)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

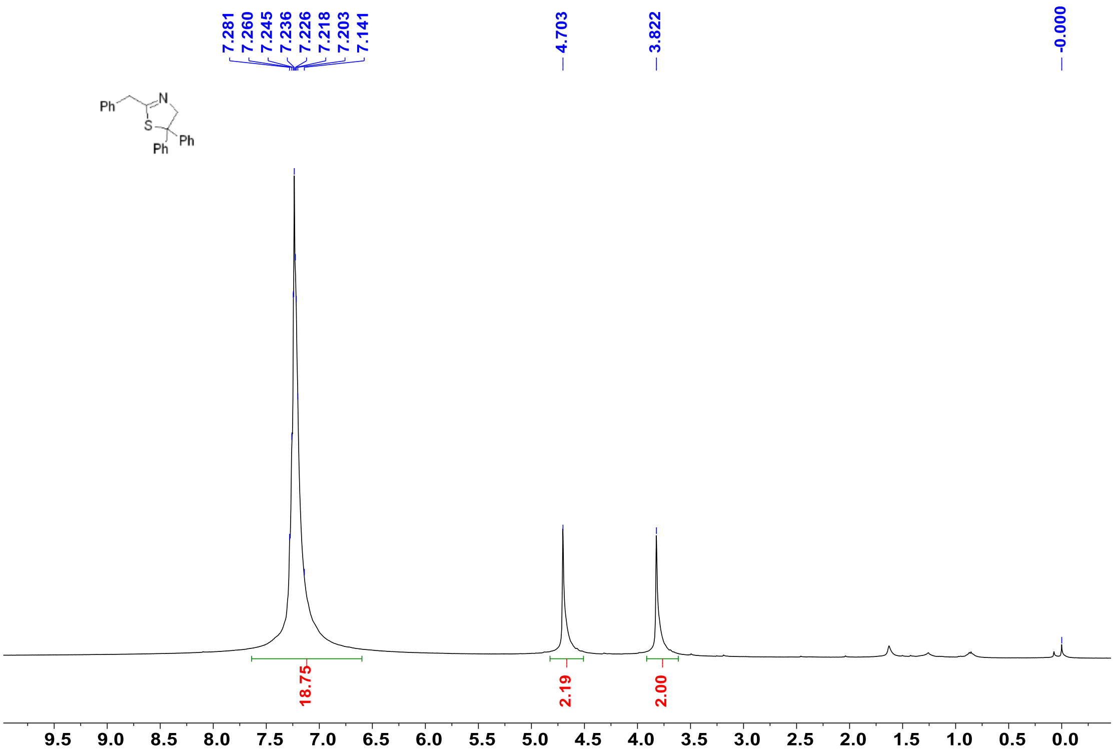


HRMS [M+H]+

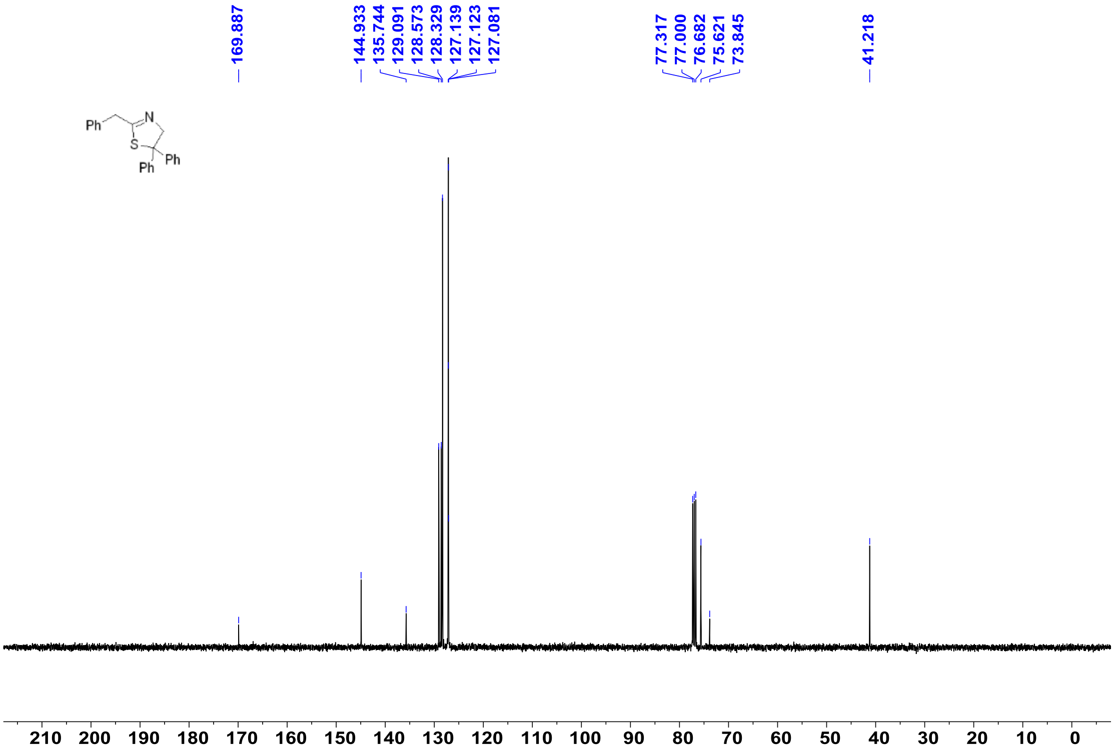


2-Benzyl-5,5-diphenyl-4,5-dihydrothiazole (3ao)

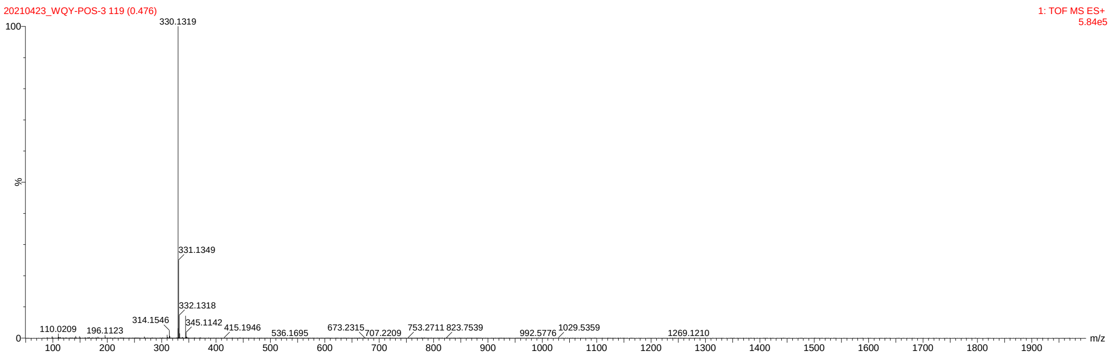
1H MNR (400 MHz, CDCl3)



^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$)

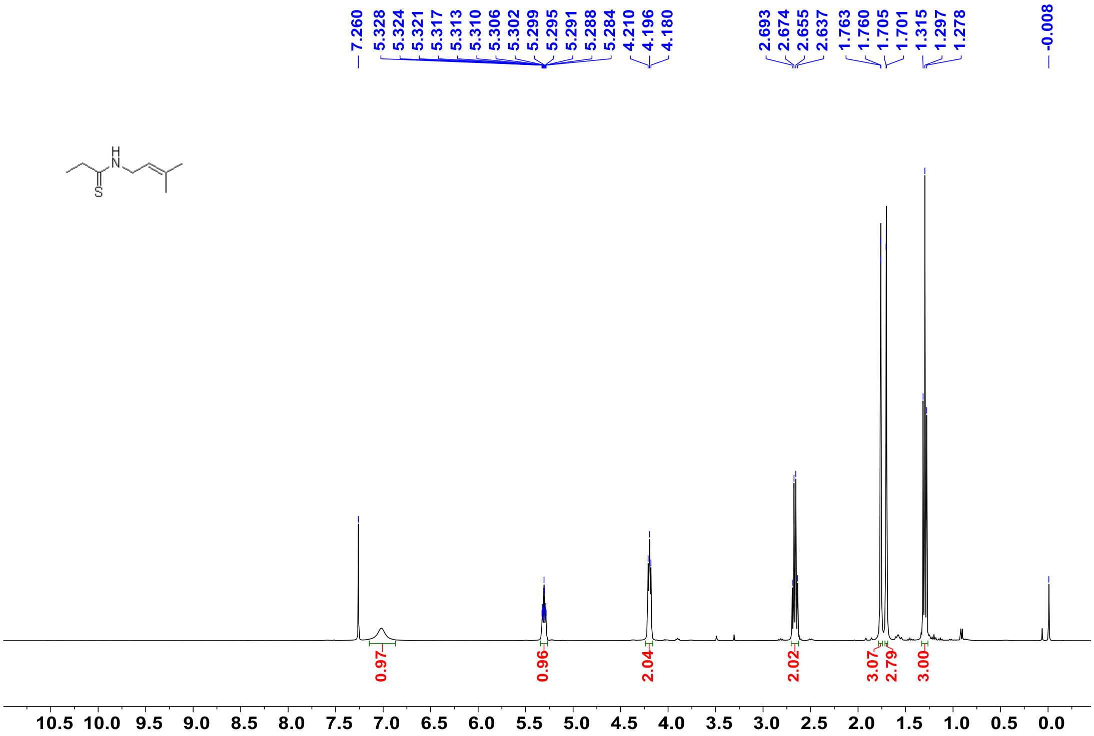


HRMS [M+H]+

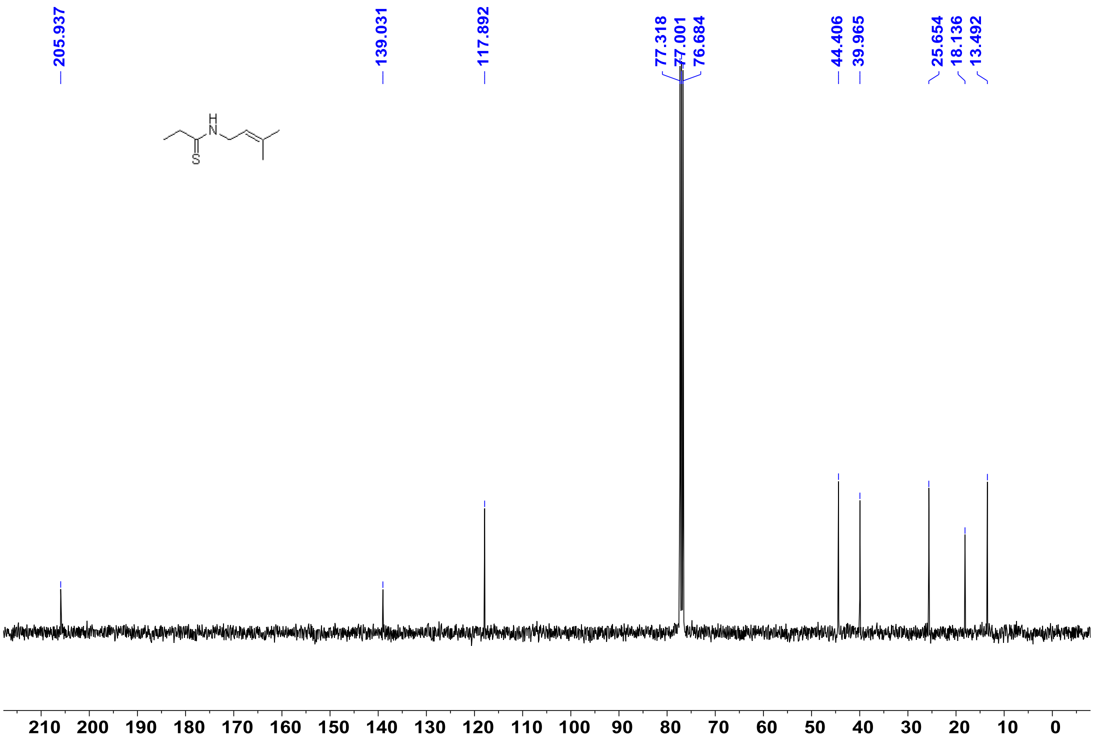


N-(3-Methylbut-2-en-1-yl)propanethioamide (9si)

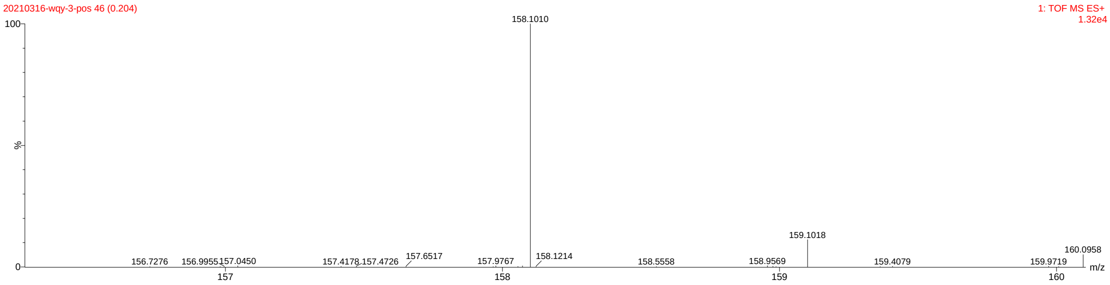
[1]H MNR (400 MHz, $CDCl_3$)



[13]C NMR{[1]H} (101 MHz, $CDCl_3$)



HRMS [M+H]$^+$



20210316-wqy-3-pos 46 (0.204)
1: TOF MS ES+
1.32e4
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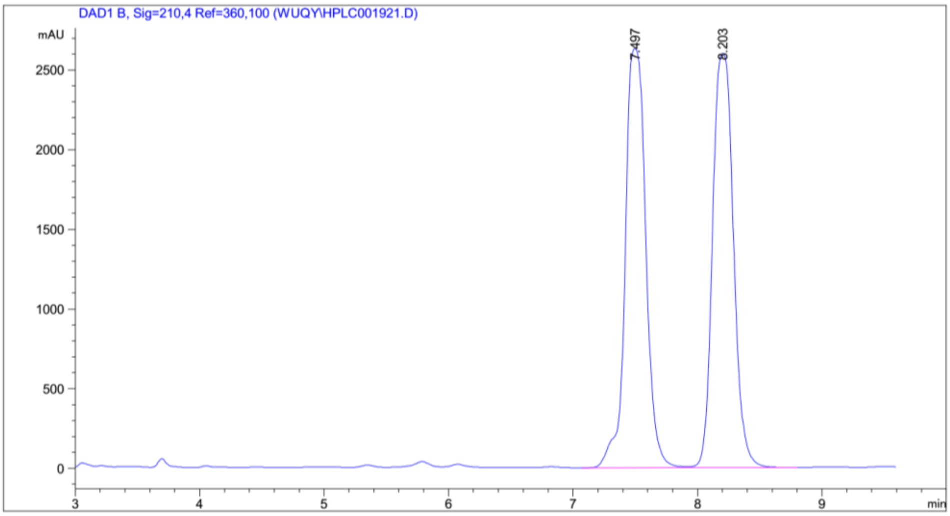
157.4726
157.6517
157.9767
158.1214
158.5558
158.9569
159.4079
159.9719
100
%
0
157
158
159
160
m/z

Copies of HPLC profiles for the enantiomeric excess determination

HPLC profile of product 3aa:

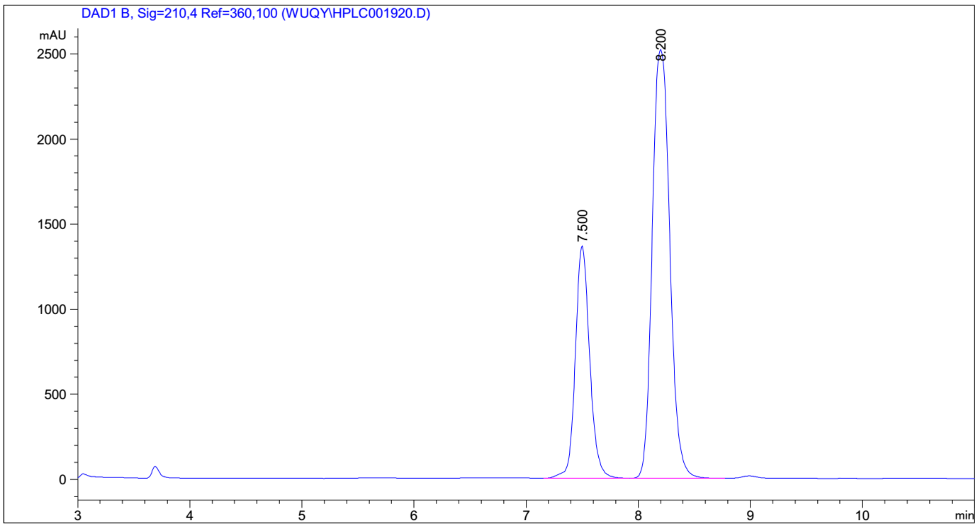
Daicel Chiralpak AD-H (*i*-PrOH/hexane = 10/90, *v*/*v*, 1.0 mL/min, 210 nm)



Peak #	Ret. Time [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.497	BV	0.1799	3.01814e4	2629.69165	50.0214
2	8.203	VB	0.1833	3.01556e4	2600.40283	49.9786

HPLC profile of product (*S*)-3aa:

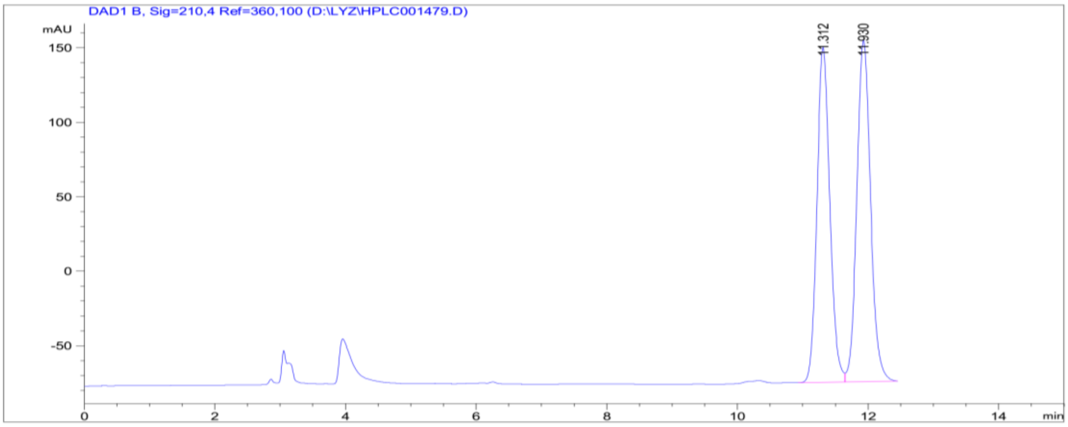
Daicel Chiralpak AD-H (*i*-PrOH/hexane = 10/90, *v*/*v*, 1.0 mL/min, 210 nm)



Peak #	Ret. Time [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.500	BB	0.1378	1.21390e4	1364.88867	30.7467
2	8.200	BV	0.1727	2.73418e4	2518.20898	69.2533

HPLC data of product 4ah:

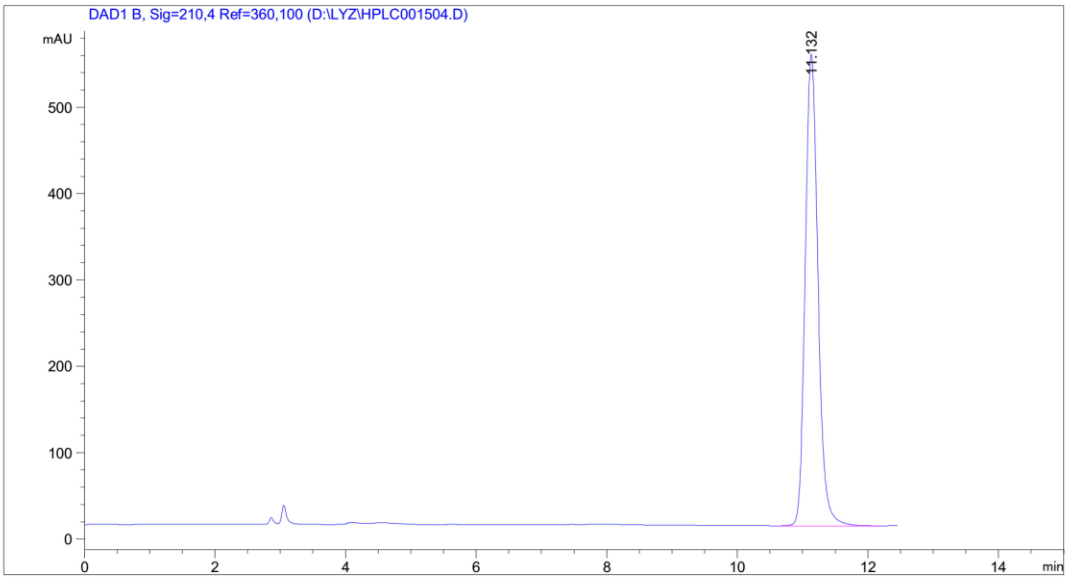
Daicel Chiralpak AD-H (*i*-PrOH/hexane = 0.9/99.1, *v*/*v*, 1.0 mL/min, 210 nm)



Peak #	Ret. Time [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.312	BV	0.2121	3083.83301	224.67834	48.0537
2	11.930	VBA	0.2238	3333.63525	229.00940	51.9463

HPLC data of product (*S*)-4ah:

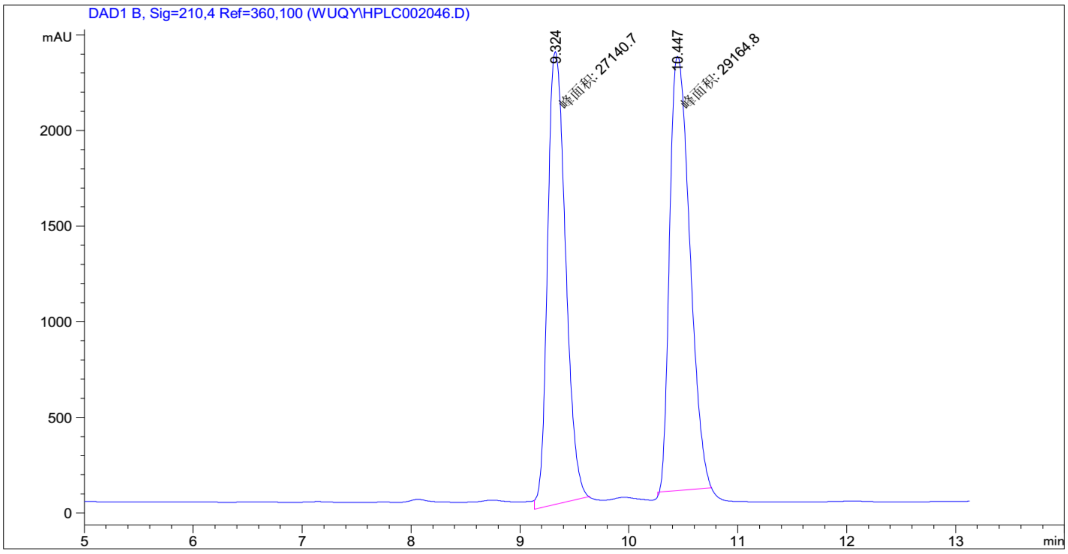
Daicel Chiralpak AD-H (*i*-PrOH/hexane = 0.9/99.1, *v*/*v*, 1.0 mL/min, 210 nm)



Peak #	Ret. Time [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.132	BB	0.2078	7386.65723	545.94849	100.0000

HPLC profile of product 4ah for gram-scaled synthesis:

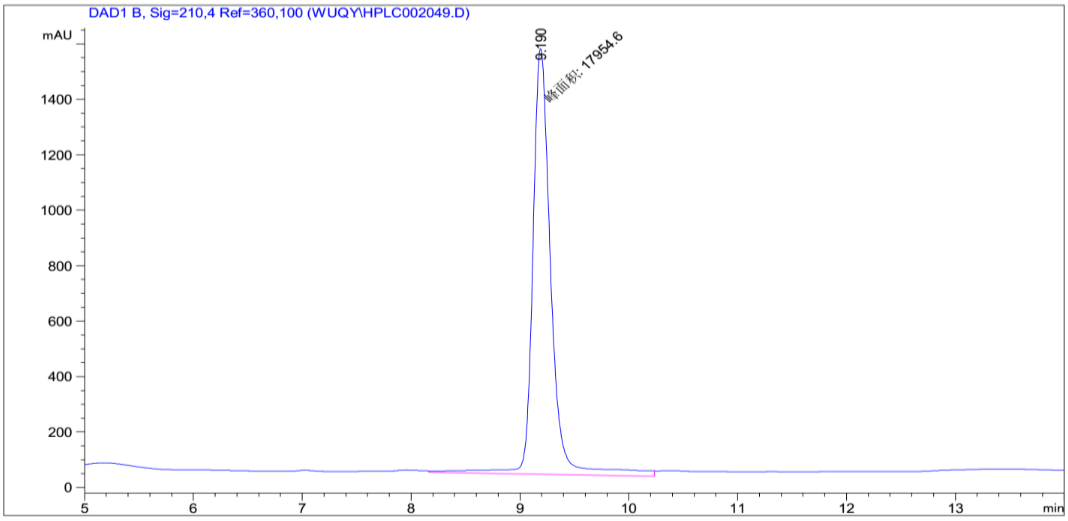
Daicel Chiralpak AD-H (*i*-PrOH/hexane = 1/99, *v*/*v*, 1.0 mL/min, 210 nm)



Peak #	Ret. Time [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.324	MM	0.1910	2.71407e4	2368.72681	48.2026
2	10.447	MM	0.2140	2.91648e4	2270.99683	51.7974

HPLC profile of product (*S*)-4ah:

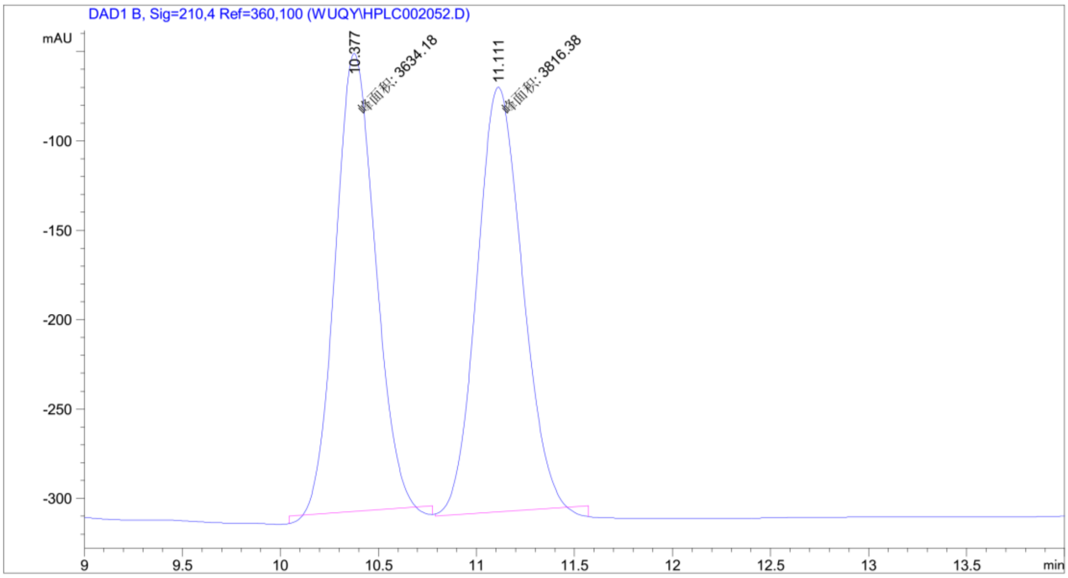
Daicel Chiralpak AD-H (*i*-PrOH/hexane = 1/99, *v*/*v*, 1.0 mL/min, 210 nm)



Peak #	Ret. Time [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.190	MM	0.1948	1.79546e4	1535.88647	100.0000

HPLC profile of product 4ai:

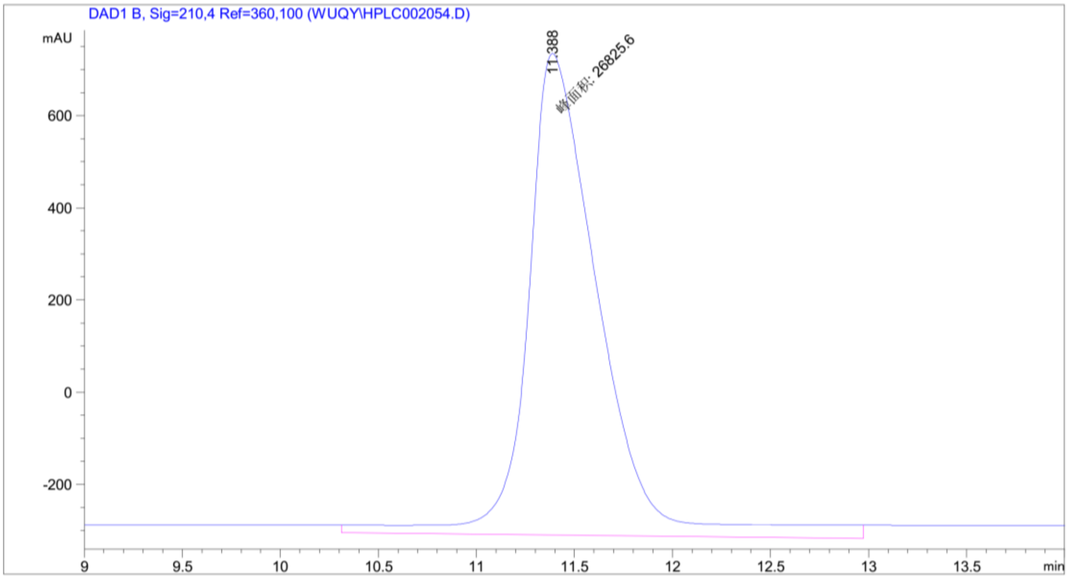
Daicel Chiralpak AS-H (*i*-PrOH/hexane = 0.1/99.9, *v*/*v*, 1.0 mL/min, 210 nm)



Peak #	Ret. Time [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.377	MM	0.2363	3634.18408	256.29239	48.7773
2	11.111	MM	0.2676	3816.37793	237.68222	51.2227

HPLC profile of product (*S*)-4ai:

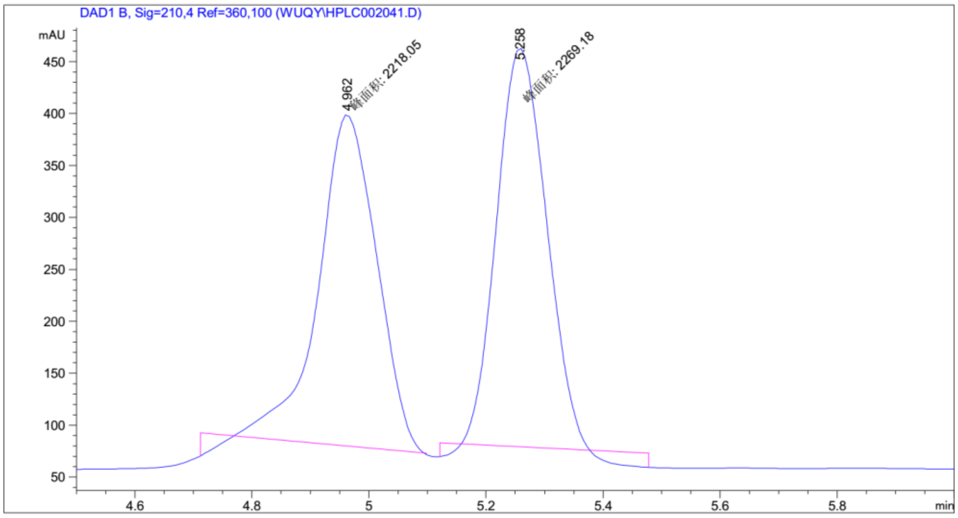
Daicel Chiralpak AS-H (*i*-PrOH/hexane = 0.1/99.9, *v*/*v*, 1.0 mL/min, 210 nm)



Peak #	Ret. Time [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.388	MM	0.4281	2.68256e4	1044.25122	100.0000

HPLC profile of product 4aj:

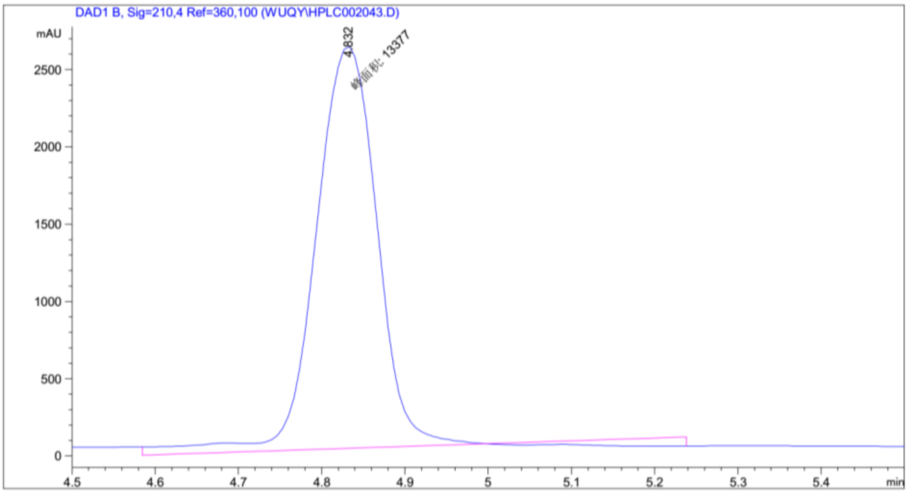
Daicel Chiralpak AD-H (*i*-PrOH/hexane = 1/99, *v*/*v*, 1.0 mL/min, 210 nm)



Peak	Ret. Time	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
1	4.962	MM	0.1159	2218.04541	319.06622	49.4303
2	5.258	MM	0.0985	2269.17603	384.02893	50.5697

HPLC profile of product (*S*)-4aj:

Daicel Chiralpak AD-H (*i*-PrOH/hexane = 1/99, *v*/*v*, 1.0 mL/min, 210 nm)



Peak	Ret. Time	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
1	4.832	MM	0.0856	1.33770e4	2605.93335	100.0000