Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Steric hindrance classified: treatment of isothiocyanatoallene with secondary amines bearing bulky substituents to generate 2-aminothiazoles

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Table of Contents

General information

Warning! *Synthesis and handling of neat allenyl isothiocyanate (**9a**) carries the risk of highly exothermic and vigorous polymerization. Measures of precaution must always be taken.*[S-1]
The produced solution of **9a** could be handled conveniently.

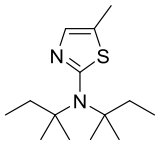
The amines used were either commercially available or were synthesized according to the literature indicated. THF was dried over sodium and benzophenone.
Since the simple reaction of allenyl isothiocyanate with a variety of different nucleophiles has already been extensively studied,[S-2] the reaction conditions presented here should only serve to synthesize the unknown 2-aminothiazoles and for their complete characterization. For this reason, an optimization of the yields was omitted.

NMR spectra were recorded on different spectrometers, e. g. on an *Inova 400* (Varian) operating at 400 MHz (^{1}H NMR) and 100.6 MHz (^{13}C NMR), the *Bruker Avance III HD 500* (500 MHz for ^{1}H and 125.8 MHz for ^{13}C) or the *Bruker Avance Neo 600* (600 MHz for ^{1}H and 150 MHz for ^{13}C). Chemical shifts δ are referenced on residual solvent signals ($CDCl_3$: 7.26 for ^{1}H and 77.00 for ^{13}C). Multiplicities are indicated by s (singulet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), m (multiplet), bs (broad signal). Multiplicities in decoupled ^{13}C NMR spectra were determined by DEPT135 experiments. All experiments were carried out at room temperature (20–25 °C), if not noted otherwise. Spectra were plotted with MestReNova V.6.0.2.
IR spectra were recorded with FT-IR spectrometer *Nicolet iS5* (ThermoFischer Scientific) in solution ($CDCl_3$ or CCl_4). IR data are given in cm^{-1}. Relative intensities are described as w (weak), m (medium), s (strong) and br (broad band).
Mass spectra were recorded on a *micrOTOF* spectrometer (Bruker).
Quantitative elementary analyses were performed on a *Vario Micro Tube* (Elementar Analysensysteme GmbH Hanau).
Melting points were determined with a *Boetius* apparatus (Pentakon Dresden). The values were not corrected.
Flash column chromatography was performed on silica 60 M (0.04–0.063) from Machery-Nagel.

General procedure for the preparation of 2-aminothiazoles 12 [GP-1]

To a solution of amine **2** (1.00 mmol) in anhydrous THF (5 mL) was added **9a**[S-2] (1.00 mmol, solution in anhydrous THF) at room temperature. Subsequently, the reaction mixture was stirred at rt or about 30 °C until the conversion was completed (as indicated by NMR). The solvent was removed in vacuum and the crude product was purified by flash column chromatography.

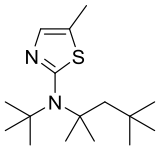
***N*,*N*-Di-*tert*-amyl-5-methylthiazol-2-amine (12a)**: According to GP-1, to a solution of *N*,*N*-di-*tert*-amylamine (**2a**)[S-3] (157 mg, 1.00 mmol) in anhydrous THF (3 mL) was added to allenyl isothiocyanate (**9a**) (97.1 mg, 1.00 mmol; solution in anhydrous THF) at room temperature. The mixture was stirred for six days at 30 °C. Flash chromatography (Et_2O/*n*-hexane, 1:2) of the crude product gave **12a** (14.3 mg, 0.06 mmol, 5.6%) as a yellow oil.



12a

^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.95 (t, ^3J = 7.4 Hz, 6H, CH_2CH_3), 1.25 (s, 12H, $C(CH_3)_2$), 1.57 (q, ^3J = 7.4 Hz, 4H, CH_2CH_3), 2.37 (d, ^4J = 1.2 Hz, 3H, $=CCH_3$), 7.12 (q, 1H, ^4J = 1.2 Hz, C*H*-4); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 9.28 (q, CH_2CH_3), 12.74 (q, $=CCH_3$), 29.08 (q, $C(CH_3)_2$), 36.35 (t, CH_2CH_3) 60.80 (s, $C(CH_3)_2$), 132.49 (s, *C*-5), 134.92 (d, *C*-4), 171.27 (s, NCS); IR ($CDCl_3$) ν = 3437 (w), 2974 (m), 2925 (m), 1440 (m), 1120 (m) cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{14}H_{27}N_2S$ $(M+H)^+$: 255.1889 (found: 255.1886).

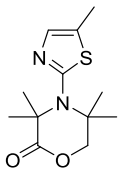
***N*-*tert*-Butyl-*N*-*tert*-octyl-5-methylthiazol-2-amine (12b)**: According to GP-1, to a solution of *N*-*tert*-butyl-*N*-*tert*-octylamine (**2b**)[S-4] (185 mg, 1.00 mmol) in anhydrous THF (5 mL) was added allenyl isothiocyanate (**9a**) (97.1 mg, 1.00 mmol) at room temperature. The mixture was stirred for 25 days. The crude product was purified by flash chromatography (Et_2O/*n*-hexane, 3:1) but the desired product **12b** could not be isolated because it underwent decomposition on attempts to remove unreacted **2b** in vacuum or in contact with SiO_2. Nevertheless, some NMR data of **12b** were measured.



12b

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.03 (s, 9H, C(CH_3)$_3$), 1.33 (s, 9H, C(CH_3)$_3$), 1.93 (s, 2H, CH_2), 2.38 (s, 3H, =CCH_3), 7.13 (s, 1H, C*H*-4), the signal for $CH_2C(CH_3)_2$ could not be clearly assigned; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ = 12.76 (q, =C*C*H$_3$), 28.89 (q, $CH_2C(CH_3)_2$), 31.69 (s, *C*(CH$_3$)$_3$), 32.05 (q, C(CH_3)$_3$), 32.59 (q, C(CH_3)$_3$), 54.36 (t, *C*H$_2$), 57.88 (s, N*C*(CH$_3$)$_3$), 62.56 (s, $CH_2C(CH_3)_2$), 132.51 (s, *C*-5), 134.82 (d, *C*-4), 170.93 (s, N*C*S).

3,3,5,5-Tetramethyl-4-(5-methylthiazol-2-yl)morpholin-2-one (12c): According to GP-1, alleny isothiocyanate (**9a**) (97.1 mg, 1.00 mmol) was added to a solution of 3,3,5,5-tetramethylmorpholin-2-one (**2c**)[S-5] (157 mg, 1.00 mmol) in anhydrous THF (5 mL). After stirring for eight days at room temperature the solvent was removed in vacuum. Flash chromatography (Et_2O/*n*-hexane, 3:1) gave **12c** (56.2 mg, 0.22 mmol, 22%) as a colorless oil.

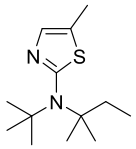


12c

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.32 (s, 6H, $CH_2C(CH_3)_2$), 1.56 (s, 6H, C(=O)C(CH_3)$_2$), 2.39 (d, ^{4}J = 1.2 Hz, 3H, =CCH_3), 4.22 (s, 2H, CH_2), 7.13 (q, ^{4}J = 1.2 Hz, 1H, C*H*-4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ = 12.39 (q, =C*C*H$_3$), 23.29 (q, $CH_2C(CH_3)_2$), 28.05 (q, C(=O)C(*C*H$_3$)$_2$), 54.36 (s, $CH_2C(CH_3)_2$), 60.57 (s, C(=O)*C*(CH$_3$)$_2$), 77.36 (t, *C*H$_2$), 131.39 (s, *C*-5'), 136.05 (d, *C*-4'), 163.71 (s, N*C*S), 173.74 (s, *C*=O); IR (CCl_4) ν = 2961 (m), 2934 (m), 2868 (m) cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{12}H_{19}N_2O_2S$ $(M+H)^+$: 255.1162 (found: 255.1151), calcd. for $C_{12}H_{18}N_2NaO_2S$ $(M+Na)^+$: 277.0981 (found: 277.0969).

***N*-*tert*-Amyl-*N*-*tert*-butyl-5-methylthiazol-2-amine (12d)**: According to GP-1, to a solution of *N*-*tert*-amyl-*N*-*tert*-butylamine (**2d**)[S-6] (143 mg, 1.00 mmol) in anhydrous THF (5 mL) was added allenyl isothiocyanate (**9a**) (97.1 mg, 1.00 mmol) at room temperature. After stirring for

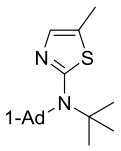
nine days at 30 °C, flash chromatography (Et_2O/*n*-hexane, 5:1) of the crude product gave **12d** (118 mg, 0.49 mmol, 49%) as a yellow oil.



12d

^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.97 (t, ^3J = 7.4 Hz, 3H, CH_2CH_3), 1.24 (s, 6H, $C(CH_3)_2$), 1.30 (s, 9H, $C(CH_3)_3$), 1.59 (q, ^3J = 7.4 Hz, 2H, CH_2CH_3), 2.37 (d, ^4J = 1.3 Hz, 3H, $=CCH_3$), 7.12 (q, ^4J = 1.3 Hz, 1H, C*H*-4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ = 9.29 (q, CH_2CH_3), 12.74 (q, $=CCH_3$), 29.45 (q, $C(CH_3)_2$), 32.18 (q, $C(CH_3)_3$), 36.17 (t, CH_2CH_3), 57.67 (s, $C(CH_3)_3$), 60.73 (s, $C(CH_3)_2$), 132.63 (s, *C*-5), 135.00 (d, *C*-4), 171.25 (s, N*C*S); IR (CCl_4) ν = 3080 (w), 2975 (m), 2925 (m), 2878 (w) cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{13}H_{25}N_2S$ $(M+H)^+$: 241.1733 (found: 241.1715).

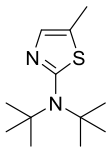
***N*-1-Adamantyl-*N*-*tert*-butyl-5-methylthiazol-2-amine (12e)**: According to GP-1, allenyl isothiocyanate (**9a**) (48.6 mg, 0.50 mmol) and *N*-1-adamantyl-*N*-*tert*-butylamine (**2e**)[S-7] (101 mg, 0.49 mmol) were reacted at 30 °C in anhydrous THF (5 mL). The mixture was stirred for four days. Flash chromatography (Et_2O/*n*-hexane, 1:1) gave **12e** (14.2 mg, 0.05 mmol, 9.5%) as a pale yellow solid.



12e

m.p. 95−96 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 1.32 (s, 9H, $C(CH_3)_3$), 1.58 (bs, 6H, 1-Ad-CH_2), 1.98 (bs, 6H, 1-Ad-CH_2), 2.03 (bs, 3H, 1-Ad-C*H*), 2.37 (d, ^4J = 1.1 Hz, 3H, $=CCH_3$), 7.12 (q, ^4J = 1.1 Hz, 1H, C*H*-4); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 12.81 (q, $=CCH_3$), 30.35 (d, 1-Ad-*C*H), 32.86 (q, $C(CH_3)_3$), 36.35 (t, 1-Ad-CH_2), 43.86 (t, 1-Ad-CH_2), 57.98 (s, $C(CH_3)_3$), 58.95 (s, 1-Ad-*C*), 132. 88 (s, *C*-5), 134.96 (d, *C*-4), 170. 22 (s, N*C*S); IR (CCl_4): [ν] 3444 (w), 2909 (m), 2851 (m), 1548 (m), 1439 (m) cm^{-1}; $C_{18}H_{28}N_2S$ (304.50): calcd. C 71.00, H 9.27, N 9.20, S 10.53; found C 69.66, H 9.05, N 8.97, S 10.38.

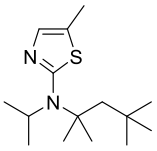
***N*,*N*-Di-*tert*-butyl-5-methylthiazol-2-amine (12f)**: According to GP-1, to a solution of *N*,*N*-di-*tert*-butylamine (**2f**)[S-8] (129 mg, 1.00 mmol) in anhydrous THF (5 mL) was added allenyl isothiocyanate (**9a**) (97.1 mg, 1.00 mmol) at room temperature. After stirring for seven days at the same temperature the solvent was removed in vacuum. Flash chromatography (*n*-hexane/Et_2O, 2:1) of the crude product gave **12f** (40 mg, 0.18 mmol, 18%) as a yellow oil.



12f

^{1}H NMR (400 MHz; $CDCl_3$) δ = 1.30 (s, 18H, C(CH_3)$_3$), 2.37 (d, ^4J = 1.2 Hz, 3H, =CCH_3), 7.12 (q, ^4J = 1.2 Hz, 1H, C*H*-4); ^{13}C NMR (100.6 MHz; $CDCl_3$) δ = 12.79 (q, =C*C*H$_3$), 32.29 (q, C(*C*H$_3$)$_3$), 57.69 (s, *C*(CH$_3$)$_3$), 132.71 (s, *C*-5), 134.89 (d, *C*-4), 170.85 (s, N*C*S); IR (CCl_4) ν = 3080 (w), 2980 (s), 2920 (s), 2140 (w), 1440 (s) cm^{-1}; HRMS (ESI) *m*/*z* calcd. for $C_{12}H_{23}N_2S$ $(M+H)^+$: 227.1576 (found: 227.1592), calcd. for $C_{12}H_{22}N_2NaS$ $(M+Na)^+$: 249.1396 (found: 249.1403).

***N*-Isopropyl-5-methyl-*N*-*tert*-octylthiazol-2-amine (12h)**: According to GP-1, *N*-isopropyl-*N*-*tert*-octylamin (**2h**)[S-9] (171 mg, 1.00 mmol) and allenyl isothiocyanate (**9a**) (97.1 mg, 1.00 mmol) were reacted in anhydrous THF (5 mL) at room temperature. After five days of stirring a flash chromatography (*n*-hexane/Et_2O, 3:1) gave **12h** (160 mg, 0.60 mmol, 60%) as a yellow oil.

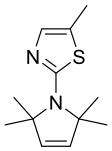


12h

^{1}H NMR (400 MHz; $CDCl_3$) δ = 1.00 (s, 9H, C(CH_3)$_3$), 1.16 (d, ^3J = 6.7 Hz, 6H, CH(CH_3)$_2$), 1.36 (s, 6H, CH$_2$C(CH_3)$_2$), 1.85 (s, 2H, CH_2), 2.34 (s, 3H, =CCH_3), 3.73 (sept, ^3J = 6.7 Hz, 1H, C*H*(CH$_3$)$_2$), 7.05 (s, 1H, C*H*-4); ^{13}C NMR (100.6 MHz; $CDCl_3$) δ = 12.48 (q, =C*C*H$_3$), 23.29 (q, CH(*C*H$_3$)$_2$), 28.87 (q, CH$_2$C(*C*H$_3$)$_2$), 31.26 (s, *C*(CH$_3$)$_3$), 31.88 (q, C(*C*H$_3$)$_3$), 47.49 (d, *C*H(CH$_3$)$_2$), 51.40 (t, *C*H$_2$), 61.68 (s, CH$_2$*C*(CH$_3$)$_2$), 128.56 (s, *C*-5), 134.76 (d, *C*-4), 166.81 (s, N*C*S); IR (CCl_4): [ν] 2960 (s), 2170 (m), 2140 (w) cm^{-1}; HRMS (ESI) m/z calcd. for $C_{15}H_{29}N_2S$

$(M+H)^+$: 269.2046 (found: 269.2044), calcd. for $C_{15}H_{28}N_2NaS$ $(M+Na)^+$: 291.1865 (found: 291.1867).

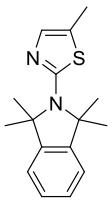
5-Methyl-2-(2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yl)thiazole (12i): According to GP-1, to a solution of 2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol (**2i**)[S-10] (125 mg, 1.00 mmol) in anhydrous THF was added allenyl isothiocyanate (**9a**) (97.1 mg, 1.00 mmol) at room temperature. The mixture was stirred overnight at 30 °C. Flash chromatography (Et_2O/ *n*-hexane, 1:2) of the crude product gave **12i** (96.5 mg, 0.43 mmol, 43%) as a pale yellow solid.



12i

m.p. 83−85 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 1.59 (s, 12H, C(CH_3)$_2$), 2.30 (d, ^4J = 1.3 Hz, 3H, =CCH_3), 5.54 (s, 2H, *H*C=C*H*), 6.83 (s, 1H, C*H*-4); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 11.53 (q, =C*C*H$_3$), 25.72 (q, C(*C*H$_3$)$_2$), 70.27 (s, *C*(CH$_3$)$_2$), 118.97 (s, *C*-5), 133.94 (d, H*C*=*C*H), 135.25 (d, *C*-4), 162.17 (s, N*C*S); IR (CCl_4) ν = 3454 (w), 3070 (w), 2968 (m), 2921 (m), 2883 (m), 1504 (s), 1451 (m), 1203 (m) cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{12}H_{19}N_2S$ $(M+H)^+$: 223.1263 (found: 223.1262).

5-Methyl-2-(1,1,3,3-tetramethylisoindolin-2-yl)thiazole (12j): According to GP-1, allenyl isothiocyanate (**9a**) (48.6 mg, 0.50 mmol) was added to a solution of 1,1,3,3-tetramethylisoindoline (**2j**)[S-11] (70.0 mg, 0.40 mmol) in anhydrous. THF (3 mL) at room temperature and stirred for two days at 30 °C. The following flash chromatography (Et_2O/ *n*-hexane, 1:3) gave **12j** (62 mg, 0.23 mmol, 57%) as a colorless, crystalline solid.

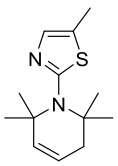


12j

m.p. 127−129 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 1.82 (s, 12H, C(CH_3)$_2$), 2.34 (s, 3H, =CCH_3), 6.90 (s, 1H, C*H*-4), 7.18 (m, 2H, CH_{arom}), 7.32 (m, 2H, CH_{arom}); ^{13}C NMR (150 MHz, $CDCl_3$)

δ = 11.54 (q, =C*C*H$_3$), 27.48 (q, C(*C*H$_3$)$_2$), 68.43 (s, *C*(CH$_3$)$_2$), 119.63 (s, *C*-5), 121.32 (d, C_{arom}), 127.65 (d, C_{arom}), 135.26 (d, *C*-4), 145.61 (s, *C*-C(CH$_3$)$_2$), 162.41 (s, N*C*S); IR (CCl_4) ν = 2970 (m), 2920 (m), 1548 (m), 1505 (m) cm^{-1}; $C_{16}H_{20}N_2S$ (272.41): calcd. C 70.55, H 7.40, N 10.28, S 11.77; found C 70.47, H 7.36, N 10.11, S 11.62.

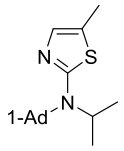
5-Methyl-2-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-1-yl)thiazole (12k): According to GP-1, allenyl isothiocyanate (**9a**) (73.0 mg, 0.75 mmol) was reacted with 2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridine (**2k**)[S-12] (70.0 mg, 0.50 mmol) in anhydrous THF (2 mL) at room temperature. After stirring for two days the solution was concentrated in vacuum. Flash chromatography (Et_2O/*n*-hexane, 1:10 to 1:6) gave **12k** (94 mg, 0.40 mmol, 80%) as a yellow oil.



12k

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.22 (s, 6H, 2'-(C*H*$_3$)$_2$), 1.24 (d, *J* = 1.0 Hz, 6H, 6'-(C*H*$_3$)$_2$), 2.09 (m, 2H, 3'-C*H*$_2$), 2.39 (s, 3H, =CC*H*$_3$), 5.55–5.65 (m, 2H, C*H*=C*H*), 7.18 (s, 1H, C*H*-4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ = 12.63 (q, =C*C*H$_3$), 27.56 (q, 2'-(*C*H$_3$)$_2$), 29.12 (q, 6'-(*C*H$_3$)$_2$), 40.42 (t, 3'-*C*H$_2$), 54.36 (s, *C*-2'), 55.81 (s, *C*-6'), 120.61 (d, *C*-4'), 132.74 (s, *C*-5), 135.75 (d, *C*-4/5'), 135.93 (d, *C*-4/5'), 167.18 (s, N*C*S); IR (CCl_4) ν = 3030 (w), 2971 (m), 2928 (m), 1517 (w), 1471 (m), 1441 (s), 1361 (m) cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{13}H_{21}N_2S$ $(M+H)^+$: 237.1420 (found: 237.1478).

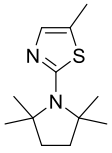
***N*-1-Adamantyl-*N*-isopropyl-5-methylthiazol-2-amine (12m)**: According to GP-1, to a solution of *N*-1-adamantyl-*N*-isopropylamine (**2m**)[S-13] (96.7 mg, 0.50 mmol) in anhydrous THF (2 mL) was added allenyl isothiocyanate (**9a**) (48.6 mg, 0.50 mmol) at room temperature. The mixture was stirred for three days. Flash chromatography (Et_2O/*n*-hexane, 1:1) of the crude product gave **12m** (95.8 mg, 0.33 mmol, 66%) as a yellow oil.



12m

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.10 (d, ^{3}J = 6.7 Hz, 6H, CH(CH_3)$_2$), 1.61 (bs, 6H, 1-Ad-CH_2), 1.90 (bs, 6H, 1-Ad-CH_2), 2.06 (bs, 3H, 1-Ad-C*H*), 2.36 (d, ^{4}J = 1.2 Hz, 3H, =CCH_3), 3.73 (sept, ^{3}J = 6.7 Hz, 1H, C*H*(CH$_3$)$_2$), 7.11 (q, ^{4}J = 1.2 Hz, 1H, C*H*-4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ = 12.63 (q, =C*C*H$_3$), 23.70 (q, CH(*C*H$_3$)$_2$), 29.87 (d, 1-Ad-*C*H), 36.48 (t, 1-Ad-*C*H$_2$), 41.35 (t, 1-Ad-*C*H$_2$), 45.06 (d, *C*H(CH$_3$)$_2$), 57.08 (s, 1-Ad-*C*), 130.78 (s, *C*-5), 135.50 (d, *C*-4), 166.21 (s, N*C*S); IR (CCl_4) ν = 2971 (m), 2907 (m), 2852 (m), 1224 (m) cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{17}H_{27}N_2S$ $(M+H)^+$: 291.1889 (found: 291.1890).

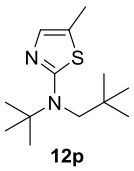
5-Methyl-2-(2,2,5,5-tetramethylpyrrolidin-1-yl)thiazole (12o): According to GP-1, 2,2,5,5-tetramethylpyrrolidine (**2o**)[S-14] (127 mg, 1.00 mmol) and allenyl isothiocyanate (**9a**) (97.1 mg, 1.00 mmol) were reacted in anhydrous THF (5 mL) at room temperature. After three hours of stirring, the solution was concentrated in vacuum. Flash chromatography (Et_2O/*n*-hexane, 1:2) gave **12o** (135 mg, 0.60 mmol, 60%) as a yellow solid.



12o

m.p. 53−54 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.49 (s, 12H, C(CH_3)$_2$), 1.87 (s, 4H, CH_2), 2.29 (d, ^{4}J = 1.3 Hz, 3H, =CCH_3), 6.82 (q, ^{4}J = 1.3 Hz, 1H, C*H*-4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ = 11.68 (q, =C*C*H$_3$), 26.21 (q, C(*C*H$_3$)$_2$), 39.79 (t, *C*H$_2$), 64.72 (s, *C*(CH$_3$)$_2$), 119.54 (s, *C*-5), 134.94 (d, *C*-4), 163.11 (s, N*C*S); IR (CCl_4) ν = 2965 (m), 1219 (m) cm^{-1}; $C_{12}H_{20}N_2S$ (224.366): calcd. C 64.24, H 8.99, N 12.49, S 14.29; found C 64.08, H 8.84, N 12.57, S 14.41.

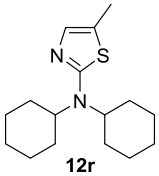
***N*-*tert*-Butyl-5-methyl-*N*-neopentylthiazol-2-amine (12p)**: According to GP-1, to a solution of *N*-*tert*-butyl-*N*-neopentylamine (**2p**)[S-15] (71.6 mg, 0.50 mmol) in anhydrous THF (2 mL) was added allenyl isothiocyanate (**9a**) (48.6 mg, 0.50 mmol) at room temperature. After stirring for one day at 30 °C, flash chromatography (Et_2O/*n*-hexane, 1:2) of the crude product gave **12p** (72.8 mg, 0.30 mmol, 61%) as a yellow oil.



12p

^{1}H NMR (600 MHz, $CDCl_3$) δ = 0.80 (s, 9H, NC(CH_3)$_3$), 1.20 (s, 9H, C(CH_3)$_3$), 2.36 (d, ^{4}J = 1.2 Hz, 3H, =CCH_3), 3.03 (s, 2H, CH_2), 7.04 (q, ^{4}J = 1.2 Hz, 1H, C*H*-4); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 12.61 (q, =CCH_3), 28.26 (q, C(CH_3)$_3$), 28.27 (q, C(CH_3)$_3$), 33.23 (s, $C(CH_3)_3$), 57.59 (s, N$C(CH_3)_3$), 61.37 (t, CH_2), 130.01 (s, *C*-5), 135.08 (d, *C*-4), 173.21 (s, N*C*S); IR (CCl_4) ν = 2973 (m), 2955 (m), 2865 (m), 1506 (m), 1480 (s), 1394 (s), 1364 (s) cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{13}H_{25}N_2S$ $(M+H)^+$: 241.1733 (found: 241.1737), calcd. for $C_{13}H_{24}N_2NaS$ $(M+Na)^+$: 263.1552 (found: 263.1556).

***N*,*N*-Dicyclohexyl-5-methylthiazol-2-amine (12r)**: According to GP-1, *N*,*N*-dicyclohexylamine (**2r**)[S-16] (181 mg, 1.00 mmol) and allenyl isothiocyanate (**9a**) (97.1 mg, 1.00 mmol) were reacted at room temperature in anhydrous THF (5 mL) for about ten minutes. Flash chromatography (Et_2O/*n*-hexane, 1:3) gave **12r** (93.4 mg, 0.34 mmol, 34%) as a brown oil.

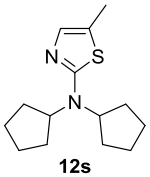


12r

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.12−1.37 (m, 6H, CH_2), 1.62−1.70 (m, 6H, CH_2), 1.80−1.83 (m, 4H, CH_2), 1.92−2.03 (m, 4H, CH_2), 2.26 (d, ^{4}J = 1.3 Hz, 3H, =CCH_3), 3.39 (tt, J = 11.9 Hz, J = 3.7 Hz, 2H, C*H*CH_2), 6.75 (q, ^{4}J = 1.3 Hz, 1H, C*H*-4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ = 11.69 (q, =CCH_3), 25.40 (t, CH_2), 26.33 (t, CH_2), 30.41 (t, CH_2), 59.65 (d, *C*HCH_2), 118.64 (s, *C*-5), 135.53 (d, *C*-4), 167.78 (s, N*C*S); IR (CCl_4) ν = 2933 (m), 2856 (m) cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{16}H_{27}N_2S$ $(M+H)^+$: 279.1889 (found: 279.1884).

***N*,*N*-Dicyclopentyl-5-methylthiazol-2-amine (12s)**: According to GP-1, allenyl isothiocyanate (**9a**) (63.1 mg, 0.65 mmol) was added to a solution of *N*,*N*-dicyclopentylamine (**2s**)[S-17] (100 mg, 0.65 mmol) in anhydrous THF (5 mL) at room temperature. After stirring for

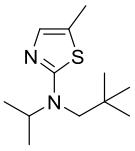
ten minutes flash chromatography (Et_2O/*n*-hexane, 1:2) gave **12s** (26.9 mg, 0.11 mmol, 17%) as a brown oil.



12s

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.52−1.61 (m, 4H, CH_2), 1.75−1.84 (m, 8H, CH_2), 1.89−1.97 (m, 4H, CH_2), 2.27 (d, ^4J = 1.3 Hz, 3H, =CCH_3), 4.00 (quint, ^3J = 8.7 Hz, 2H, CHCH_2), 6.76 (q, ^4J = 1.3 Hz, 1H, CH-4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ = 11.77 (q, =CCH$_3$), 24.43 (t, CH$_2$), 28.48 (t, CH$_2$), 60.60 (d, CHCH$_2$), 119.34 (s, C-5), 135.63 (d, C-4), 167.46 (s, NCS); IR (CCl_4) ν = 2957 (m), 2871 (m) cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{14}H_{23}N_2S$ $(M+H)^+$: 251.1576 (found: 251.1566).

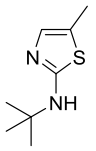
***N*-Isopropyl-5-methyl-*N*-neopentylthiazol-2-amine (12t)**: According to GP-1, allenyl isothiocyanate (**9a**) (48.6 mg, 0.50 mmol) was added to a solution of *N*-isopropyl-*N*-neopentylamine (**2t**)[S-18] (40.0 mg, 0.31 mmol) in anhydrous THF (2 mL) at room temperature. After stirring for four days, flash chromatography (Et_2O/*n*-hexane, 1:2) of the crude product gave **12t** (33.5 mg, 0.15 mmol, 48%) as a pale yellow oil.



12t

^{1}H NMR (600 MHz, $CDCl_3$) δ = 0.98 (s, 9H, C(CH_3)$_3$), 1.36 (d, ^3J = 6.8 Hz, 6H, CH(CH_3)$_2$), 2.27 (d, ^4J = 1.2 Hz, 3H, =CCH_3), 3.13 (s, 2H, CH_2), 3.72 (sept, ^3J = 6.8 Hz, 1H, CH(CH$_3$)$_2$), 6.77 (s, 1H, CH-4); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 11.79 (q, =CCH$_3$), 19.48 (q, CH(CH$_3$)$_2$), 28.53 (q, C(CH$_3$)$_3$), 33.82 (s, C(CH$_3$)$_3$), 56.38 (d, CH(CH$_3$)$_2$), 62.81 (t, CH$_2$), 120.33 (s, C-5), 135.28 (d, C-4), 170.68 (s, NCS); IR (CCl_4) ν = 3051 (w), 2961 (m), 2867 (m), 1529 (s), 1509 (s), 1365 (m) cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{12}H_{23}N_2S$ $(M+H)^+$: 227.1576 (found: 227.1578).

***N*-*tert*-Butyl-5-methylthiazol-2-amine (13b)**: According to GP-1, to a solution of *N*-*tert*-butylamine (0.11 g, 0.16 mL, 1.50 mmol) in anhydrous THF (7 mL) was added allenyl isothiocyanate (**9a**) (97.1 mg, 1.00 mmol) at room temperature. After one hour of stirring the solvent was removed in vacuum. Flash chromatography (Et_2O/*n*-hexane, 5:1) and subsequent sublimation (50 °C and $5 \cdot 10^{-3}$ mbar) gave **13b** (76.9 mg, 0.45 mmol, 45%) as a pale yellow solid.



13b

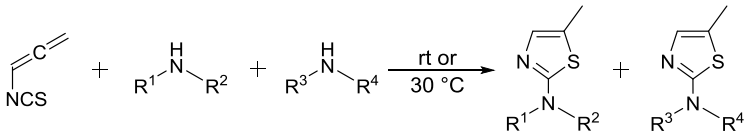
m.p. 96−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.39 (s, 9H, C(C*H*$_3$)$_3$), 2.27 (d, ^4J = 1.2 Hz, 3H, =CC*H*$_3$), 4.94 (bs, 1H, N*H*), 6.74 (q, ^4J = 1.2 Hz, 1H, C*H*-4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ = 11.83 (q, =C*C*H$_3$), 29.05 (q, C(*C*H$_3$)$_3$), 52.47 (s, *C*(CH$_3$)$_3$), 121.50 (s, *C*-5), 135.05 (d, *C*-4), 166.24 (s, N*C*S); IR (CCl_4): [ν] 3432 (w), 2973 (w), 2902 (w) cm^{-1}; $C_8H_{14}N_2S$ (170.274): calcd. C 56.43, H 8.29, N 16.45, S 18.83%; found C 56.62, H 8.30, N 16.06, S 18.87.

General procedure for the competition experiments [GP-2]

In order to determine the relative rates of the reactions of amines **2a**−**t**, which led to the thiazoles **12a**−**t**, equimolar amounts of two secondary amines were treated with **9a** in tetrahydrofuran at room temperature or 30 °C. After low conversation of the amines the ratio of the corresponding products were measured with the help of ^{1}H NMR spectroscopy.

Survey of competition experiments

The following overview shows all competition reactions and the determined relative rates for the amines **2a**–**t** during this work. The amine that reacted slower with **9a** was always set equal to 1.



9a **2** **2'** **12** **12'**

2a R^1 = *t*-Amyl, R^2 = *t*-Amyl
2b R^1 = *t*-Bu, R^2 = *t*-Octyl
2c 3,3,5,5-Tetramethylmorpholin-2-one
2d R^1 = *t*-Bu, R^2 = *t*-Amyl
2e R^1 = *t*-Bu, R^2 = 1-Ad
2f R^1 = *t*-Bu, R^2 = *t*-Bu
2g 2,2,6,6-Tetramethylpiperidin-4-one
2h R^1 = *i*-Pr, R^2 = *t*-Octyl
2i 2,2,5,5-Tetramethylpyrroline
2j 1,1,3,3-Tetramethylisoindoline
2k 2,2,6,6-Tetramethyl-1,2,3,4-tetrahydropyridine
2l 2,2,6,6-Tetramethylpiperidine
2m R^1 = *i*-Pr, R^2 = 1-Ad
2n R^1 = *i*-Pr, R^2 = *t*-Bu
2o 2,2,5,5-Tetramethylpyrrolidine
2p R^1 = *t*-Bu, R^2 = Neopentyl
2q R^1 = *i*-Pr, R^2 = *i*-Pr
2r R^1 = Cy, R^2 = Cy
2s R^1 = Cyclopentyl, R^2 = Cyclopentyl
2t R^1 = *i*-Pr R^2 = Neopentyl

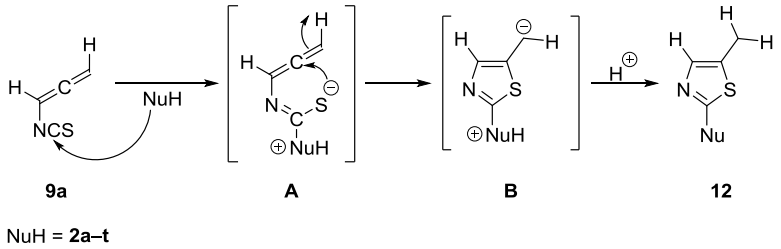
Table S-1 Overview of all competition reactions done and the determined relative rates.

Comparison of	Conversion [%]	Relative rate	T [°C]e	Comparison of	Conversion [%]	Relative rate	T [°C]
2a:2b	8.4	1:1.94	30 °C	**2a:2d**	---	---[a]	30 °C
2b:2d	21.3	1:1.61	30 °C	**2c:2d**	19.7	1:1.41	30 °C
2d:2e	25.4	1:2.24	30 °C	**2e:2f**	34.1	1:1.76	30 °C
2c:2d	3.3	1:1.46	rt	**2c:2f**	9.9	1:4.28	rt
2c:2g	---	---[a]	rt	**2d:2h**	---	---[a]	rt
2f:2g	2.7	1:1.37	rt	**2f:2h**	7.5	1:6.69	rt
2f:2l	---	---[a]	rt	**2f:2n**	---	---[a]	rt
2g:2l	7.1	1:13.24	rt	**2h:2n**	3.4	1:3.71	rt
2i:2o	7.9	1:4.56	rt	**2j:2o**	9.5	1:4.33	rt
2k:2l	10.5	1:1.61	rt	**2l:2m**	9.1	1:1.32	rt
2l:2n	8.4	1:2.08	rt	**2l:2o**	8.0	1:2.63	rt
2l:2q	6.5	1:28.59[b]	rt	**2m:2n**	12.1	1:1.71	rt
2n:2q	3.9	9.27[b]	rt	**2q:2r**	5.1	1:1.13[b]	rt
2q:2s	7.5	1:1.89[c]	rt	**2r:2t**	8.8	1:4.82[b]	rt
2s:2t	6.9	1:2.73[c]	rt	**2l:2p**	30.7	1:5.40	rt
2n:2p	44.7	1:2.58	rt				
		---[b]				---[b]	
2d:2f	---	1:2.93 (calcd.)	rt	**2d:2f**	---	1:3.96 (calcd.)	30 °C

[a] At the time of measurement, no product formation starting from the slower amine **2**, no rate determinable; [b] Reaction according to GP-2 but quenched after a short time at −70 °C, NMR measurement at −60 °C; [c] Only a very small amount of **9a** was added to the mixture of two amines; [d] The ^{1}H NMR signals of both products overlap, making a determination in the direct comparison inaccurate. However, it is possible to calculate the relative rates by other comparisons.

Reaction kinetics based on the reaction of the amine 2

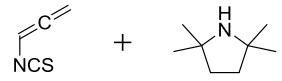
The reaction of **9a** with amine **2** is a second-order reaction.



9a **A** **B** **12**

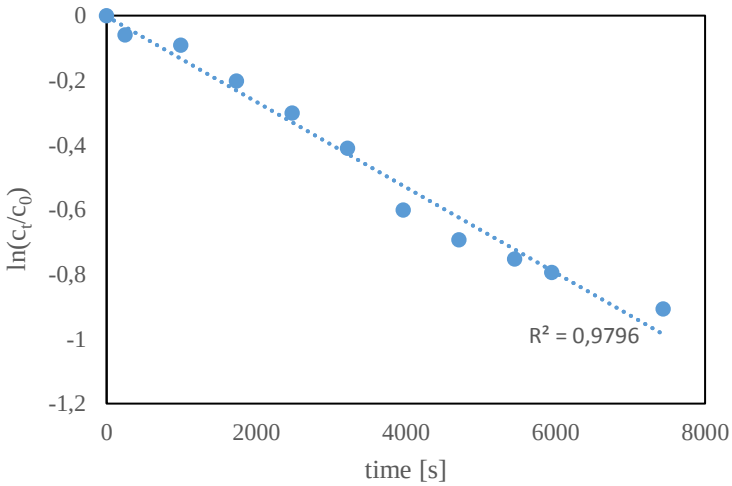
NuH = **2a–t**

If **2**, for example **2o**, is added to a large excess of **9a**, the conversion of the amine can be set equal to a first-order reaction. In order to prove the assumption that only one molecule of the nucleophilic amine **2o** was needed to form the species **B** followed by intramolecular protonation (no protonation by a second molecule), a kinetic measurement was performed for the reaction of **9a** with **2o**.



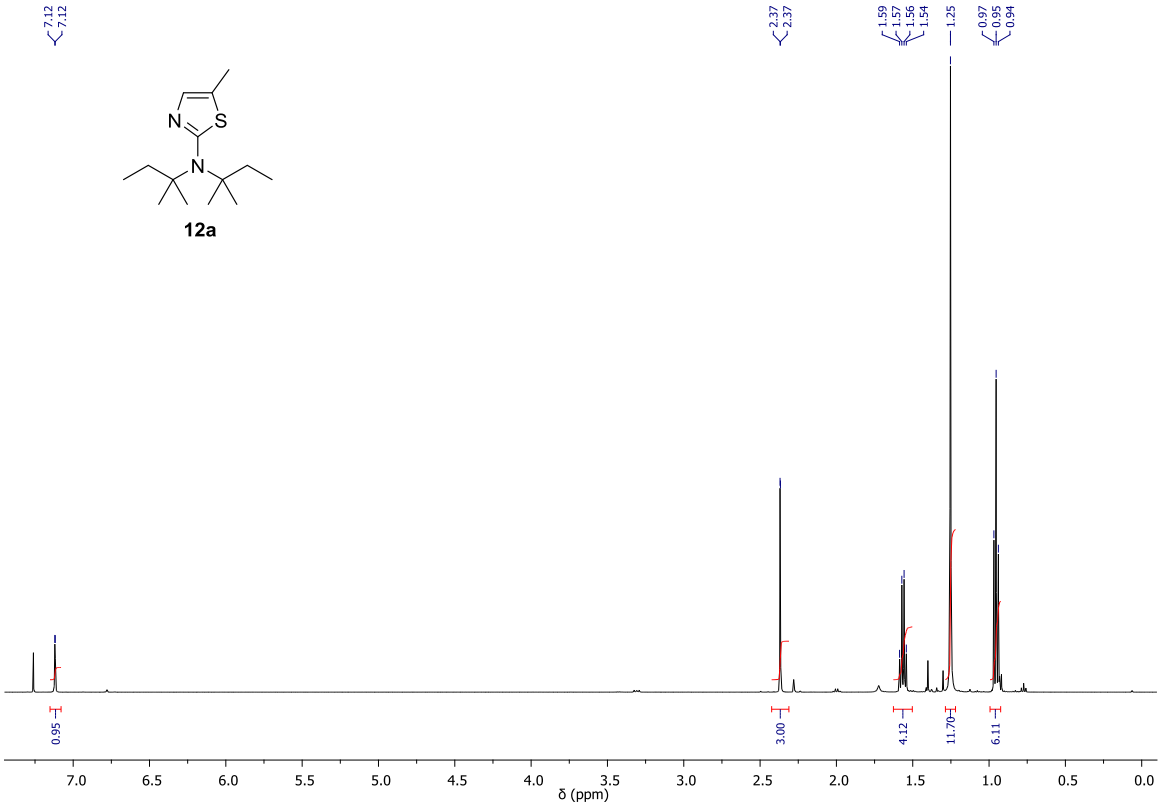
excess of **9a** **2o**

^{1}H NMR integral (Amine 2o)	**Time [s]**	**$\ln(c_t/c_0)$**
1.04	0	0
0.98	248	-0,0594
0.95	992	-0,0905
0.85	1736	-0,2017
0.77	2480	-0,3006
0.69	3224	-0,4103
0.57	3968	-0,6013
0.52	4712	-0,6931
0.49	5456	-0,7526
0.47	5952	-0,7942
0.42	7440	-0,9067

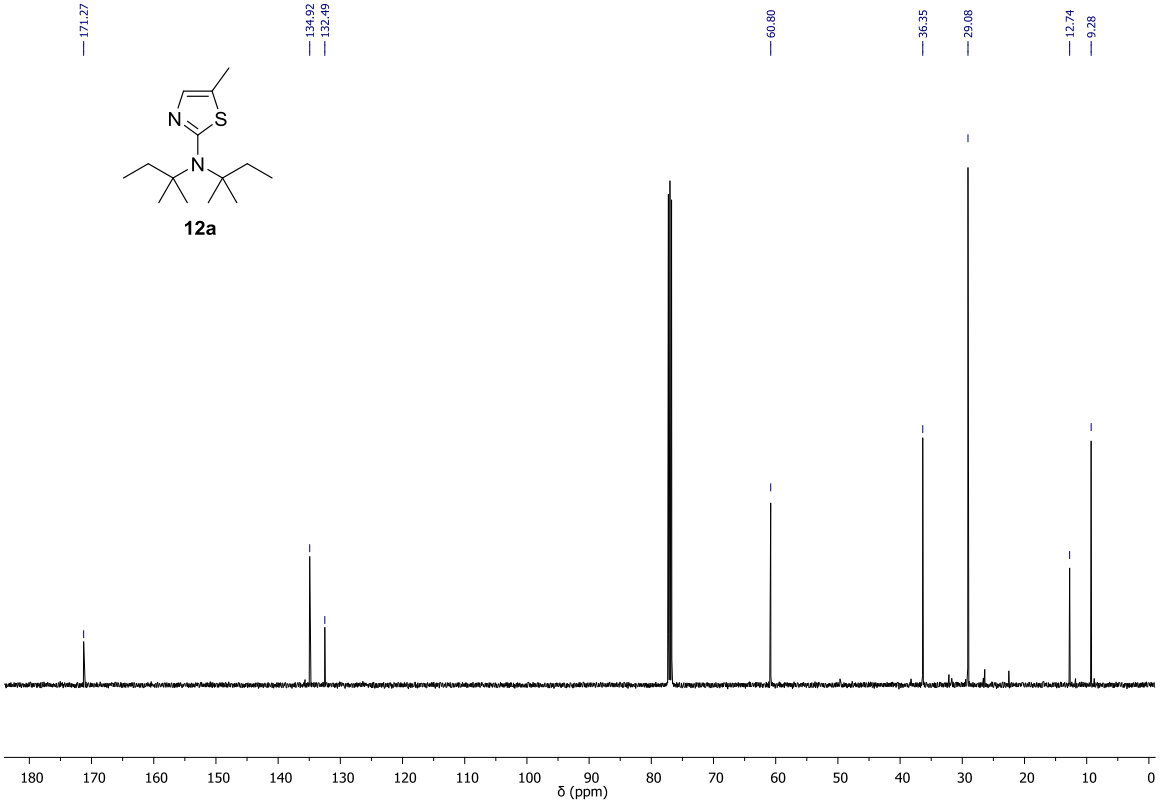


NMR spectra

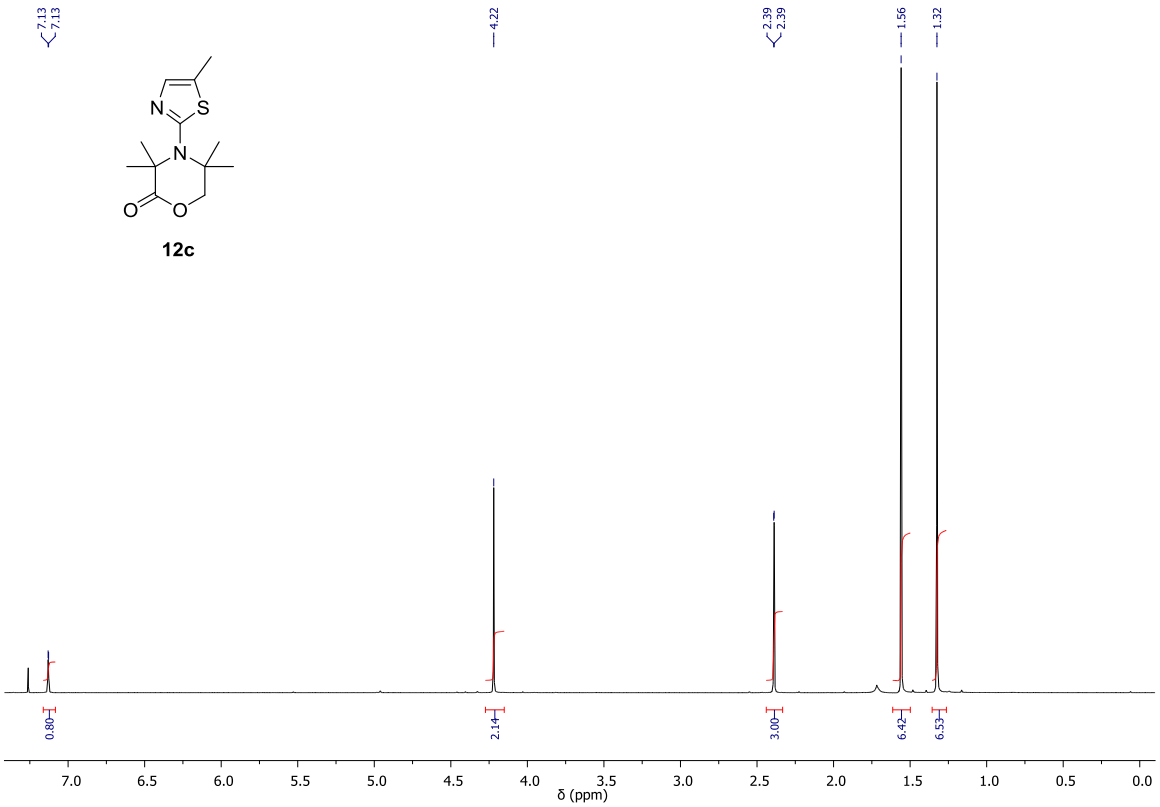
^{1}H NMR Spectrum of *N*,*N*-Di-*tert*-amyl-5-methylthiazol-2-amine (**12a**) in $CDCl_3$



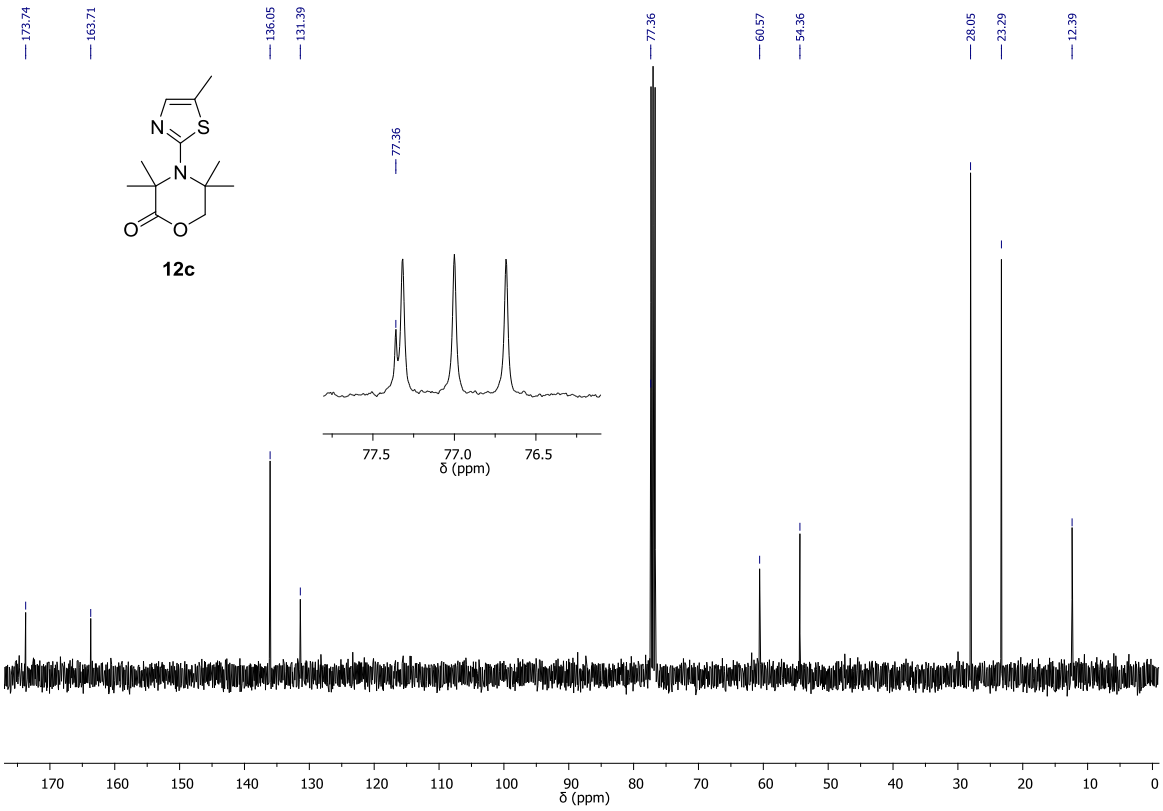
^{13}C NMR Spectrum of *N*,*N*-Di-*tert*-amyl-5-methylthiazol-2-amine (**12a**) in $CDCl_3$



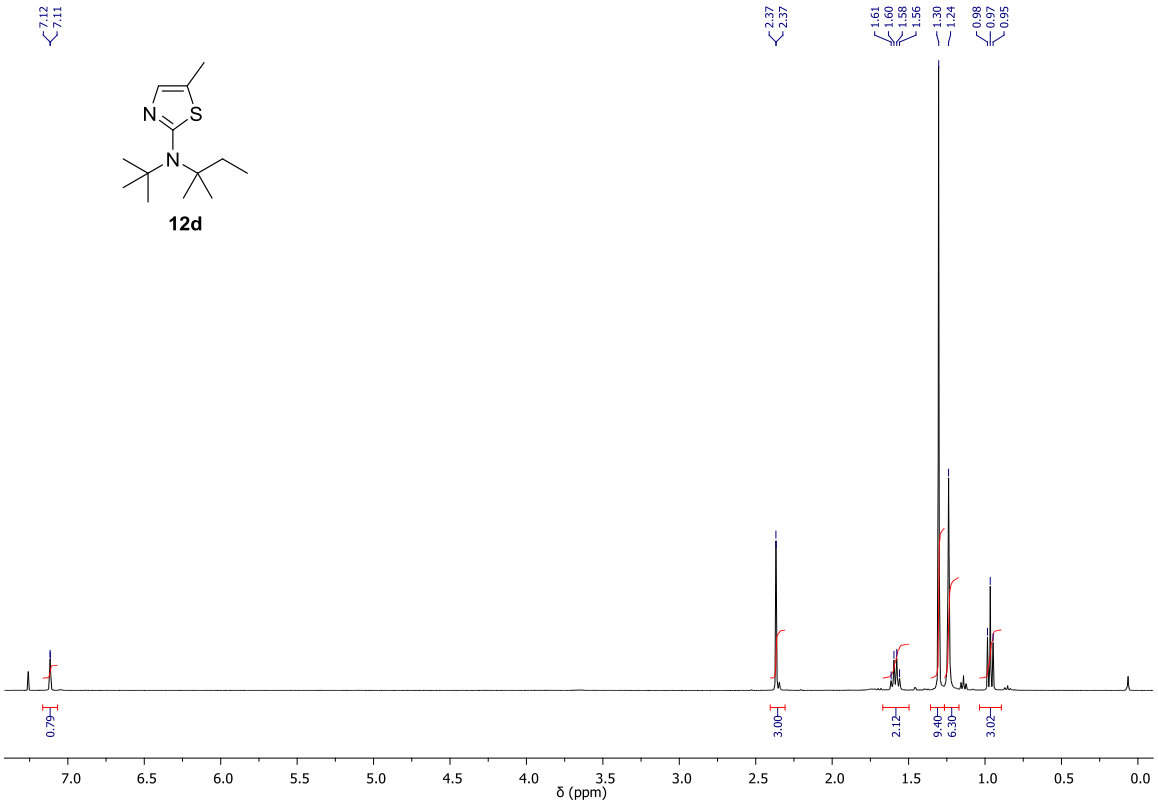
^{1}H NMR Spectrum of 3,3,5,5-Tetramethyl-4-(5-methylthiazol-2-yl)morpholin-2-one (**12c**) in $CDCl_3$



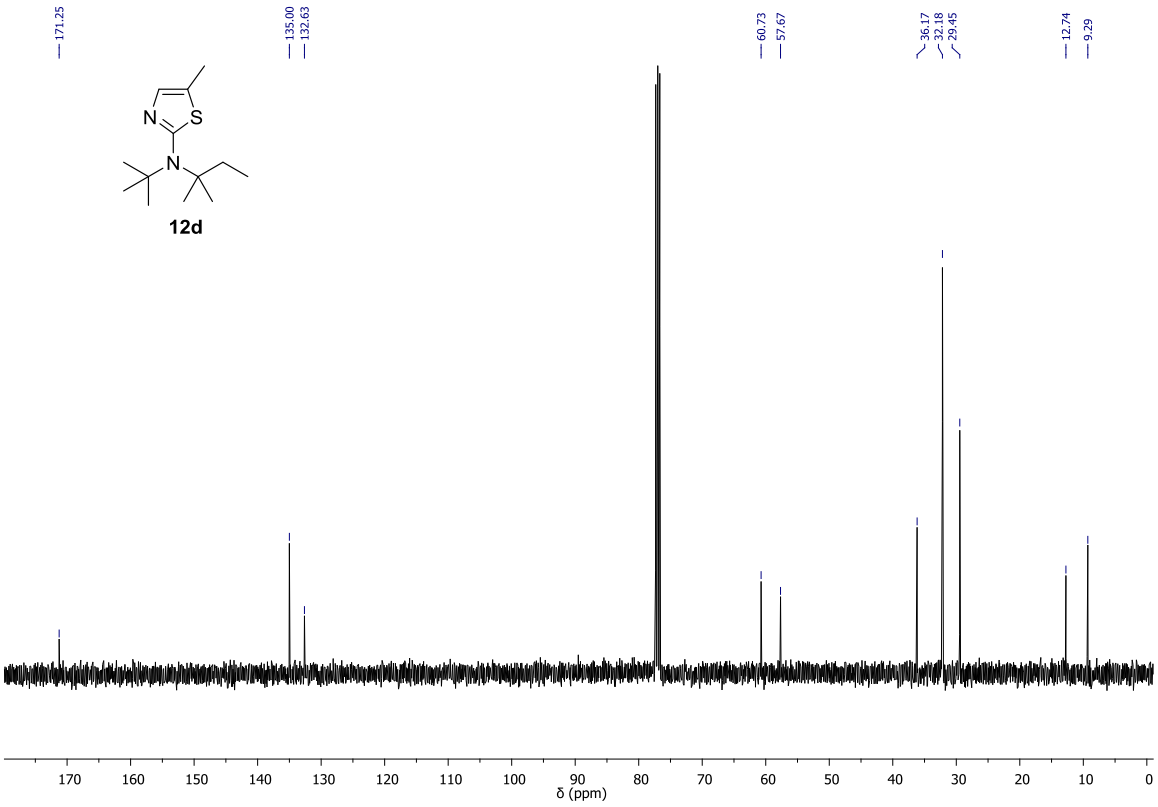
^{13}C NMR Spectrum of 3,3,5,5-Tetramethyl-4-(5-methylthiazol-2-yl)morpholin-2-one (**12c**) in $CDCl_3$



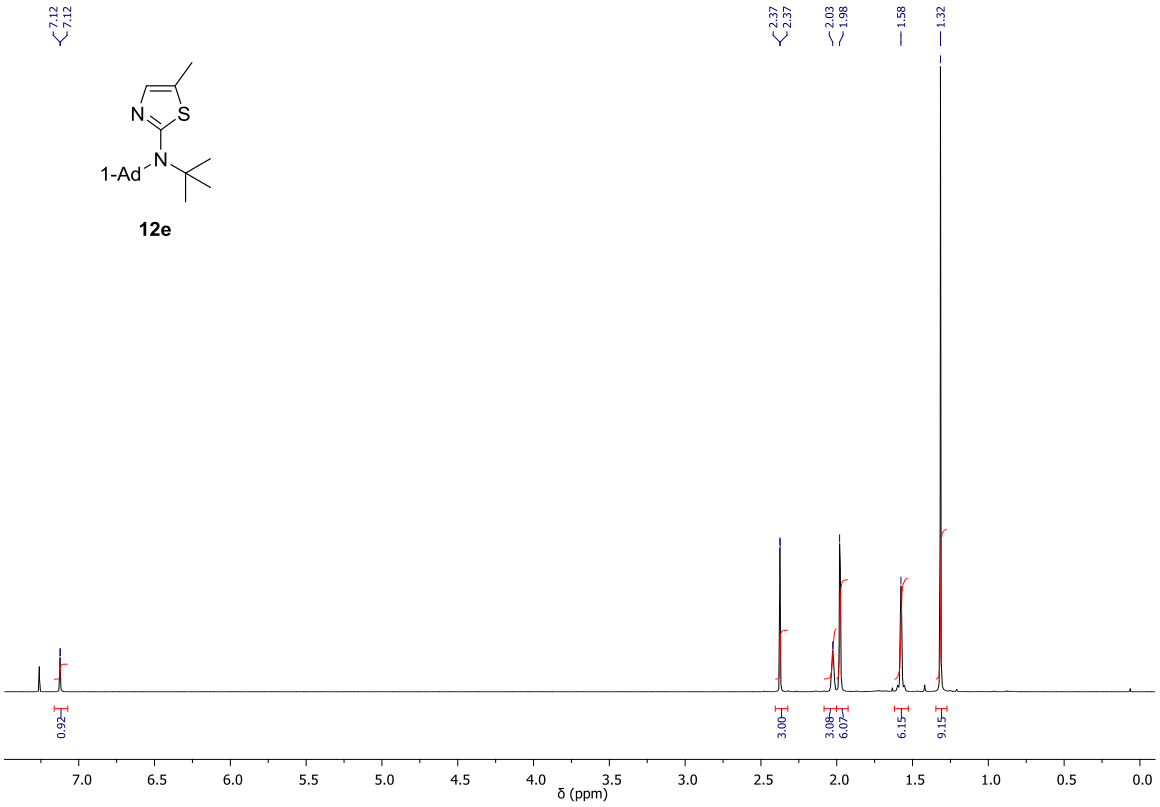
^{1}H NMR Spectrum of *N*-*tert*-Amyl-*N*-*tert*-butyl-5-methylthiazol-2-amine (**12d**) in $CDCl_3$



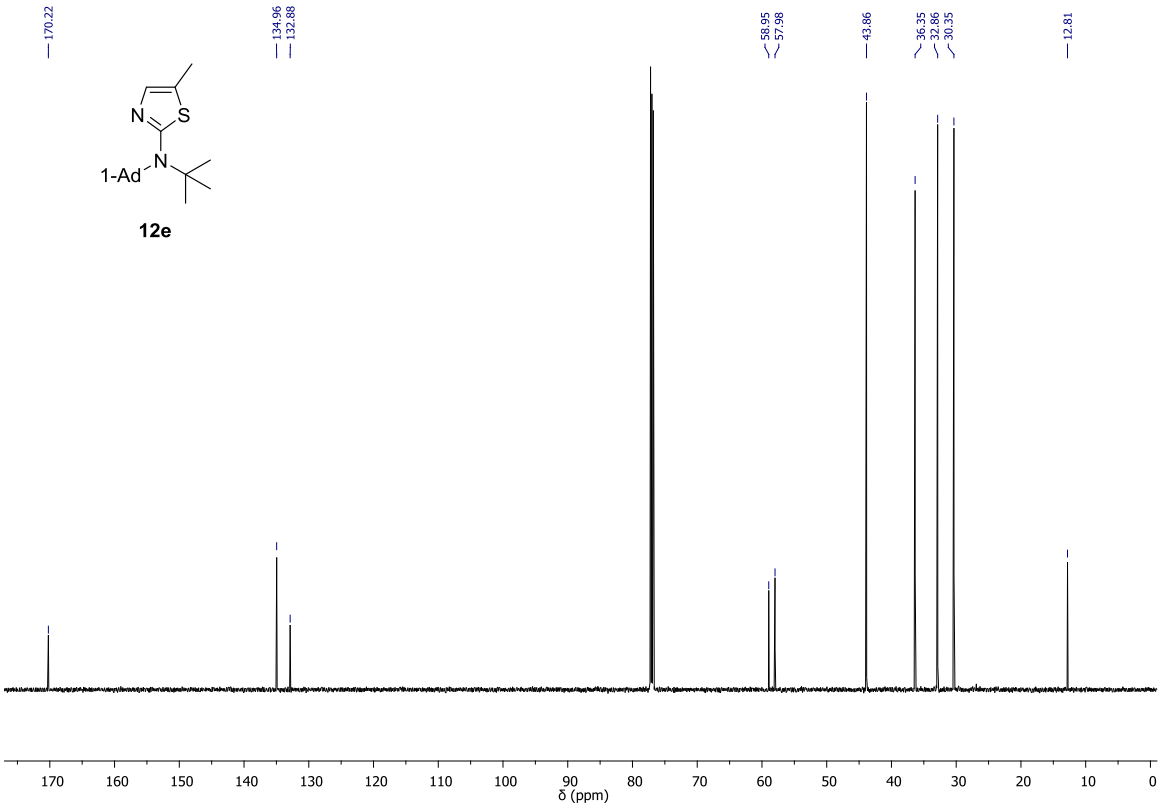
^{13}C NMR Spectrum of *N*-*tert*-Amyl-*N*-*tert*-butyl-5-methylthiazol-2-amine (**12d**) in $CDCl_3$



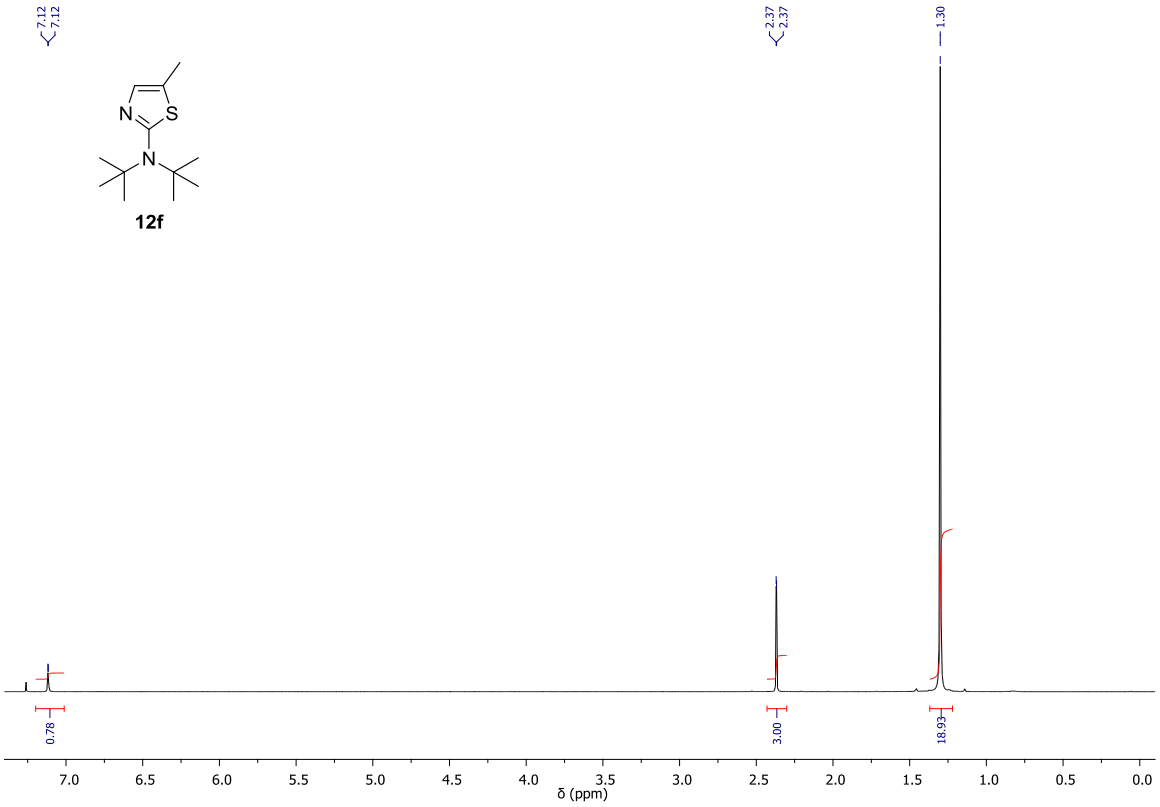
^{1}H NMR Spectrum of *N*-1-Adamantyl-*N*-*tert*-butyl-5-methylthiazol-2-amine (**12e**) in $CDCl_3$



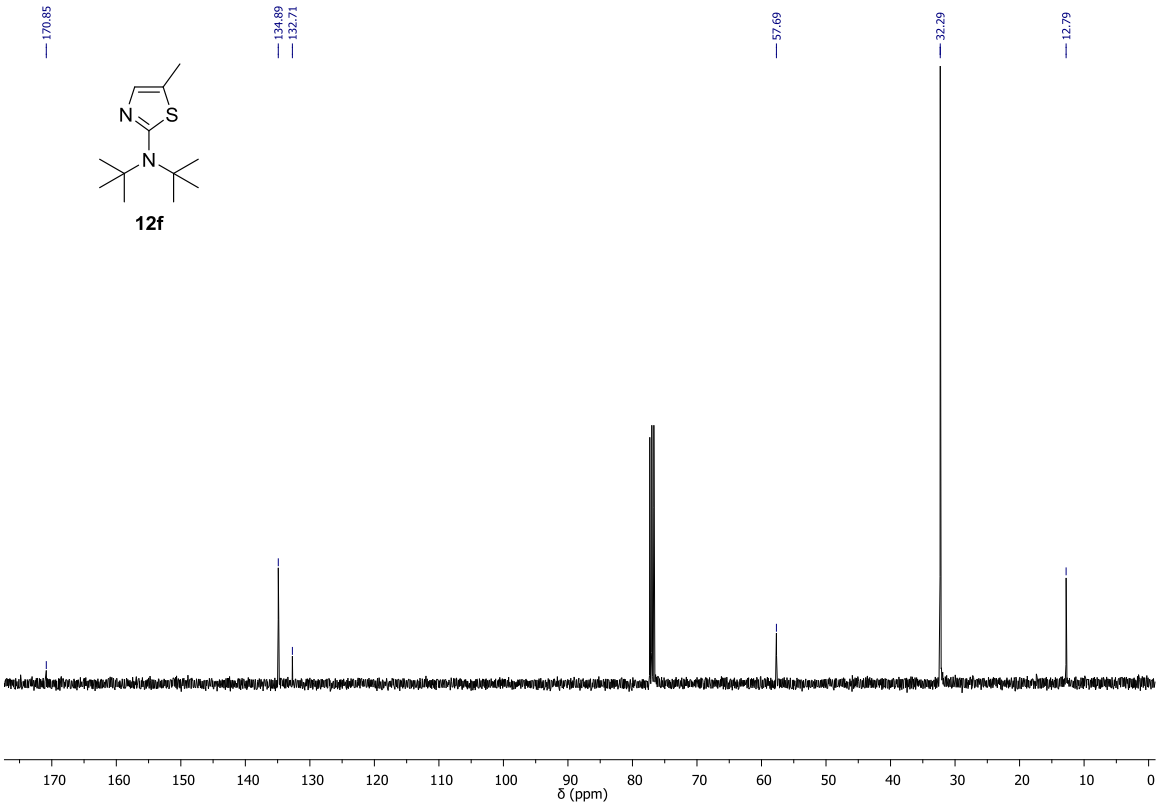
^{13}C NMR Spectrum of *N*-1-Adamantyl-*N*-*tert*-butyl-5-methylthiazol-2-amine (**12e**) in $CDCl_3$



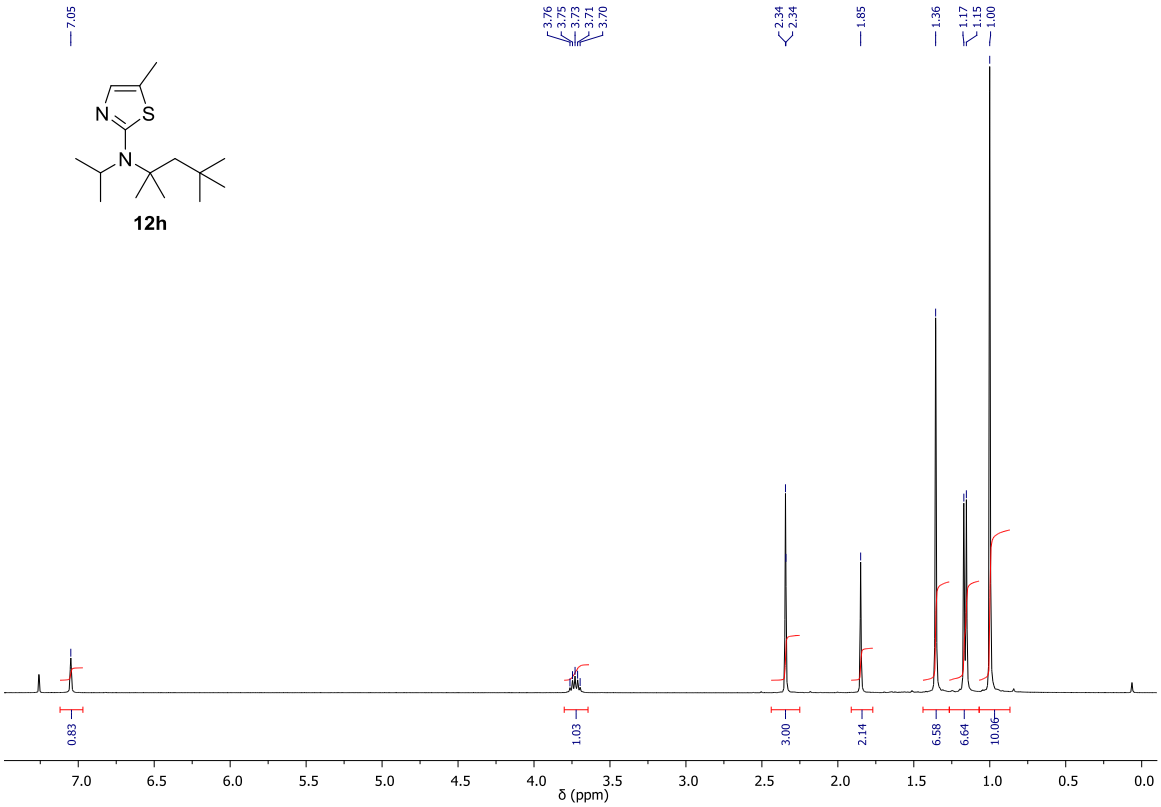
^{1}H NMR Spectrum of *N*,*N*-Di-*tert*-butyl-5-methylthiazol-2-amine (**12f**) in $CDCl_3$



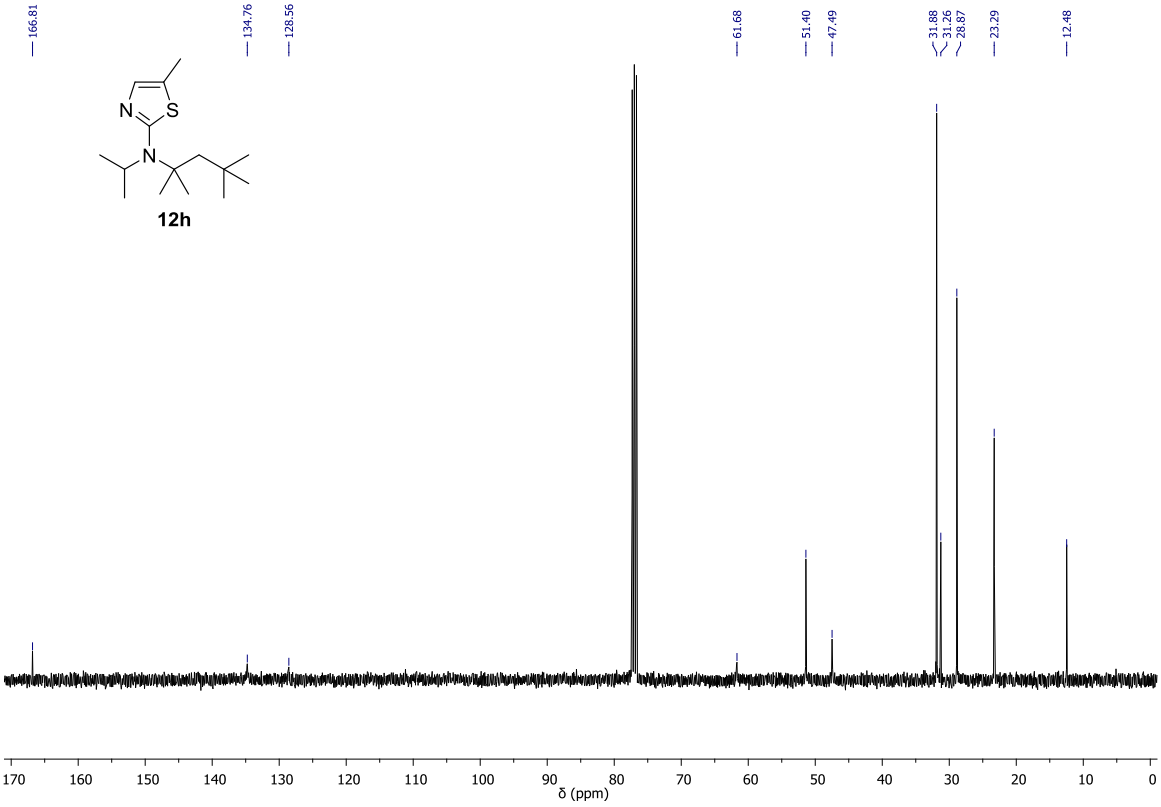
^{13}C NMR Spectrum of *N*,*N*-Di-*tert*-butyl-5-methylthiazol-2-amine (**12f**) in $CDCl_3$



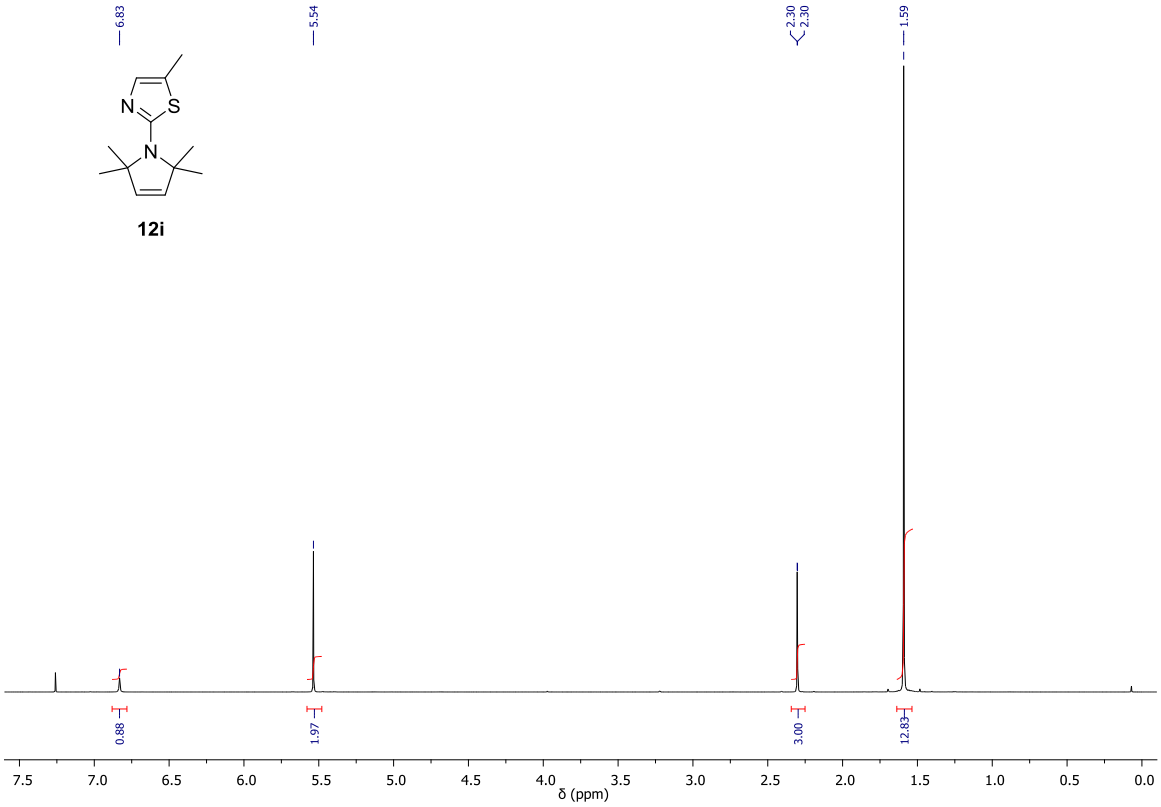
^{1}H NMR Spectrum of *N*-Isopropyl-5-methyl-*N*-*tert*-octylthiazol-2-amine (**12h**) in $CDCl_3$



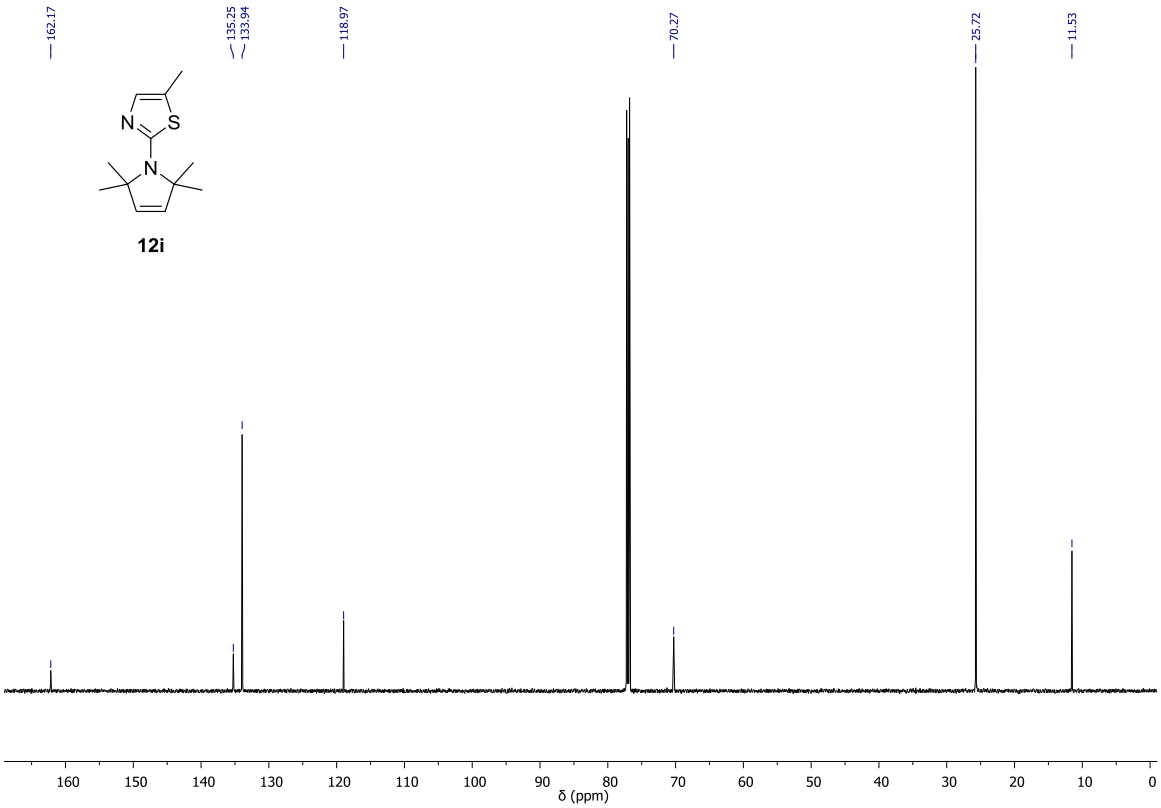
^{13}C NMR Spectrum of *N*-Isopropyl-5-methyl-*N*-*tert*-octylthiazol-2-amine (**12h**) in $CDCl_3$



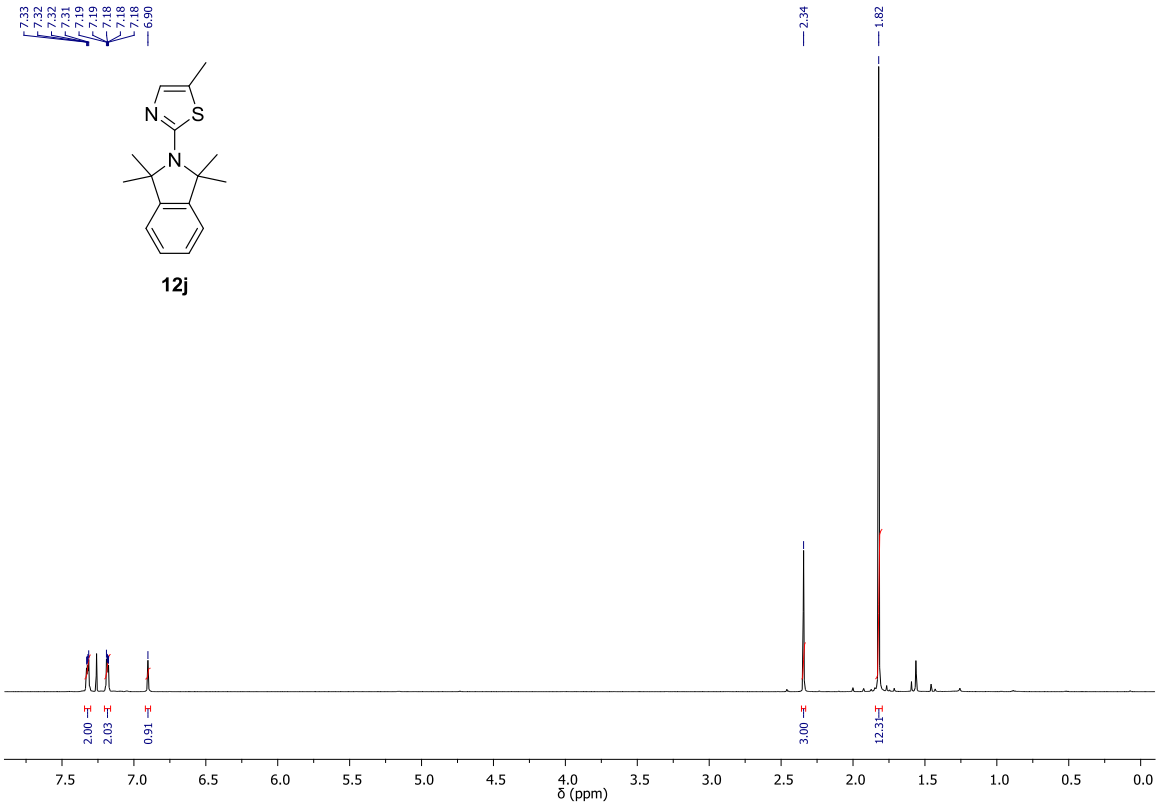
^{1}H NMR Spectrum of 5-Methyl-2-(2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yl)thiazole (**12i**) in $CDCl_3$



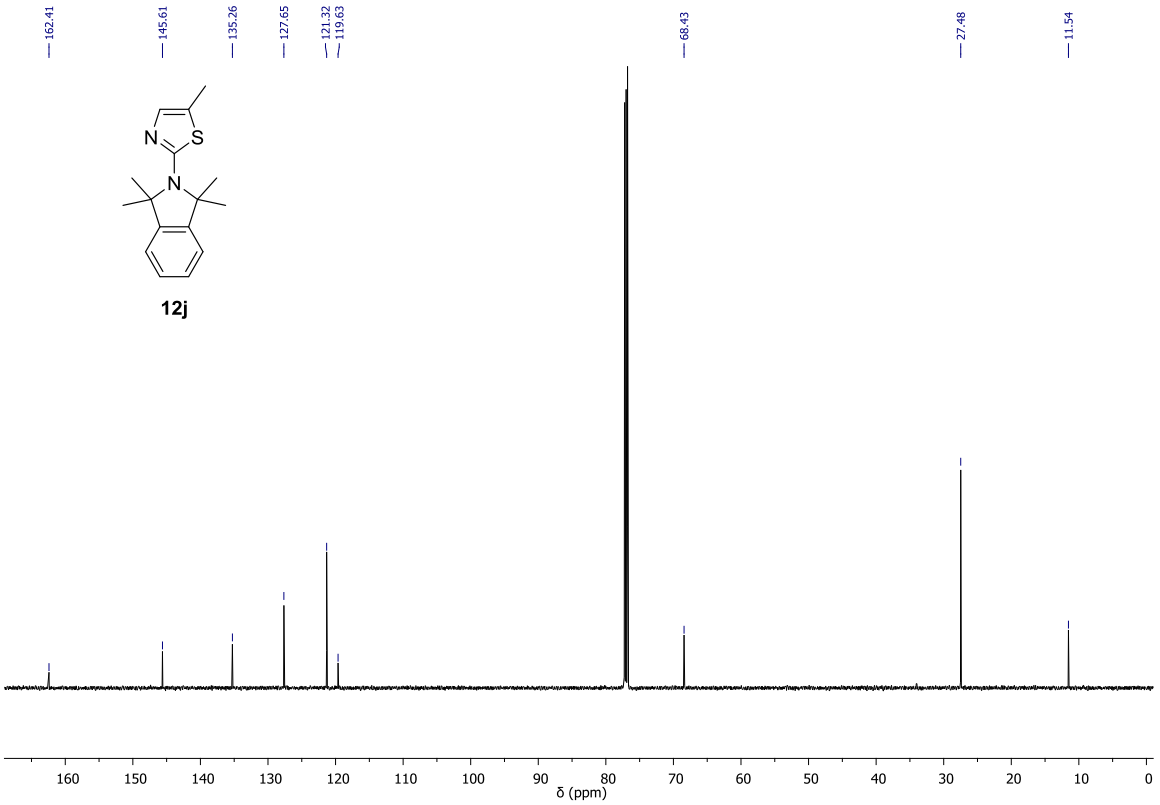
^{13}C NMR Spectrum of 5-Methyl-2-(2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yl)thiazole (**12i**) in $CDCl_3$



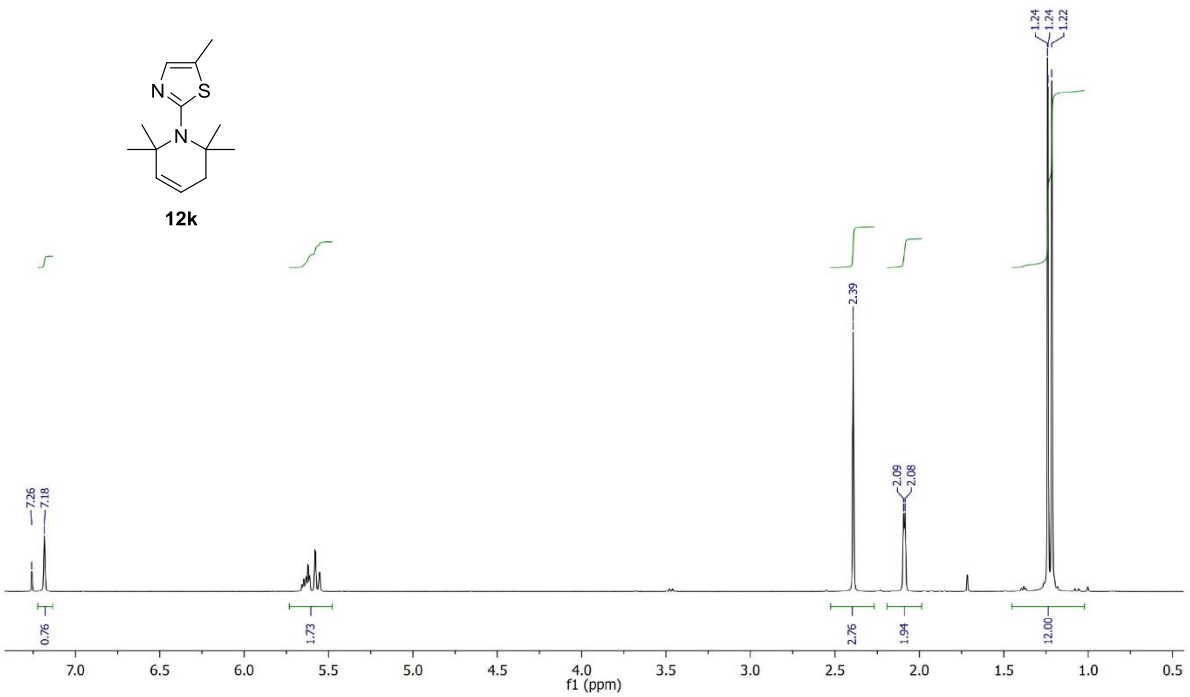
^{1}H NMR Spectrum of 5-Methyl-2-(1,1,3,3-tetramethylisoindolin-2-yl)thiazole (**12j**) in $CDCl_3$



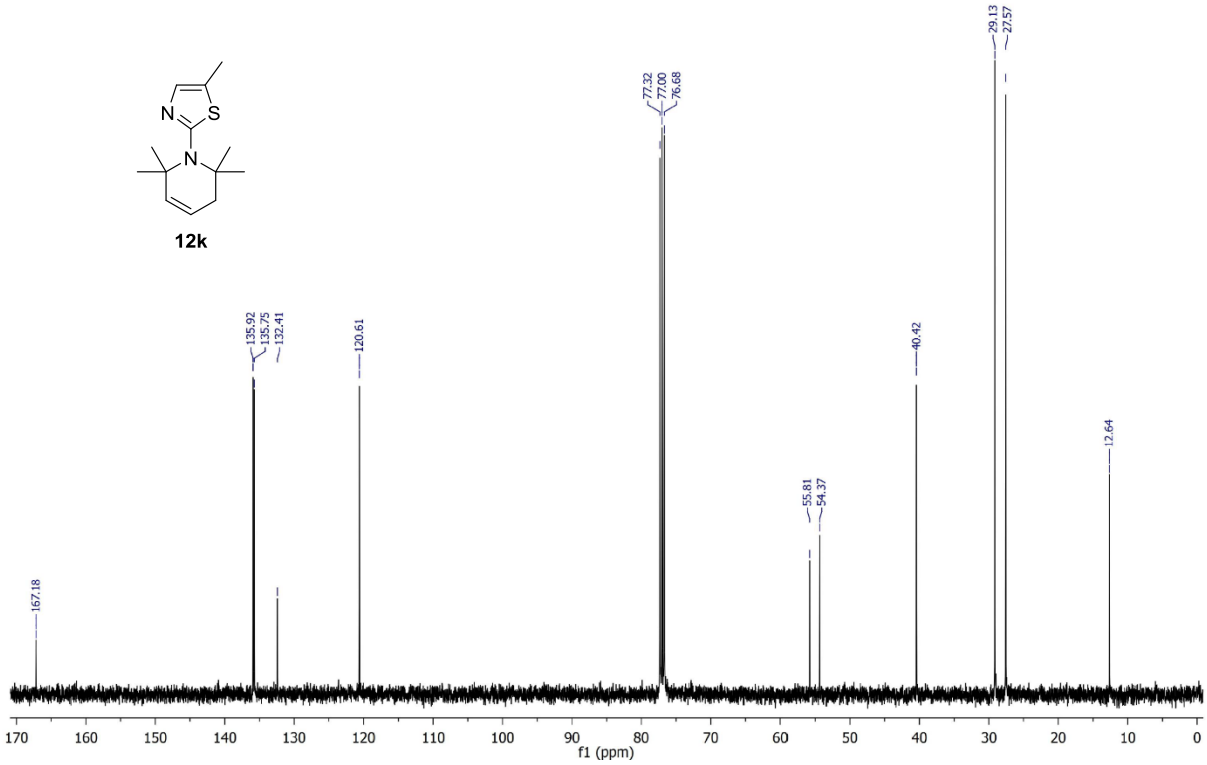
^{13}C NMR Spectrum of 5-Methyl-2-(1,1,3,3-tetramethylisoindolin-2-yl)thiazole (**12j**) in $CDCl_3$



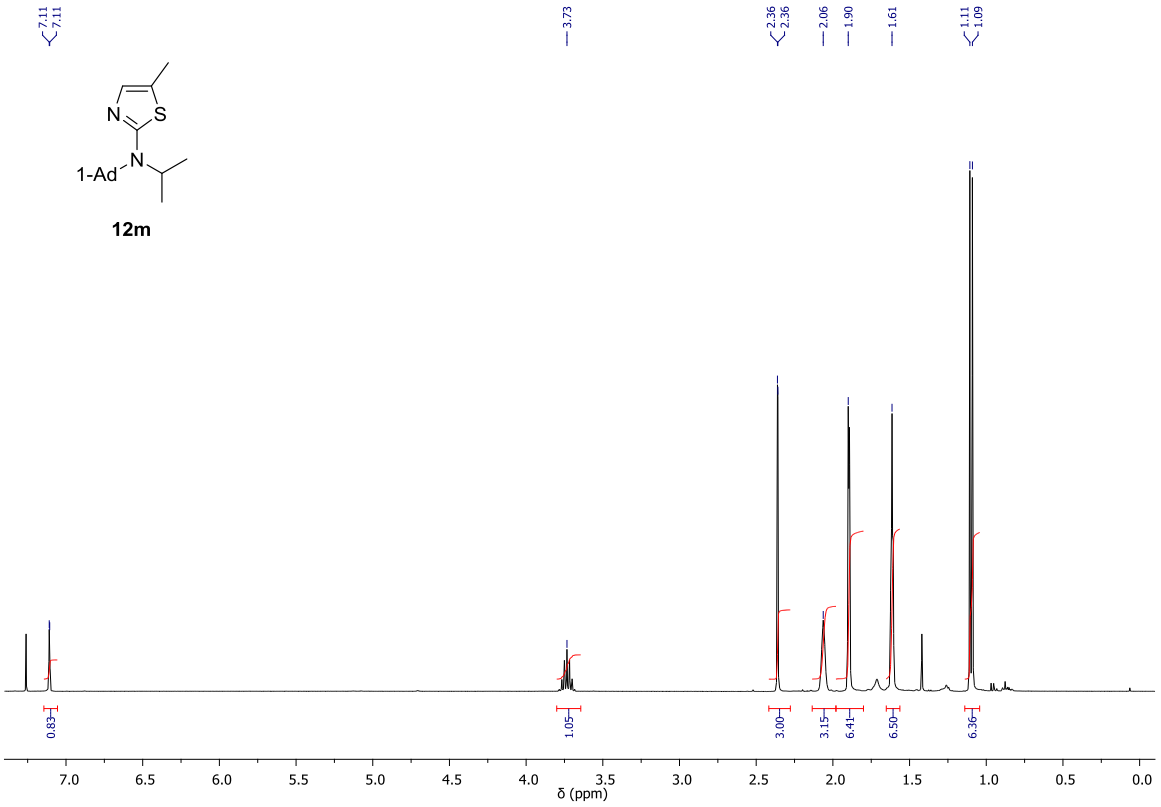
^{1}H NMR Spectrum of 5-Methyl-2-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-1-yl)thiazole (**12k**) in $CDCl_3$



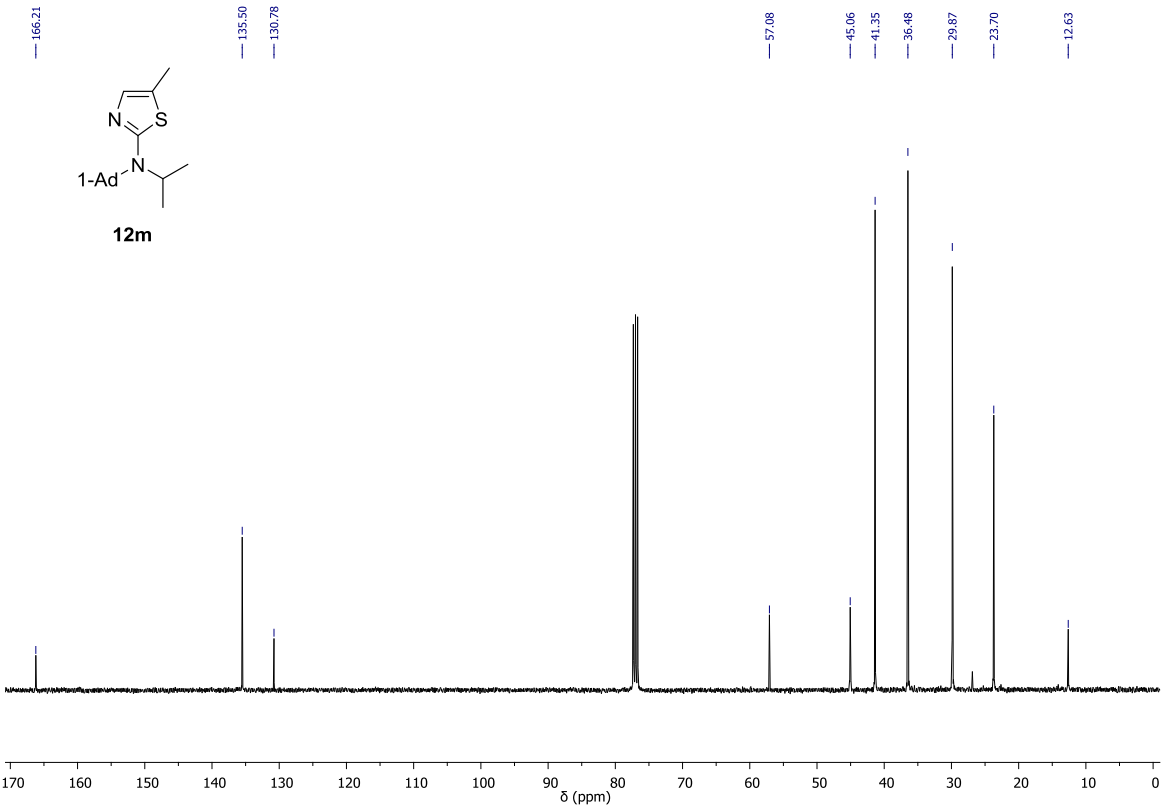
^{13}C NMR Spectrum of 5-Methyl-2-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-1-yl)-thiazole (**12k**) in $CDCl_3$



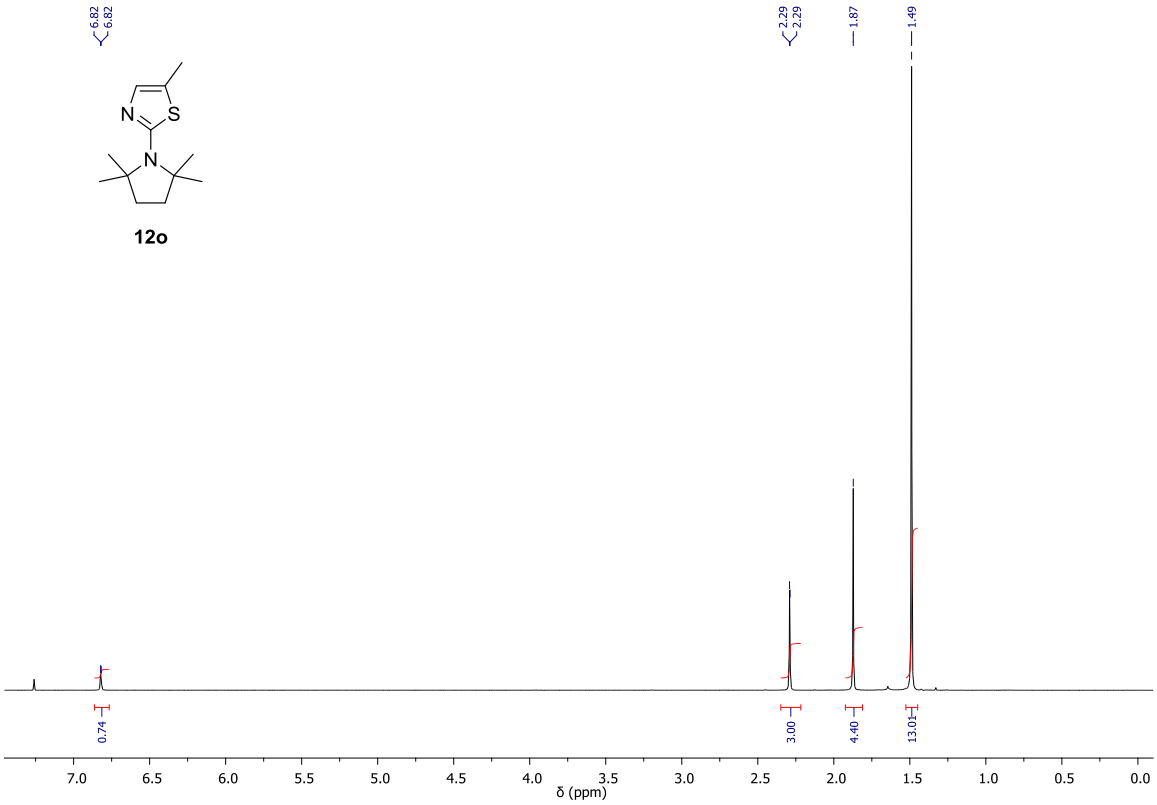
^{1}H NMR Spectrum of *N*-1-Adamantyl-*N*-isopropyl-5-methylthiazol-2-amine (**12m**) in $CDCl_3$



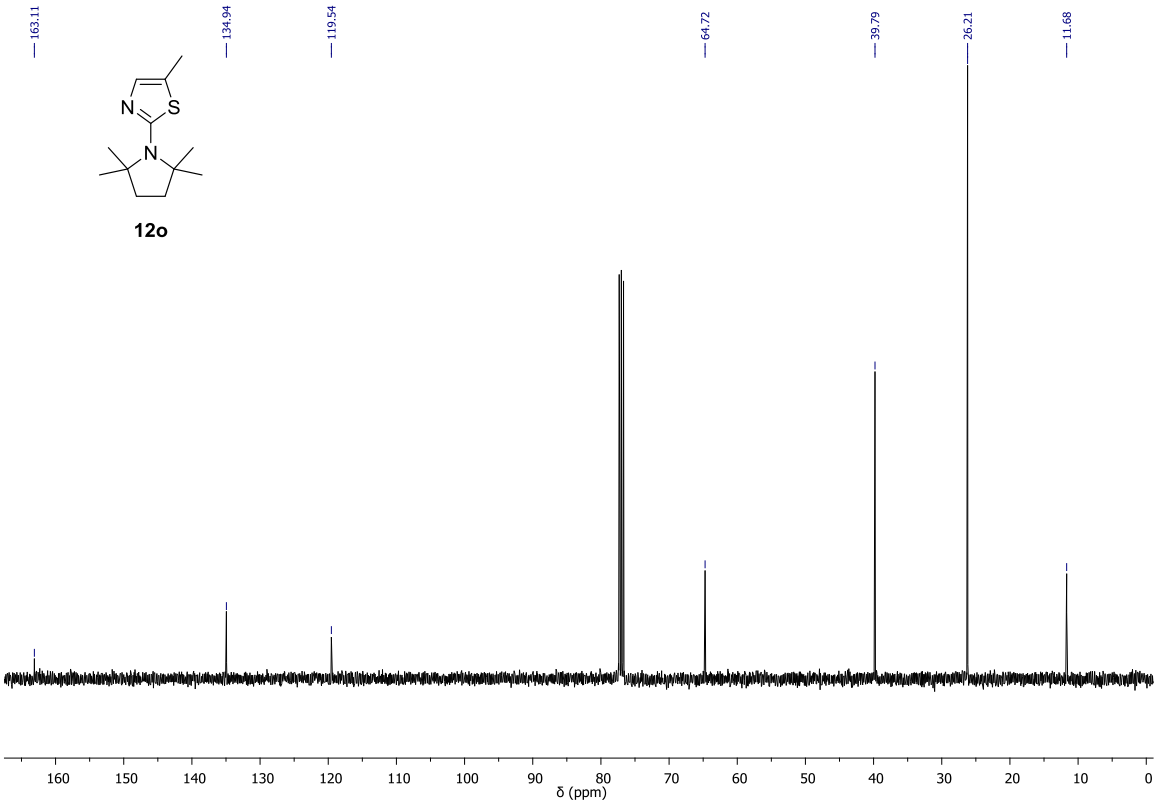
^{13}C NMR Spektrum of *N*-1-Adamantyl-*N*-isopropyl-5-methylthiazol-2-amine (**12m**) in $CDCl_3$



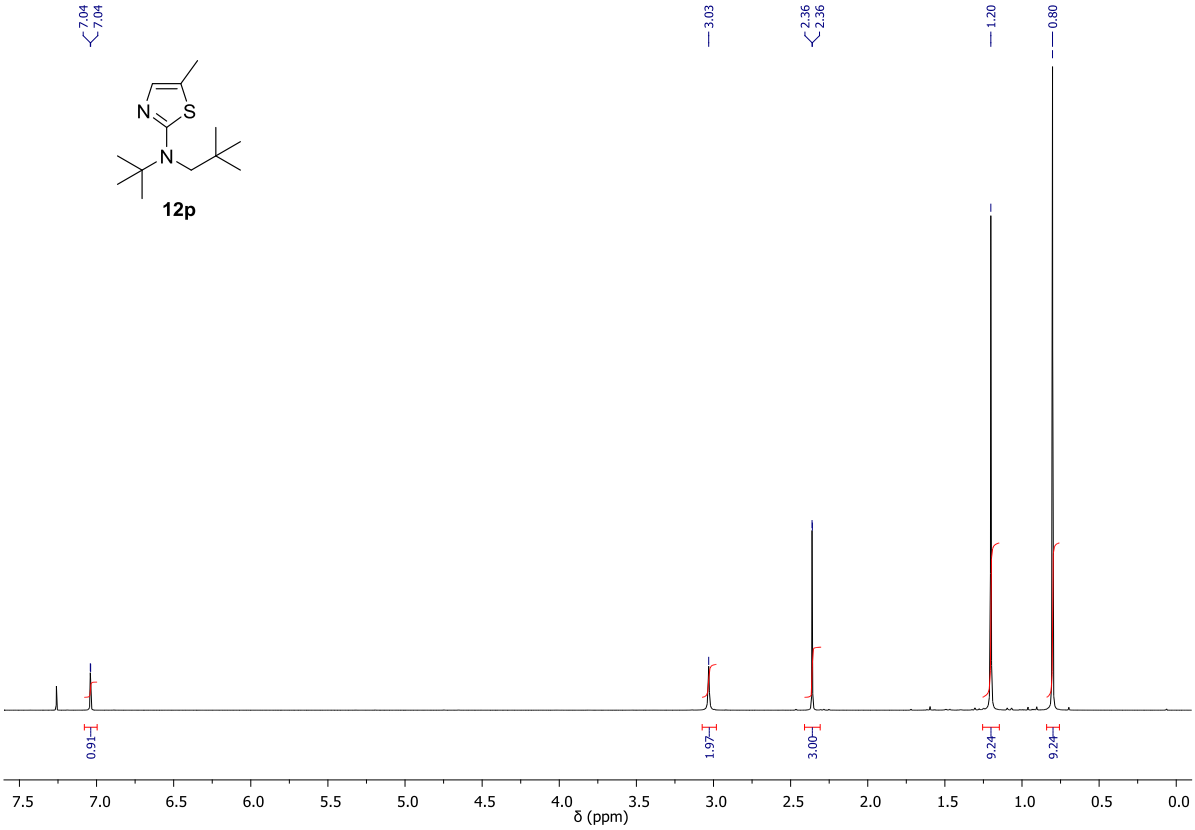
^{1}H NMR Spectrum of 5-Methyl-2-(2,2,5,5-tetramethylpyrrolidin-1-yl)thiazole (**12o**) in $CDCl_3$



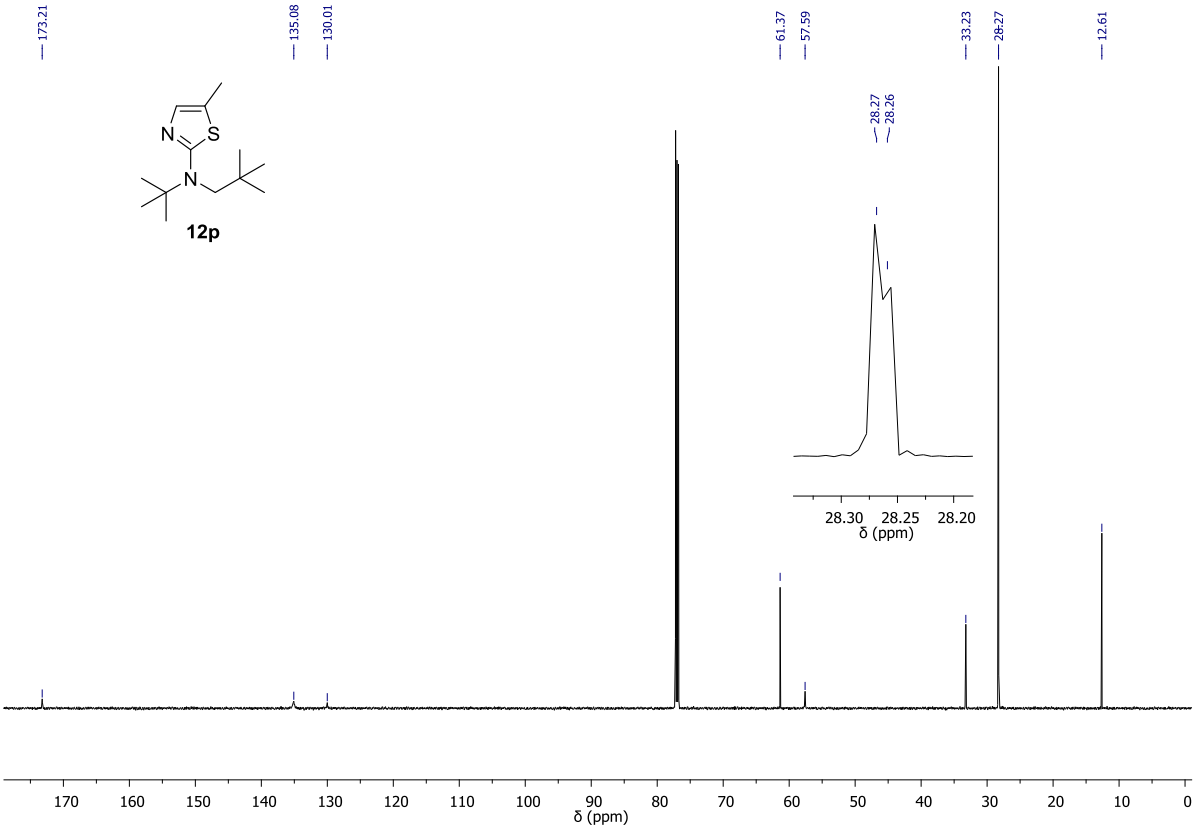
^{13}C NMR Spectrum of 5-Methyl-2-(2,2,5,5-tetramethylpyrrolidin-1-yl)thiazole (**12o**) in $CDCl_3$



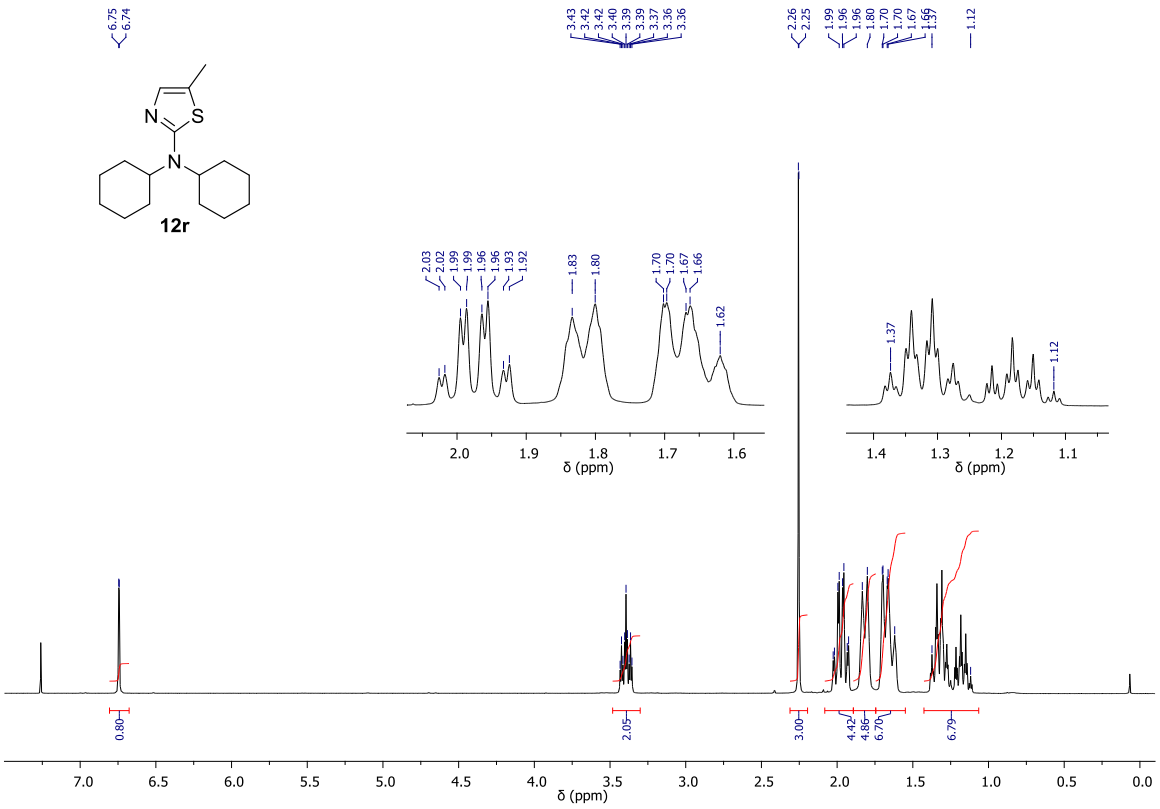
^{1}H NMR Spectrum of *N*-*tert*-Butyl-5-methyl-*N*-neopentylthiazol-2-amine (**12p**) in $CDCl_3$



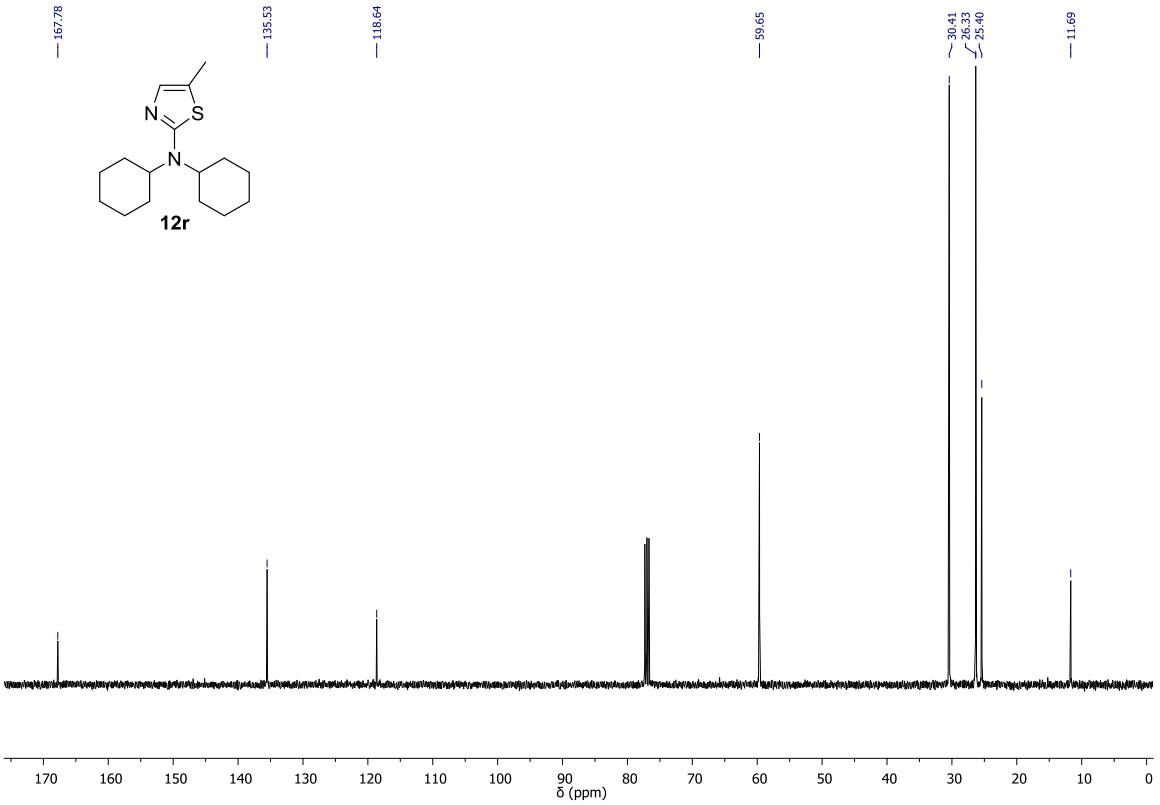
^{13}C NMR Spectrum of *N*-*tert*-Butyl-5-methyl-*N*-neopentylthiazol-2-amine (**12p**) in $CDCl_3$



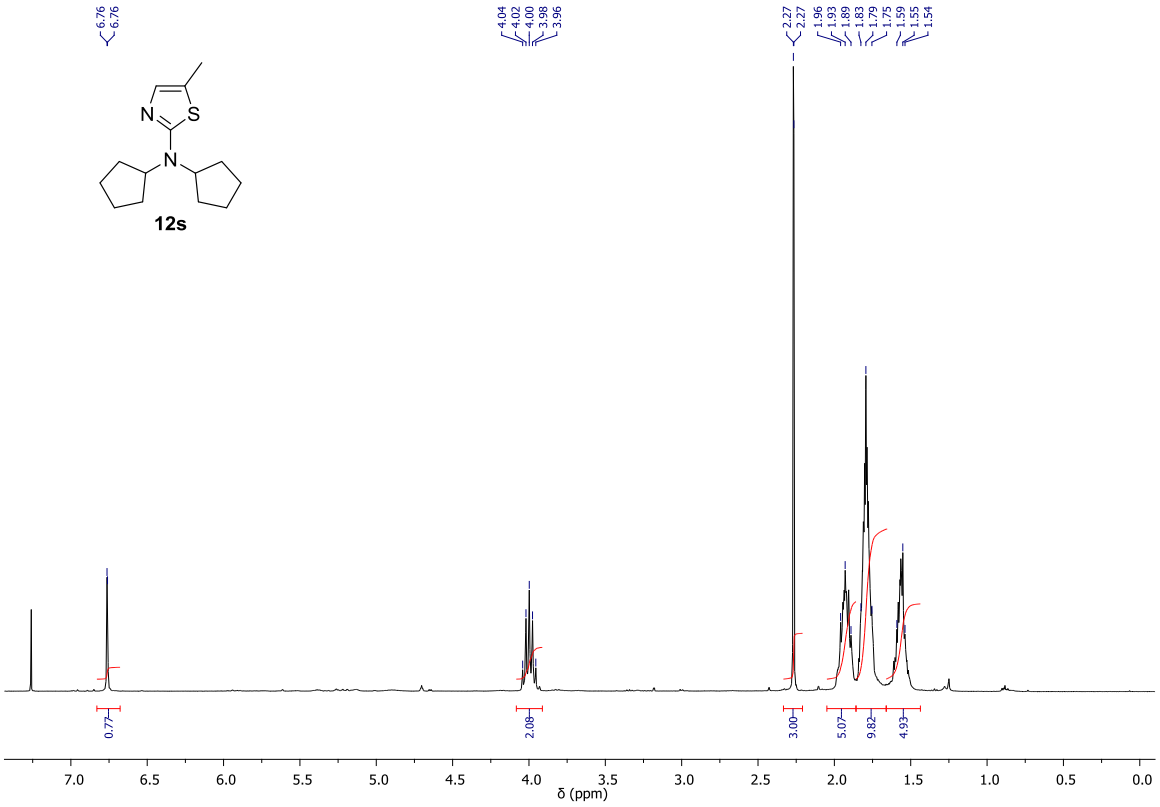
^{1}H NMR Spectrum of *N*,*N*-Dicyclohexyl-5-methylthiazol-2-amine (**12r**) in $CDCl_3$



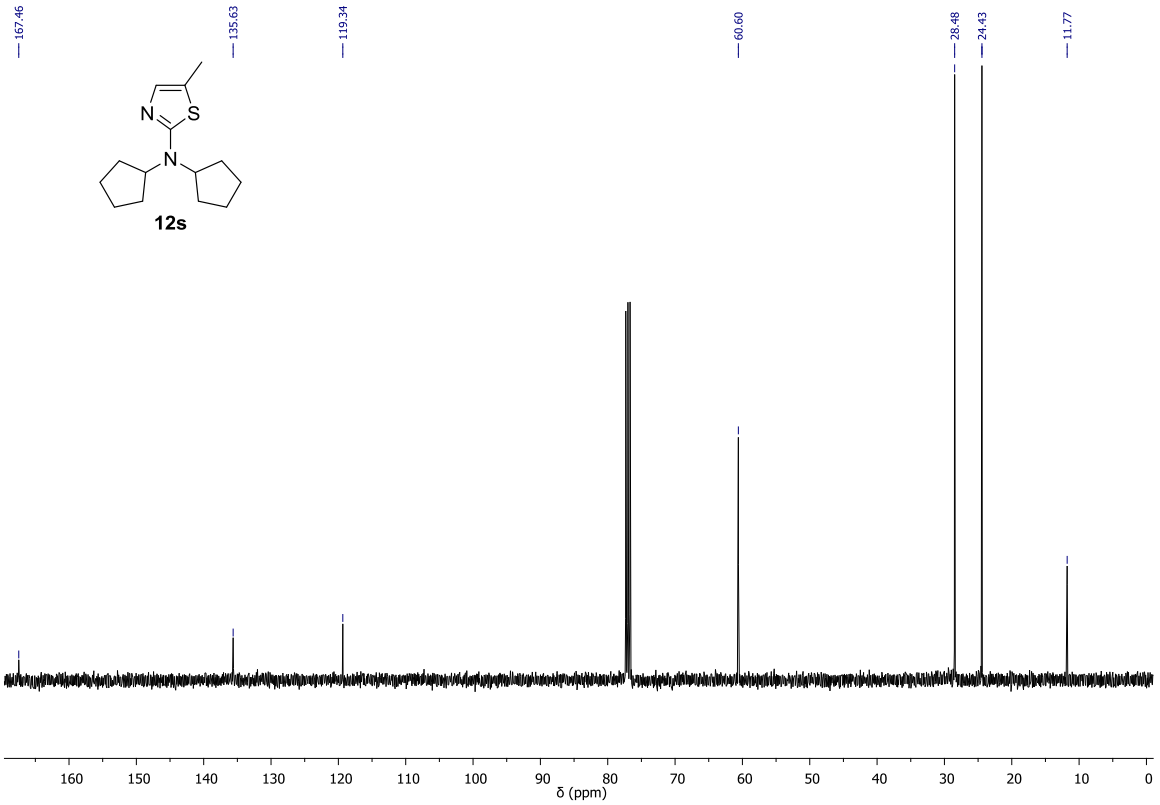
^{13}C NMR Spectrum of *N*,*N*-Dicyclohexyl-5-methylthiazol-2-amine (**12r**) in $CDCl_3$



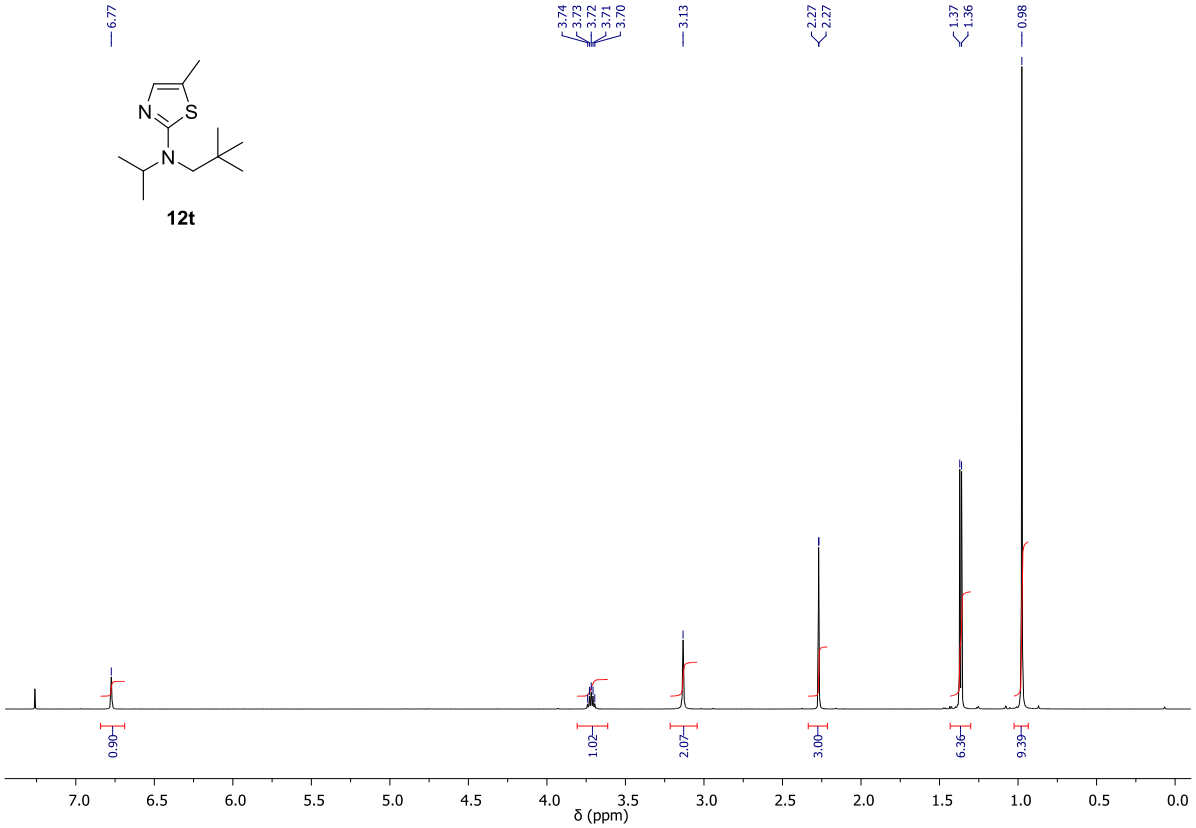
^{1}H NMR Spectrum of *N*,*N*-Dicyclopentyl-5-methylthiazol-2-amine (**12s**) in $CDCl_3$



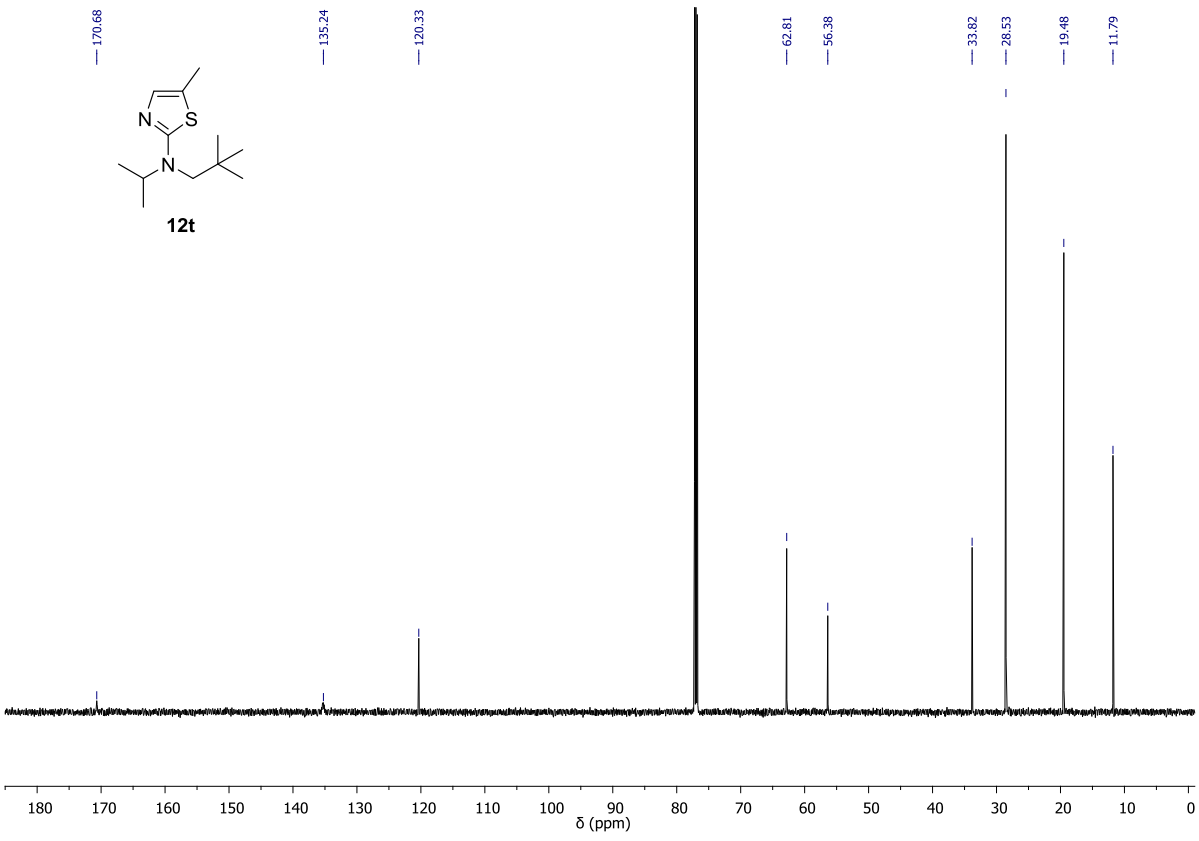
^{13}C NMR Spectrum of *N*,*N*-Dicyclopentyl-5-methylthiazol-2-amine (**12s**) in $CDCl_3$



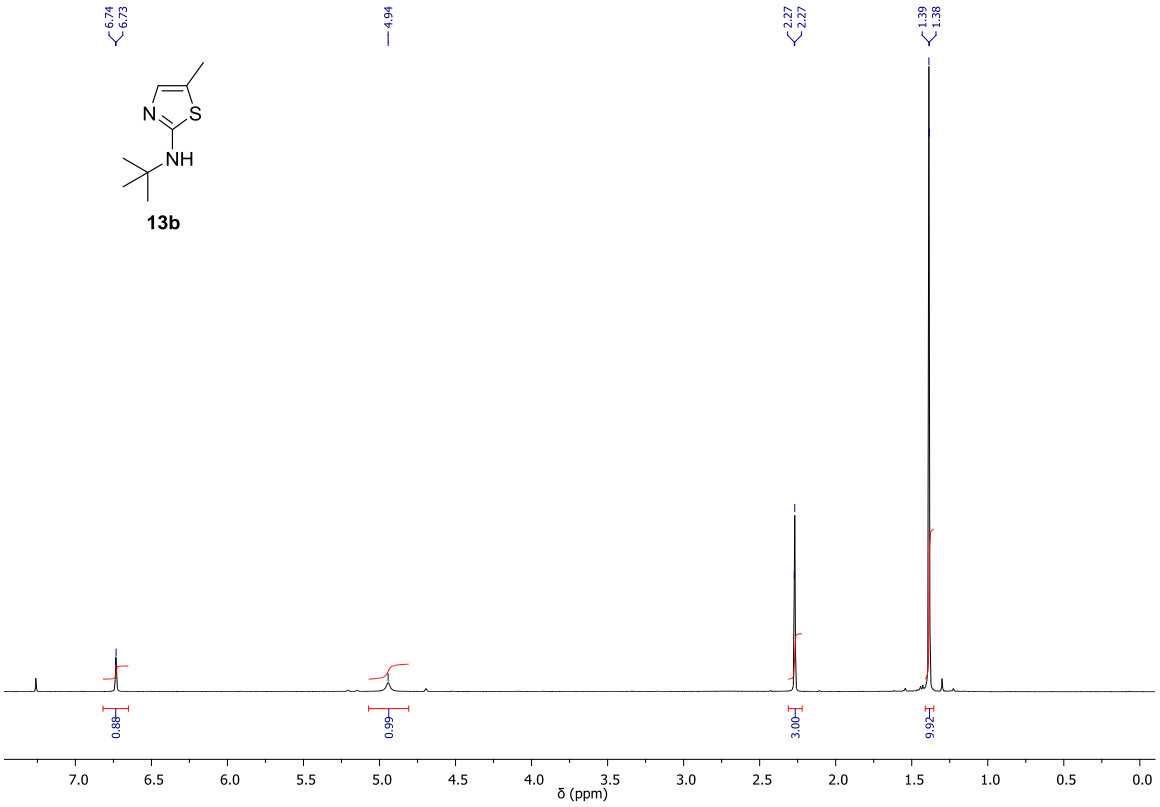
^{1}H NMR Spectrum of *N*-Isopropyl-5-methyl-*N*-neopentylthiazol-2-amine (**12t**) in $CDCl_3$



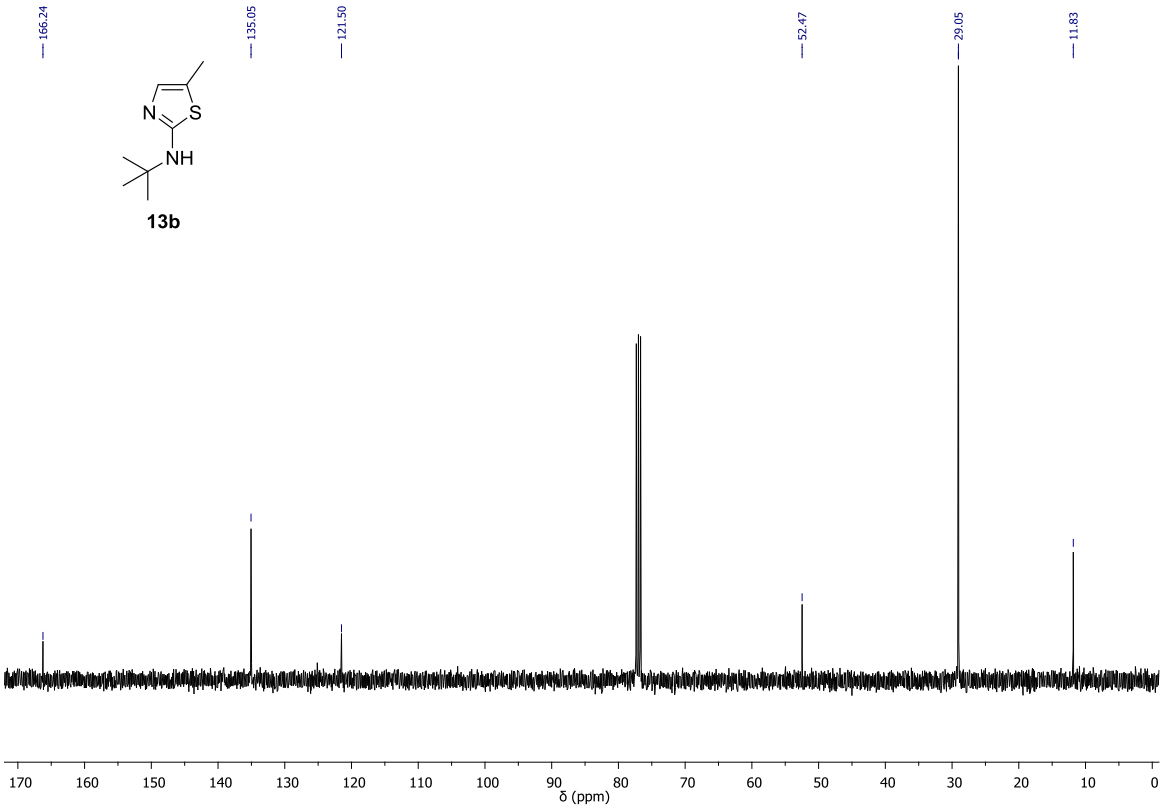
^{13}C NMR Spectrum of *N*-Isopropyl-5-methyl-*N*-neopentylthiazol-2-amine (**12t**) in $CDCl_3$



^{1}H NMR Spektrum of *N*-*tert*-Butyl-5-methylthiazol-2-amine (**13b**) in $CDCl_3$



^{13}C NMR Spectrum of *N*-*tert*-Butyl-5-methylthiazol-2-amine (**13b**) in $CDCl_3$



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