

Sabinene a new green solvent: use in the synthesis of thiazolo[5,4-*b*]pyridines by thermal or microwave activation.

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Supporting Information

Experimental part

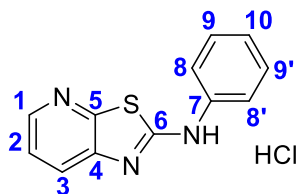
All reagents were purchased from commercial suppliers and used without further purification, ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX 250 (^{13}C , 62.9 MHz) (Bruker, Wissembourg, France), Bruker Avance II 250.13 (^{13}C , 63 MHz), Bruker Avance 400.13 (^{13}C , 101 MHz) (Bruker, Wissembourg, France), or on a Bruker Avance III HD nanobay 400.13 (^{13}C , 101 MHz) (Bruker, Wissembourg, France). Chemical shifts are expressed in parts per million (ppm) and were calibrated on deuterated or residual non-deuterated solvent peaks for ^1H and ^{13}C spectra. The following abbreviations are used for proton spectra multiplicities: b: broad, s: singlet, d: doublet, t: triplet, q: quartet, p: pentuplet, m: multiplet. Microwave-assisted reactions were carried out in a Biotage Initiator microwave synthesis instrument and temperatures were measured by an IR sensor (Biotage, Uppsala, Sweden). Melting points (p.m. [$^{\circ}\text{C}$]) were taken on samples placed in open capillary tubes on a Thermo Fisher Melting Point Instrument Digital 9000 Series IA9200X6 and were not corrected. High-resolution mass spectra (HRMS) were performed on a Bruker 4G Maxis UHR-q-TOF mass spectrometer (Bruker, Wissembourg, France), with an electrospray ionization (ESI) mode. The numbering of the atoms on the molecules has been chosen arbitrarily and is indicated on the drawings of the molecules for a better understanding of the NMR spectra

General procedure (1) : Substituted 3-amino-2-chloropyridine (1.65 mmol; 1.1 equiv.) and substituted isothiocyanate (1.5 mmol; 1 equiv.) were dissolved in 1mL sabinene and stirred at 100°C for 16 h. The mixture was allowed to cool to room temperature. The mixture was then filtered and washed with ethyl acetate followed by diethyl ether. The product was isolated without further purification.

General procedure (2) : In a sealed tube, substituted 3-amino-2-chloropyridine (1,65 mmol ; 1,1 equiv.) and substituted isothiocyanate (1,5 mmol ; 1 equiv.) were dissolved in 1.0 mL of sabinene. The mixture is placed under microwave irradiation during 2 h at 130°C . The mixture was allowed to cool to room temperature. Then, the reaction was filtered and washed with ethyl acetate followed by diethyl ether. The product was isolated without further purification.

General procedure (3) : In a sealed tube, substituted 3-amino-2-chloropyridine (1.65 mmol; 1.1 equiv.) and substituted isothiocyanate (1.5 mmol; 1 equiv.) were dissolved in the solvent consisting of 0.75 ml sabinene and 0.25 ml acetonitrile. The mixture was placed under microwave irradiation for 2 h at 130°C . After cooling to room temperature, the reaction mixture was filtered and washed with ethyl acetate followed by diethyl ether. The product was isolated without further purification

N-phenylthiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 1 was applied to phenyl isothiocyanate and 3-amino-2-chloropyridine to give *N*-phenylthiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 65% yield.

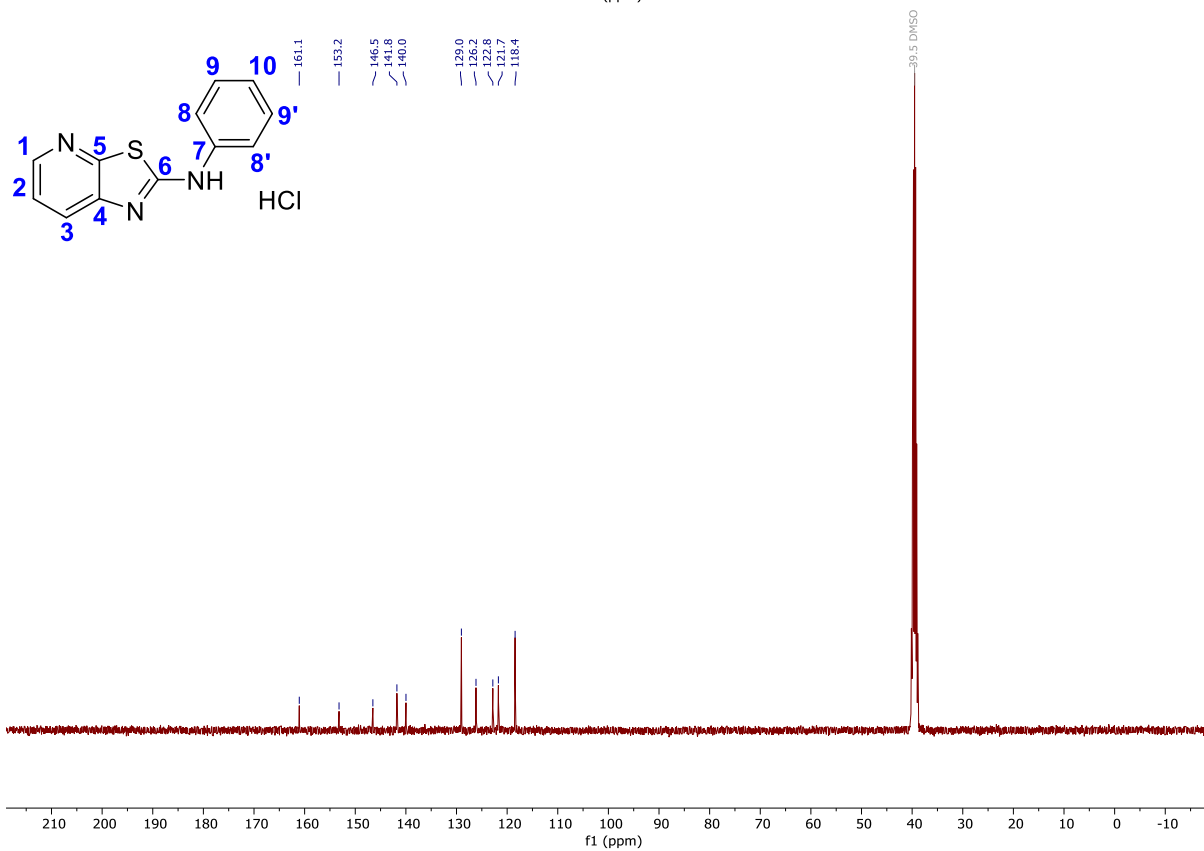
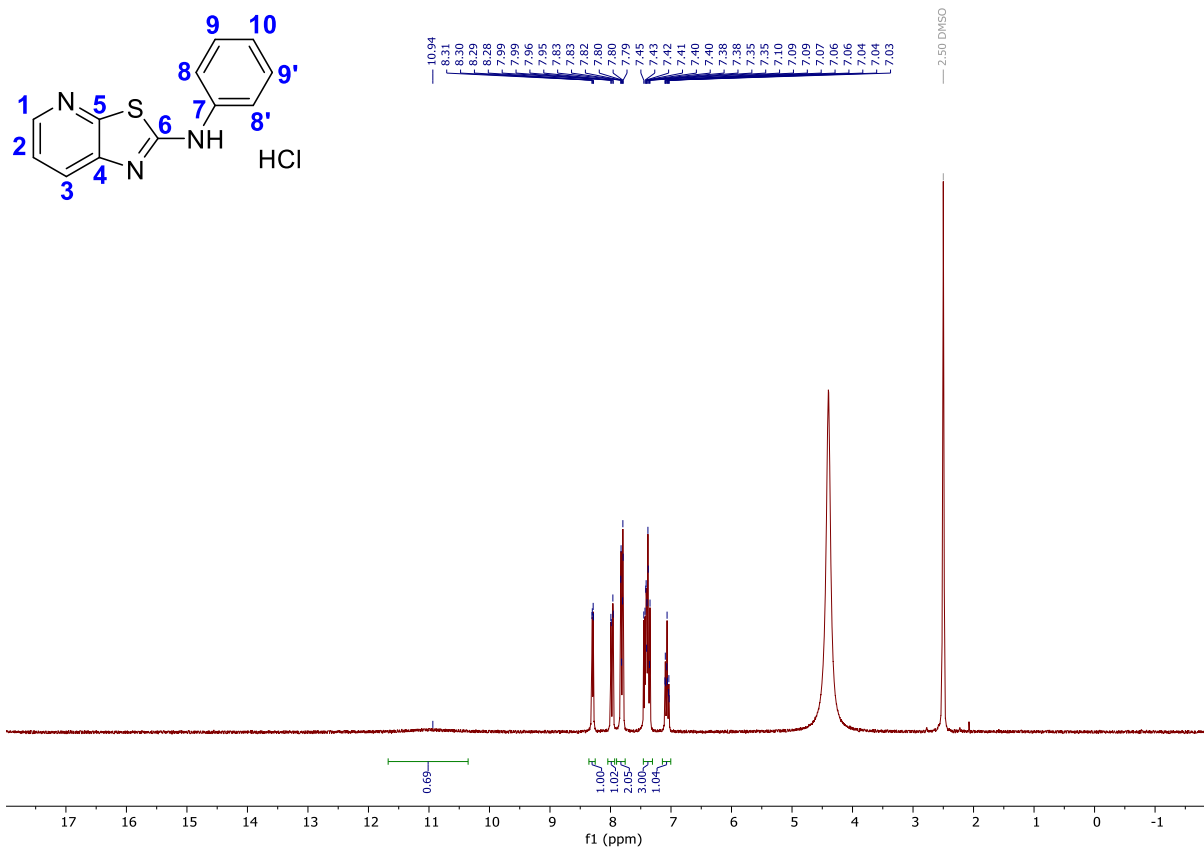
Aspect : beige powder

Melting point : 273°C (lit. 284-285°C) [40]

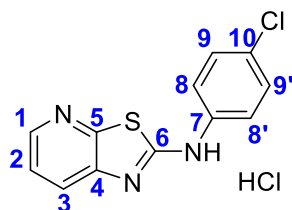
HRMS (ESI+): m/z calculated for $C_{12}H_{10}N_3S$ [$M + H^+$] = 228.0590 ; found = 228.0588

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 7.07 (tt, J = 7.3, 1.2 Hz, 1H, $^{10}H_{Ar}$), 7.32-7.41 (m, 2H, $^9H_{Ar}$ and $^8H_{Ar}$), 7.42 (dd, J = 8.1, 5.0 Hz, 1H, $^2H_{Ar}$), 7.81 (dd, J = 7.5, 1.3 Hz, 2H, $^8H_{Ar}$ and $^8'H_{Ar}$), 7.97 (dd, J = 8.2, 1.5 Hz, 1H, $^3H_{Ar}$), 8.29 (dd, J = 5.0, 1.5 Hz, 1H, $^1H_{Ar}$), 10.94 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 118.4 ($^8CH_{Ar}$ and $^8'CH_{Ar}$), 121.7 ($^2CH_{Ar}$), 122.8 ($^{10}CH_{Ar}$), 126.2 ($^3CH_{Ar}$), 129.0 ($^9CH_{Ar}$ and $^9'CH_{Ar}$), 140.0 ($^7C^{IV}$), 141.8 ($^1CH_{Ar}$), 146.5 ($^4C^{IV}$), 153.2 ($^5C^{IV}$) and 161.1 ($^6C^{IV}$).



N-(4-chlorophenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 1 was applied to 4-chlorophenyl isothiocyanate and 3-amino-2-chloropyridine to give *N*-(4-chlorophenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 59% yield.

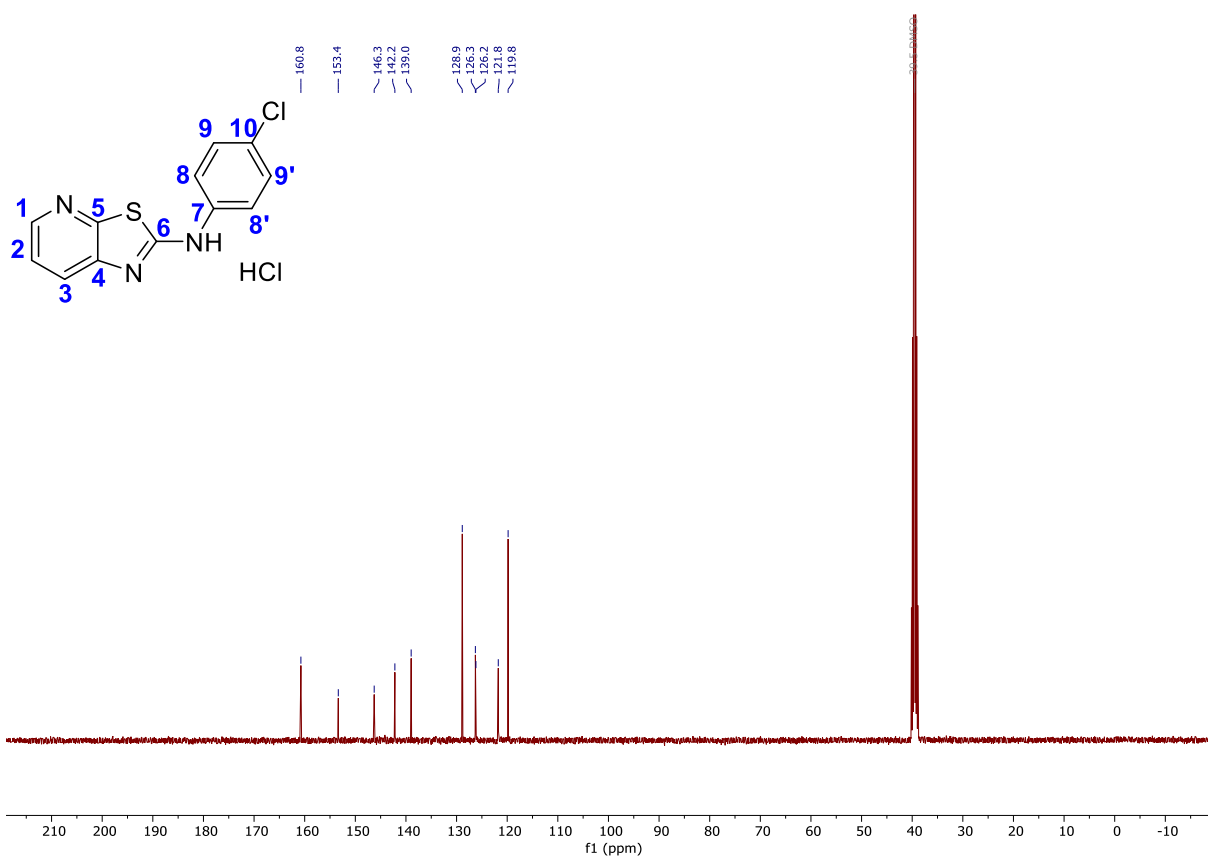
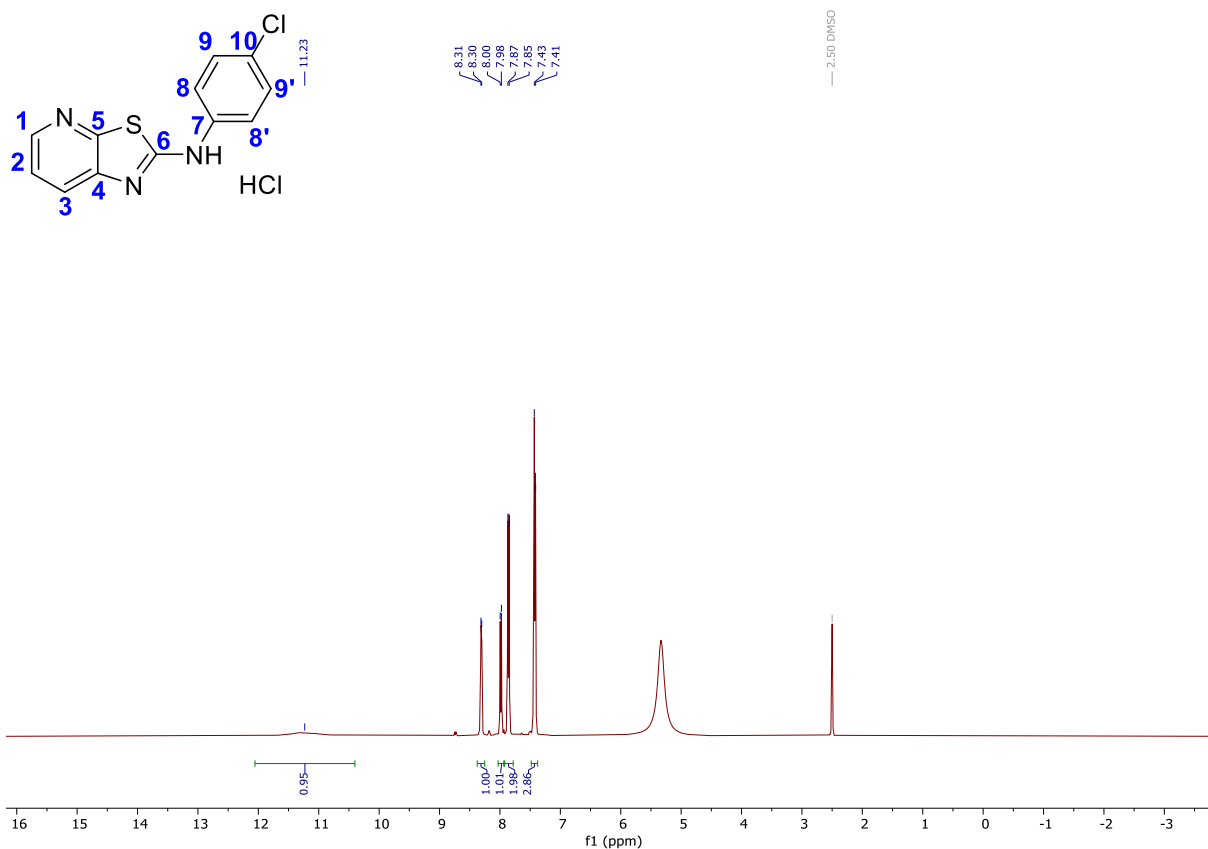
Aspect : beige powder

Melting point : 258°C

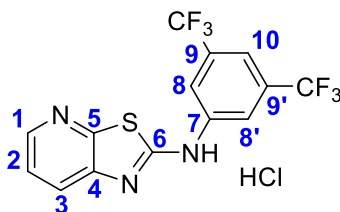
HRMS (ESI+): m/z calculated for $C_{12}H_9ClN_3S$ [$M + H^+$] = 262.0200 ; found = 262.0198

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 7.39-7.46 (m, 3H, $^2H_{Ar}$ + $^8H_{Ar}$ + $^8H_{Ar}$), 7.86 (d, J = 8.0 Hz, 2H, $^9H_{Ar}$ and $^9H_{Ar}$), 7.98 (d, J = 8.2 Hz, 1H, $^3H_{Ar}$), 8.31 (d, J = 5.2 Hz, 1H, $^1H_{Ar}$), 11.23 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 119.8 ($^9CH_{Ar}$ and $^9CH_{Ar}$), 121.8 ($^2CH_{Ar}$), 126.2 ($^{10}C^{IV}$), 126.3 ($^3CH_{Ar}$), 128.9 ($^8CH_{Ar}$ and $^8CH_{Ar}$), 139.0 ($^7C^{IV}$), 142.2 ($^1CH_{Ar}$), 146.3 ($^4C^{IV}$), 153.4 ($^5C^{IV}$) and 160.8 ($^6C^{IV}$).



N-(3,5-bis(trifluoromethyl)phenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 3 was applied to 3,5-Bis(trifluoromethyl)phenylisothiocyanate and 3-amino-2-chloropyridine to give *N*-(3,5-bis(trifluoromethyl)phenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 54% yield.

Aspect : colourless powder

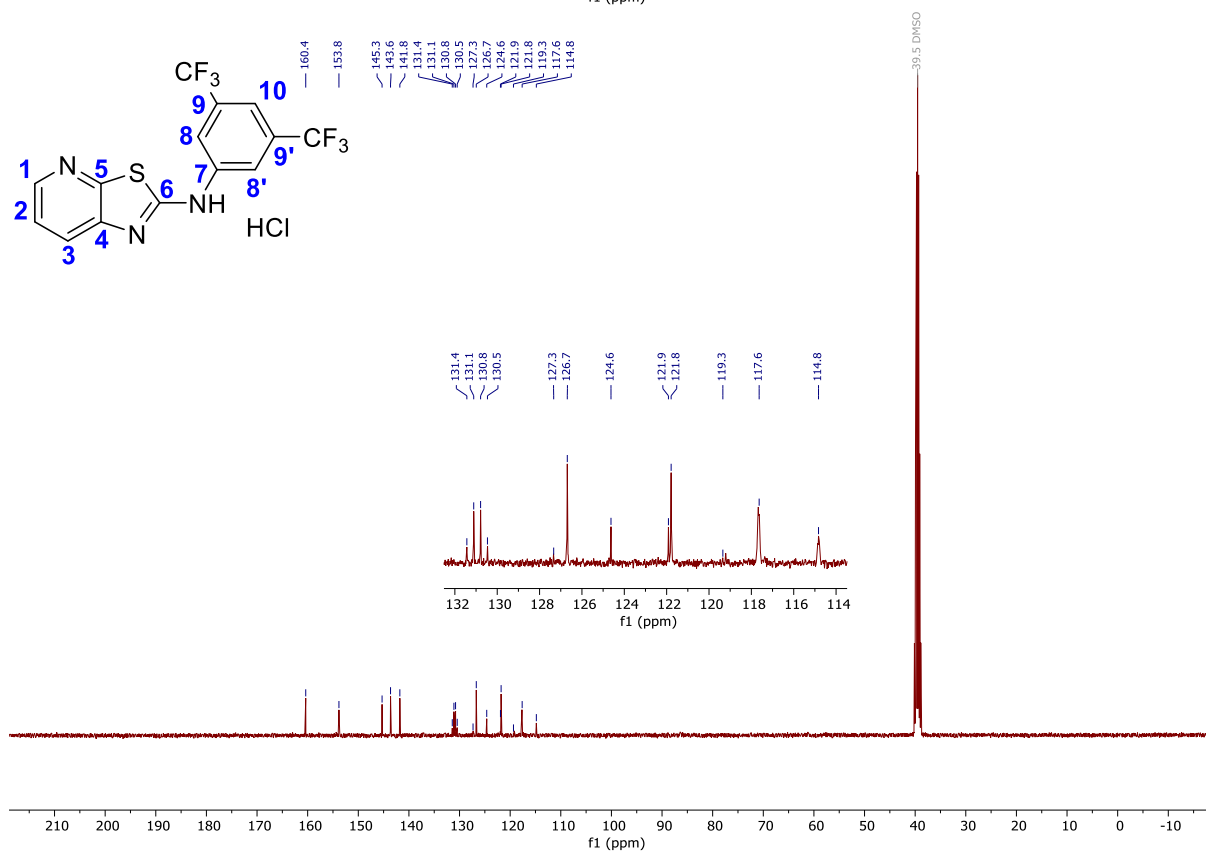
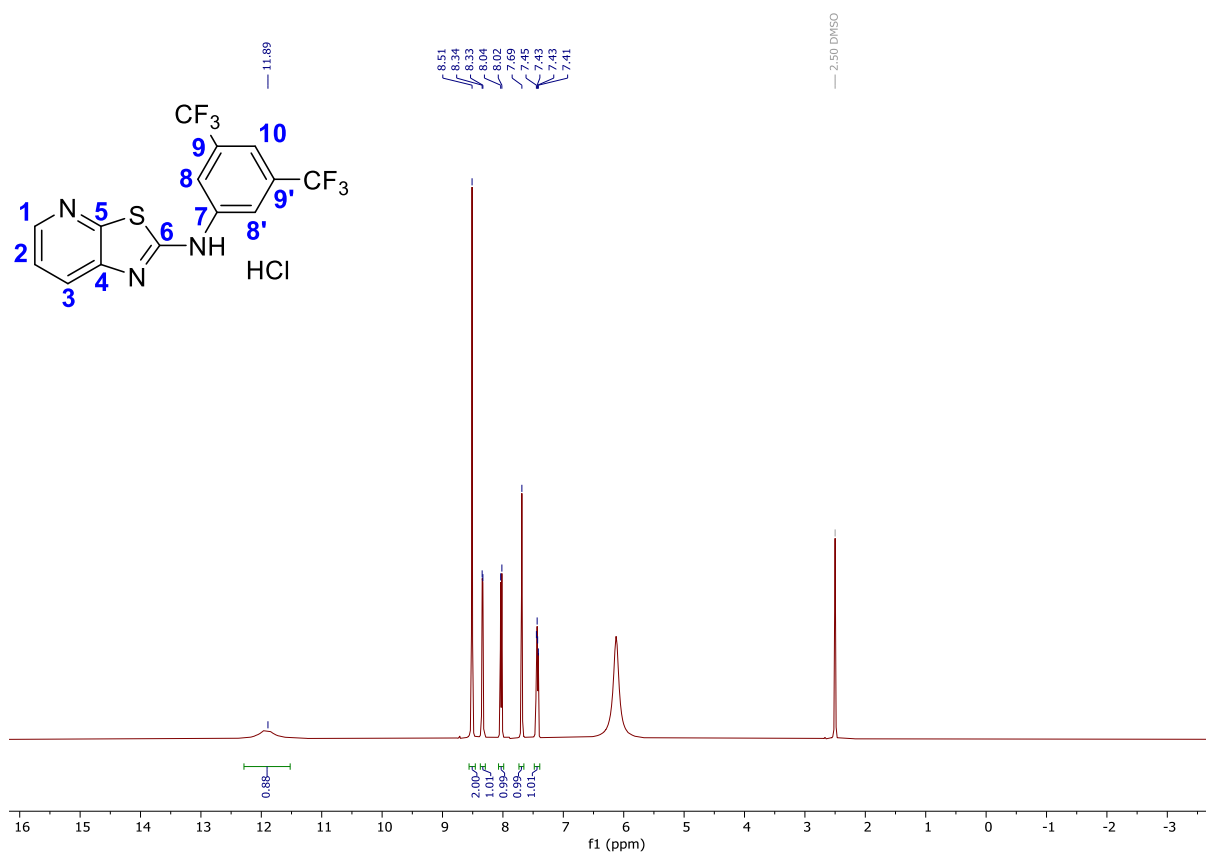
Melting point : 231°C

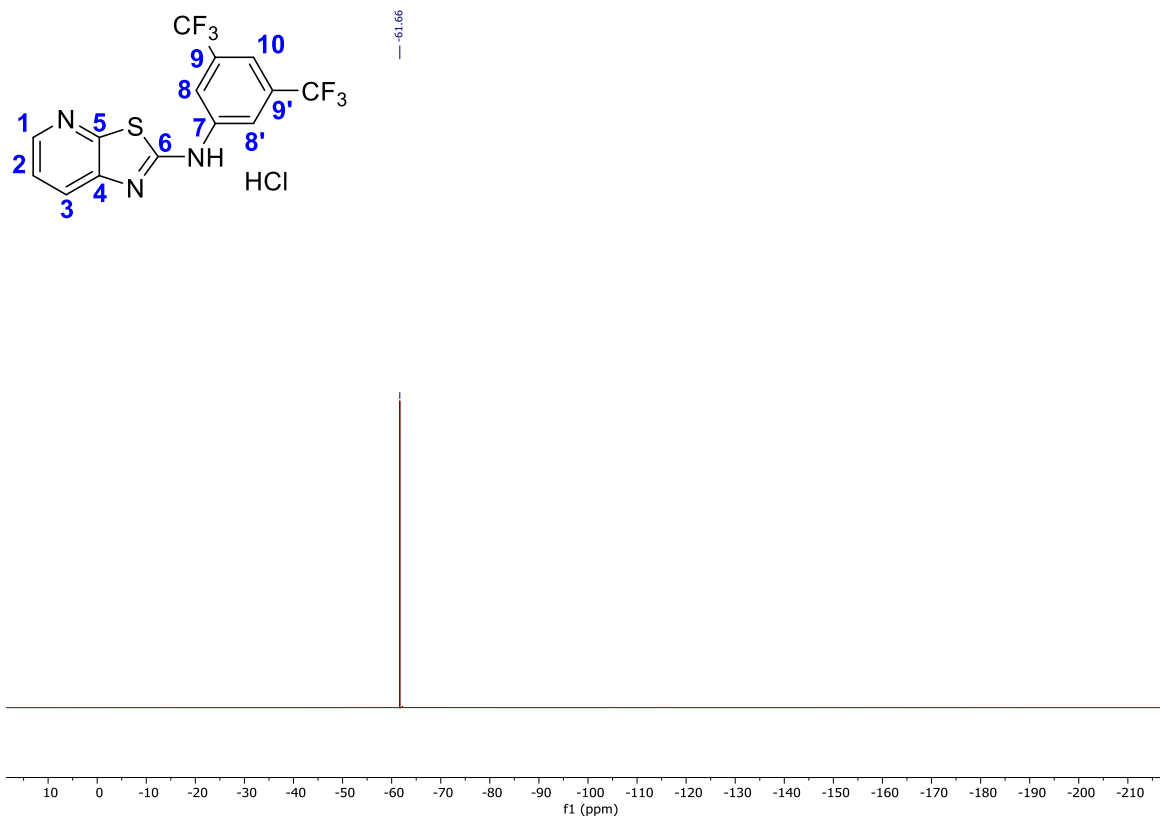
HRMS (ESI+): m/z calculated for $C_{14}H_8F_6N_3S$ [$M + H^+$] = 364.0338 ; found = 364.0341

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 7.43 (dd, J = 8.2, 4.9 Hz, 1H, $^2H_{Ar}$), 7.69 (s, 1H, $^{10}H_{Ar}$), 8.03 (d, J = 8.1 Hz, 1H, $^3H_{Ar}$), 8.34 (d, J = 4.9 Hz, 1H, $^1H_{Ar}$), 8.51 (s, 2H, $^8H_{Ar}$ and $^8'H_{Ar}$), 11.89 (bs, 1H, N-H).

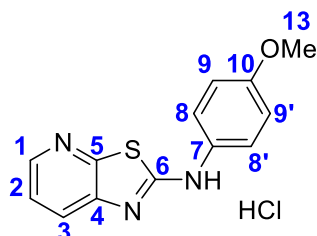
^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 114.8 ($^{10}CH_{Ar}$), 117.6 ($^8CH_{Ar}$ and $^8'CH_{Ar}$), 121.8 ($^2CH_{Ar}$), 123.3 (q, 1J = 274 Hz, $^{11}CF_3$ and $^{11'}CF_3$), 126.7 ($^3CH_{Ar}$), 130.9 (q, 2J = 32 Hz, $^9C^{IV}$ and $^9'C^{IV}$), 141.8 ($^7C^{IV}$), 143.6 ($^1CH_{Ar}$), 145.3 ($^4C^{IV}$), 153.8 ($^5C^{IV}$) and 160.4 ($^6C^{IV}$).

^{19}F NMR (DMSO-*d*₆, 376 MHz) : δ_F = -61.66.





N-(4-methoxyphenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 1 was applied to 4-methoxyphenyl isothiocyanate and 3-amino-2-chloropyridine to give *N*-(4-methoxyphenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 54% yield.

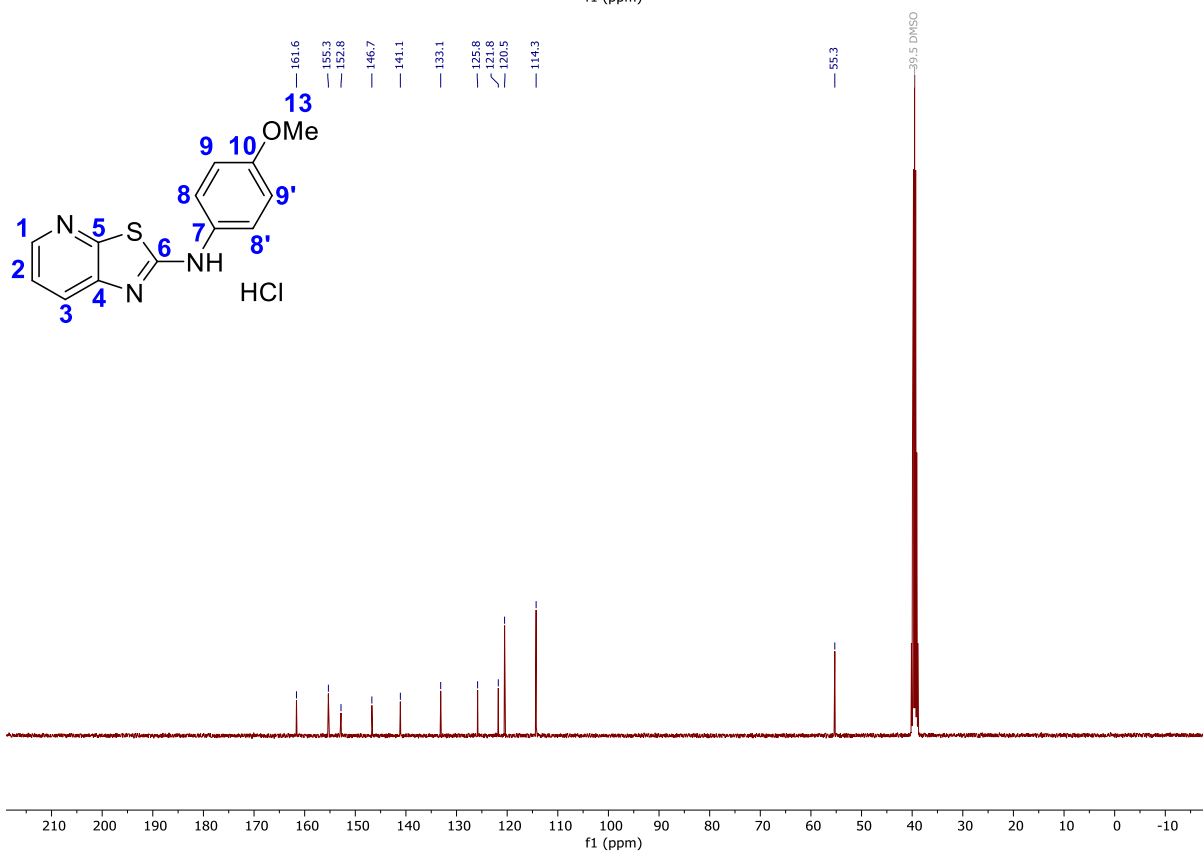
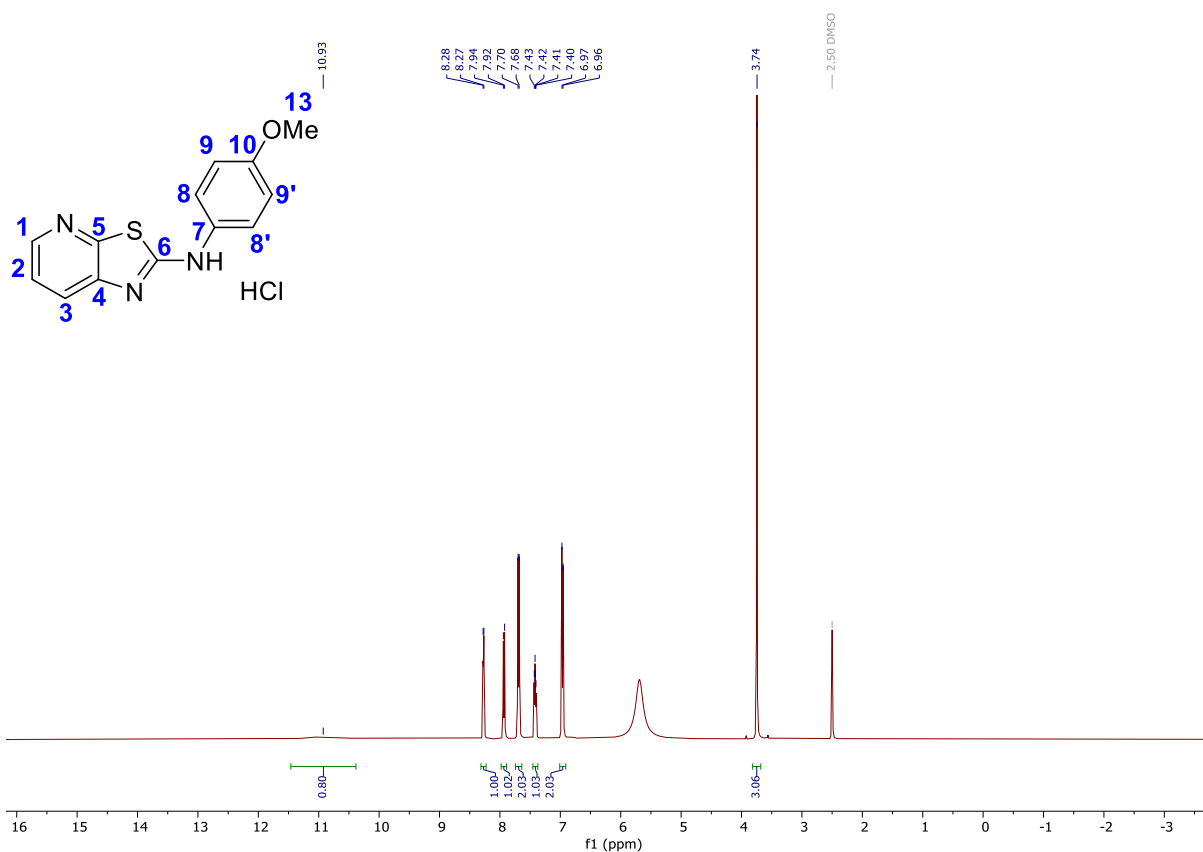
Aspect : yellow powder

Melting point : 241°C

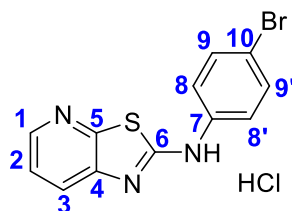
HRMS (ESI+): m/z calculated for $C_{13}H_{12}N_3OS$ [$M + H^+$] = 258.0695 ; found = 258.0693

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 3.74 (s, 3H, $^{11}CH_3$ -O), 6.96 (d, J = 7.0 Hz, 2H, $^8CH_{Ar}$ and $^8'CH_{Ar}$), 7.41 (dd, J = 8.1, 5.0 Hz, 1H, $^2CH_{Ar}$), 7.69 (d, J = 7.0 Hz, 2H, $^9CH_{Ar}$ and $^9'CH_{Ar}$), 7.93 (d, J = 8.1 Hz, 1H, $^3CH_{Ar}$), 8.27 (d, J = 5.1 Hz, 1H, $^1CH_{Ar}$), 10.93 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 55.3 ($^{11}CH_3$ -O), 114.3 ($^8CH_{Ar}$ and $^8'CH_{Ar}$), 120.5 ($^9CH_{Ar}$ and $^9'CH_{Ar}$), 121.8 ($^2CH_{Ar}$), 125.8 ($^3CH_{Ar}$), 133.1 ($^7C^{IV}$), 141.1 ($^1CH_{Ar}$), 146.7 ($^4C^{IV}$), 152.8 ($^5C^{IV}$), 155.3 ($^{10}C^{IV}$) and 161.6 ($^6C^{IV}$).



N-(4-bromophenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 1 was applied to 4-bromophenyl isothiocyanate and 3-amino-2-chloropyridine to give *N*-(4-bromophenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 66% yield.

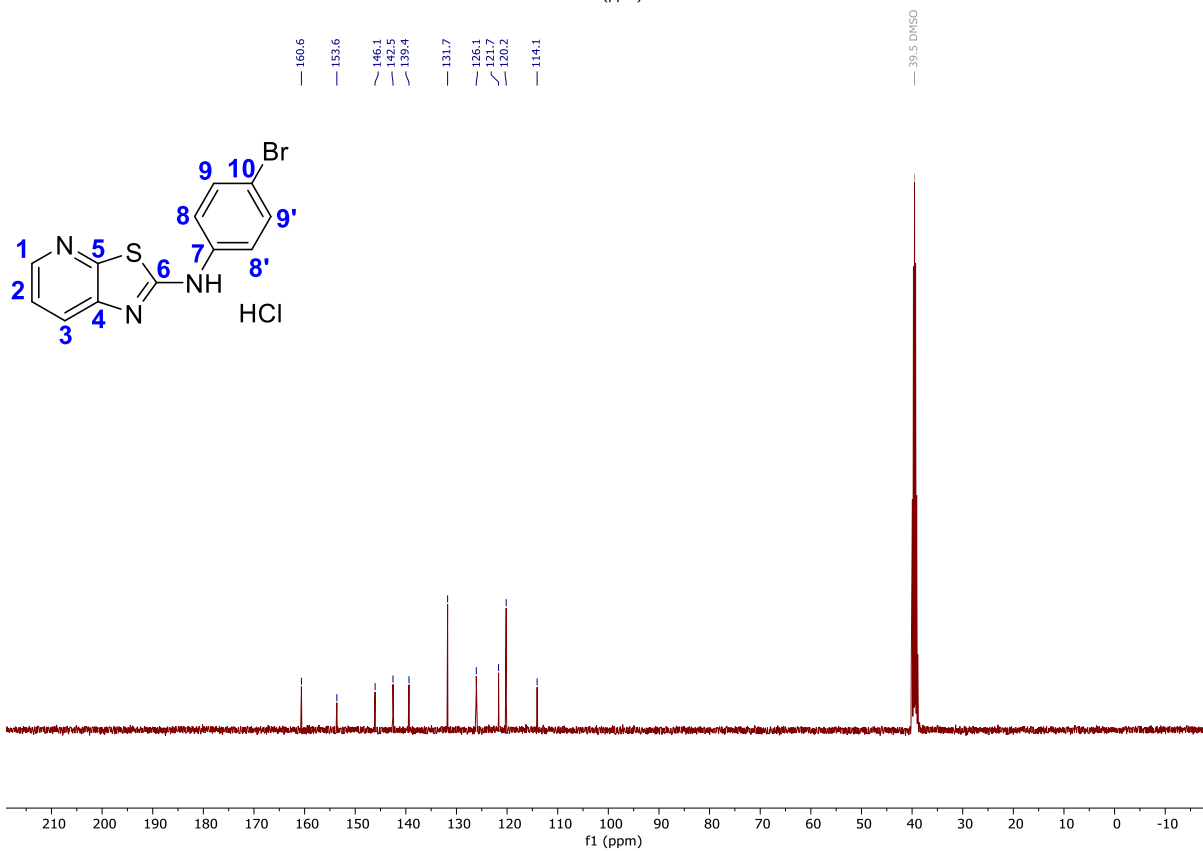
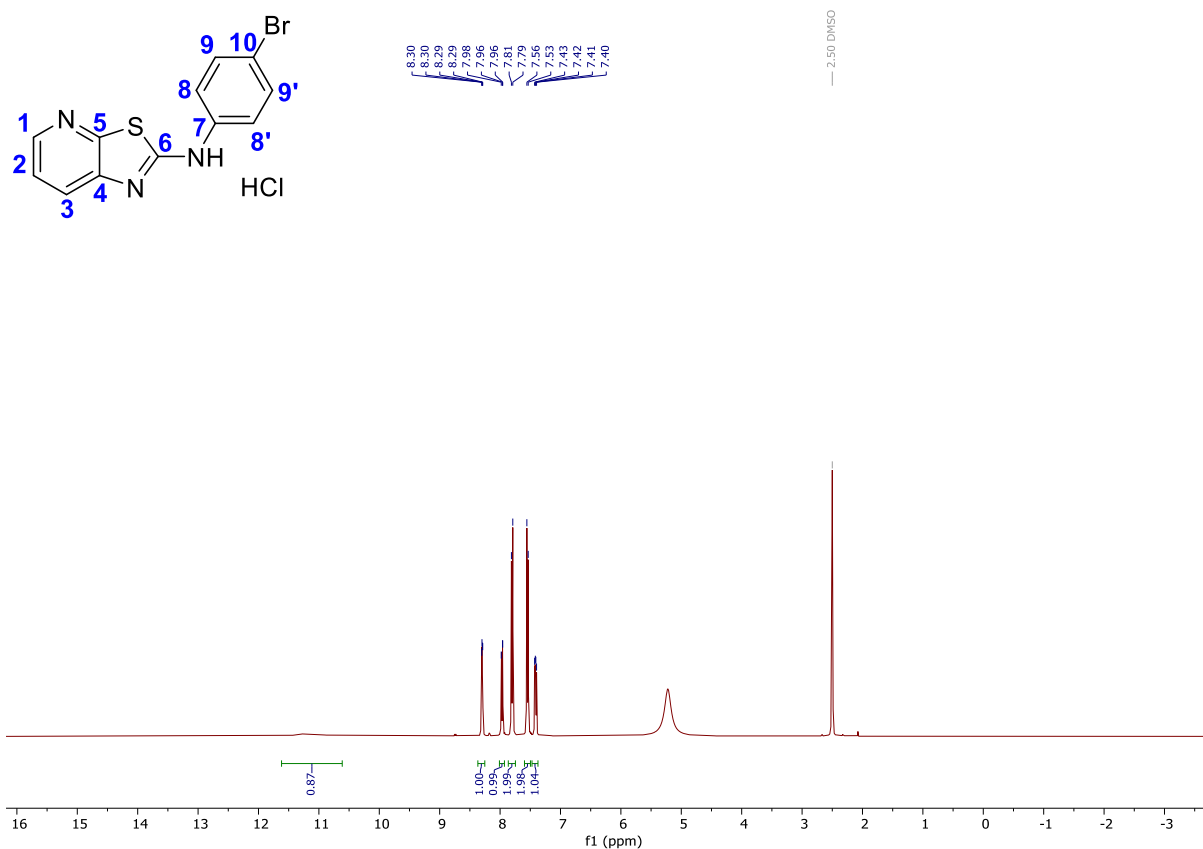
Aspect : beige powder

Melting point : 264°C (decomposition.)

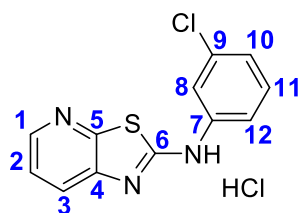
HRMS (ESI+): m/z calculated for $C_{12}H_9BrN_3S$ [$M + H^+$] = 305.9695 ; found = 305.9698

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 7.41 (dd, J = 8.1, 4.9 Hz, 1H, $^2H_{Ar}$), 7.55 (d, J = 8.8 Hz, 2H, $^8H_{Ar}$ and $^8'H_{Ar}$), 7.80 (d, J = 8.9 Hz, 2H, $^9H_{Ar}$ and $^9'H_{Ar}$), 7.97 (dd, J = 8.2, 1.6 Hz, 1H, $^3H_{Ar}$), 8.30 (dd, J = 4.9, 1.6 Hz, 1H, $^1H_{Ar}$), 11.16 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 114.1 ($^{10}C^{IV}$), 120.2 ($^9CH_{Ar}$ and $^9'CH_{Ar}$), 121.7 ($^2CH_{Ar}$), 126.1 ($^3CH_{Ar}$), 131.8 ($^8CH_{Ar}$ and $^8'CH_{Ar}$), 139.4 ($^7C^{IV}$), 142.5 ($^1CH_{Ar}$), 146.1 ($^4C^{IV}$), 153.6 ($^5C^{IV}$) and 160.6 ($^6C^{IV}$).



N-(3-chlorophenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 1 was applied to 3-chlorophenyl isothiocyanate and 3-amino-2-chloropyridine to give *N*-(3-chlorophenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 63% yield.

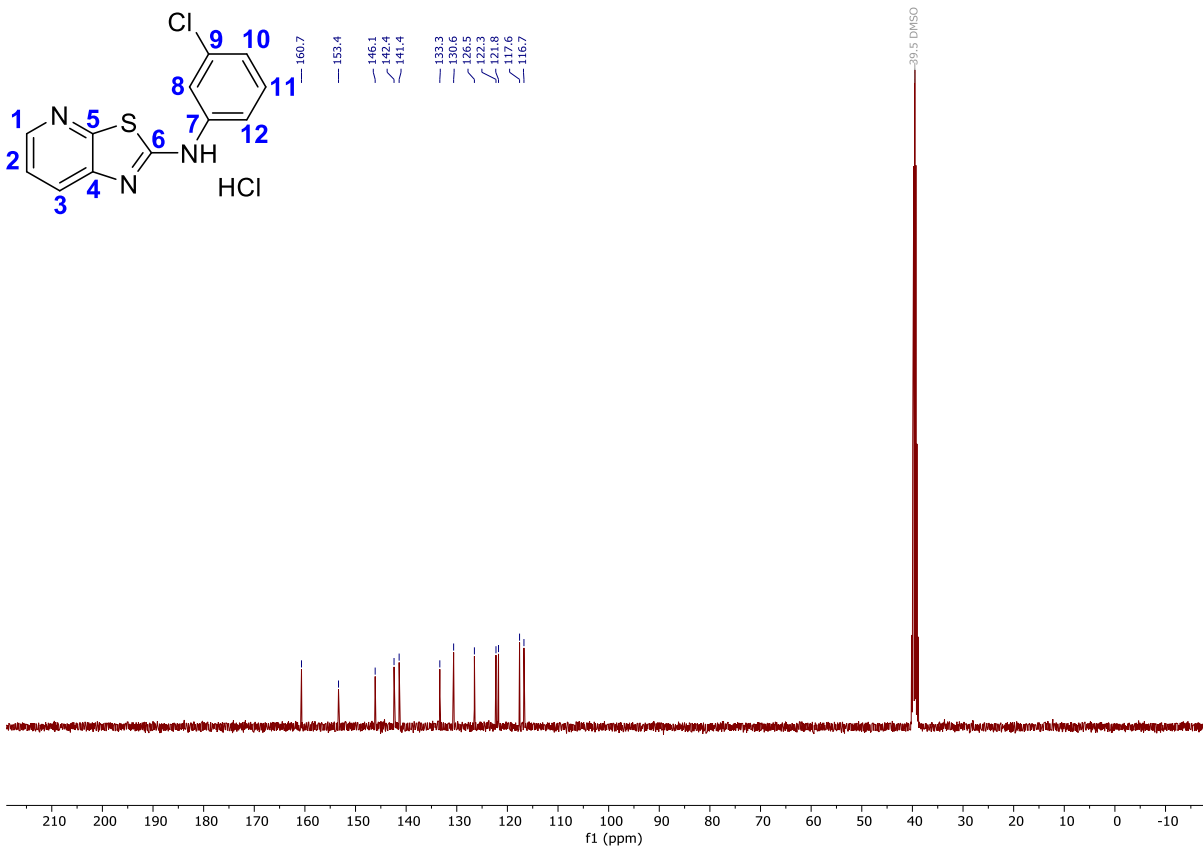
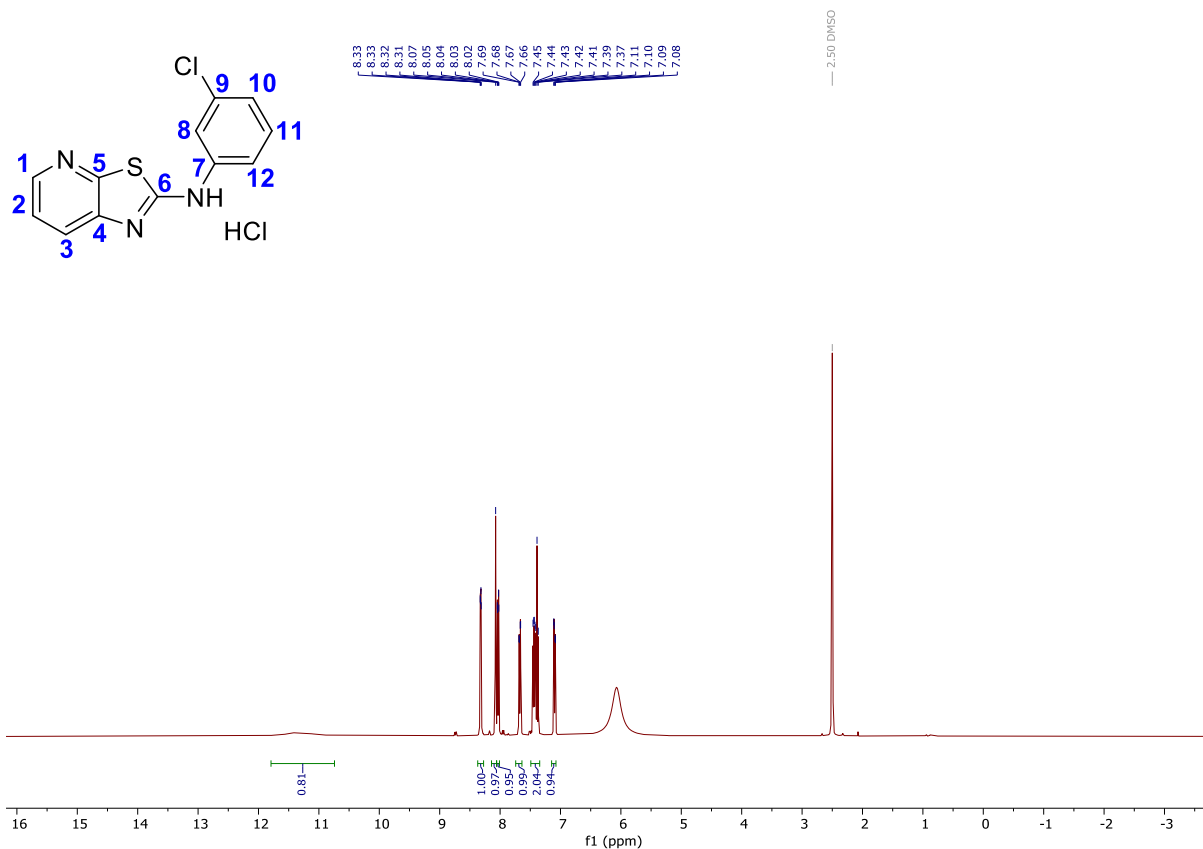
Aspect : beige powder

Melting point : 205°C.

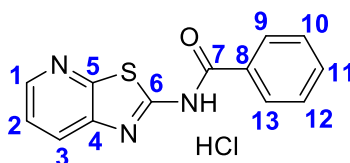
HRMS (ESI+): m/z calculated for $C_{12}H_9ClN_3S$ [$M + H^+$] = 262.0200 ; found = 262.0202

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 7.10 (dd, J = 7.8, 2.4 Hz, 1H, $^{12}H_{Ar}$), 7.39 (t, J = 8.2 Hz, 1H, $^{11}H_{Ar}$), 7.44 (dd, J = 8.0, 4.9 Hz, 1H, $^2H_{Ar}$), 7.67 (dd, J = 8.2, 2.6 Hz, 1H, $^{10}H_{Ar}$), 8.03 (dd, J = 8.2, 1.6 Hz, 1H, $^3H_{Ar}$), 8.07 (m, 1H, $^8H_{Ar}$), 8.32 (dd, J = 4.9, 1.6 Hz, 1H, $^1H_{Ar}$), 11.32 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 116.7 ($^{10}CH_{Ar}$), 117.6 ($^8CH_{Ar}$), 121.8 ($^2CH_{Ar}$), 122.3 ($^{12}CH_{Ar}$), 126.5 ($^3CH_{Ar}$), 130.6 ($^{11}CH_{Ar}$), 133.3 ($^9C^{IV}$), 141.4 ($^7C^{IV}$), 142.4 ($^1CH_{Ar}$), 146.1 ($^4C^{IV}$), 153.4 ($^5C^{IV}$) and 160.7 ($^6C^{IV}$).



N-benzamidethiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 1 was applied to benzoyl isothiocyanate and 3-amino-2-chloropyridine to give *N*-benzamidethiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 46% yield.

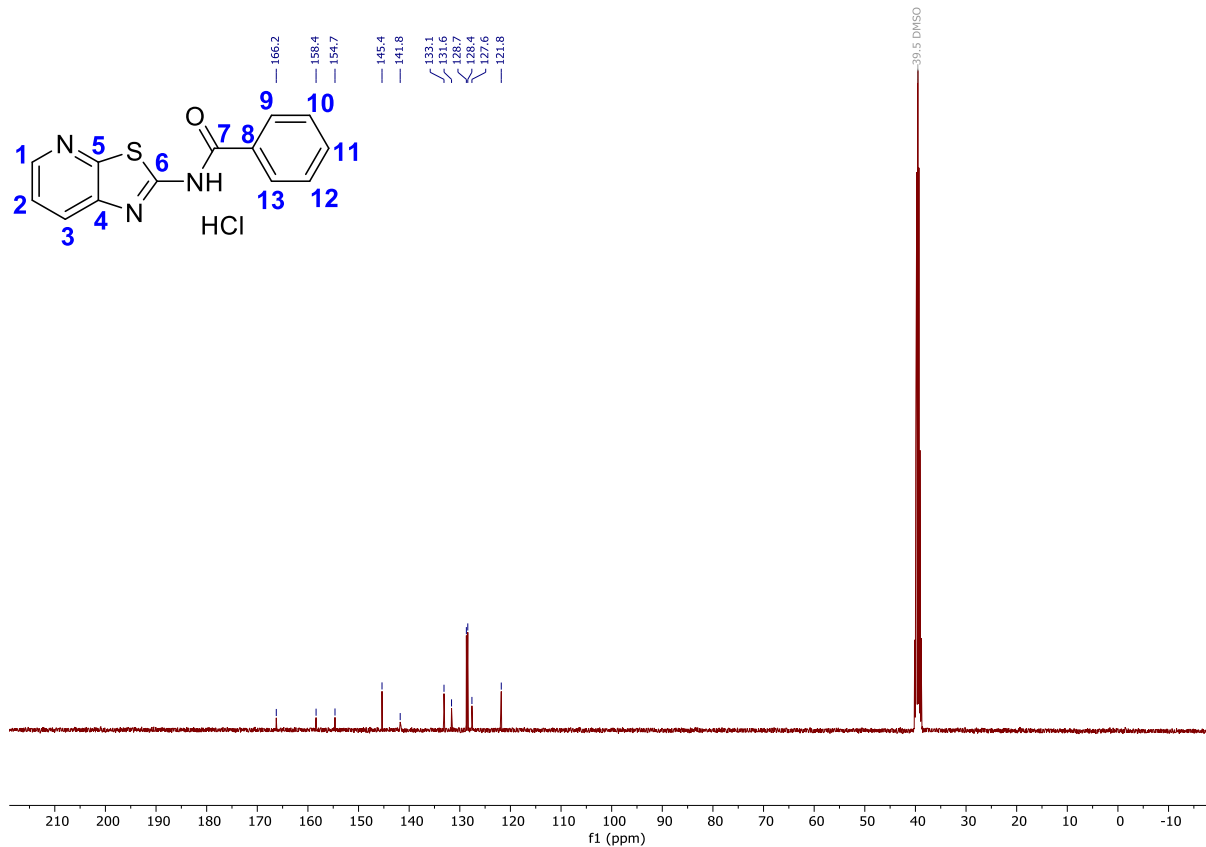
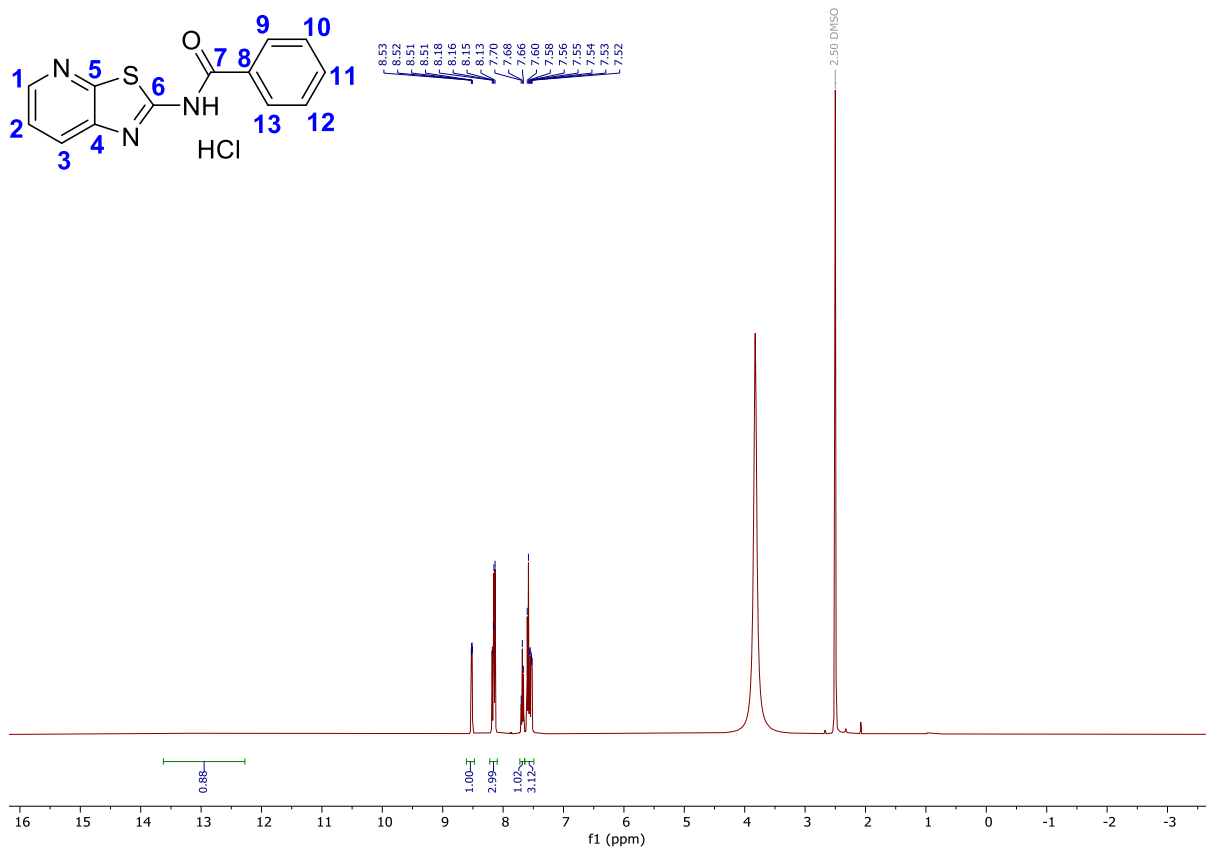
Aspect : Beige powder

Melting point : 183°C.

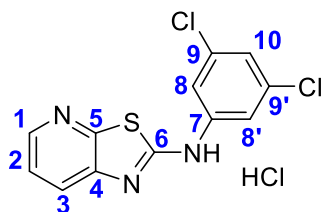
HRMS (ESI+): m/z calculated for $C_{13}H_{10}N_3OS$ [$M + H^+$] = 256.0539 ; found = 256.0541.

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 7.54 (dd, J = 8.2, 4.6 Hz, 1H, $^2H_{Ar}$), 7.58 (t, J = 7.6 Hz, 2H, $^{10}H_{Ar}$ and $^{10'}H_{Ar}$), 7.67-7.71 (m, 1H, H_{Ar}), 8.11-8.20 (m, 3H, $^9H_{Ar}$ + $^9'H_{Ar}$ + $^3H_{Ar}$), 8.52 (dd, J = 4.8, 1.4 Hz, 1.0H, $^1H_{Ar}$), 12.95 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 121.8 ($^2CH_{Ar}$), 127.6 ($^3CH_{Ar}$), 128.4 ($^9CH_{Ar}$ and $^9'CH_{Ar}$), 128.7 ($^{10}CH_{Ar}$ and $^{10'}CH_{Ar}$), 131.6 ($^8C^{IV}$), 133.1 ($^{11}CH_{Ar}$), 141.8 ($^4C^{IV}$), 145.4 ($^1CH_{Ar}$), 154.7 ($^5C^{IV}$), 158.4 ($^6C^{IV}$) and 166.3 ($^7C^{IV}=O$).



N-(3,5-dichlorophenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 3 was applied to 3,5-dichlorophenyl isothiocyanate and 3-amino-2-chloropyridine to give *N*-(3,5-dichlorophenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 66% yield.

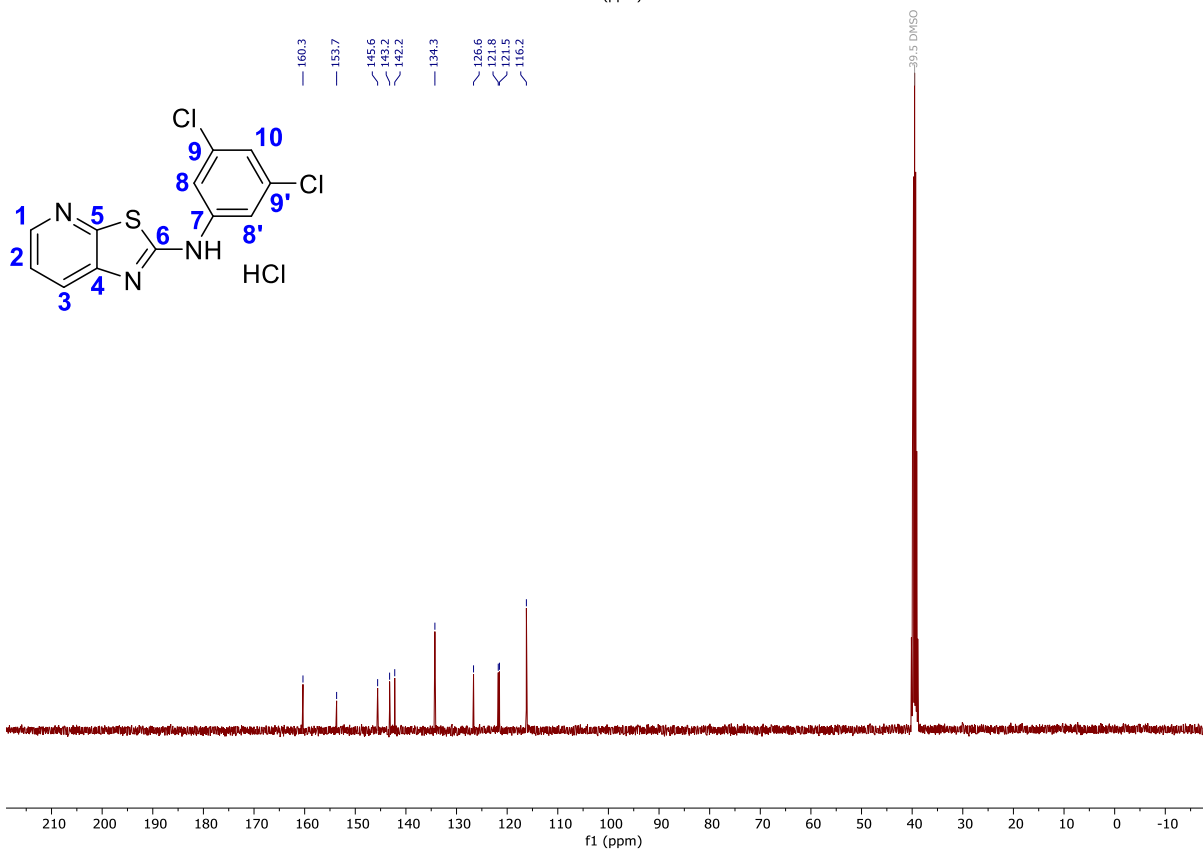
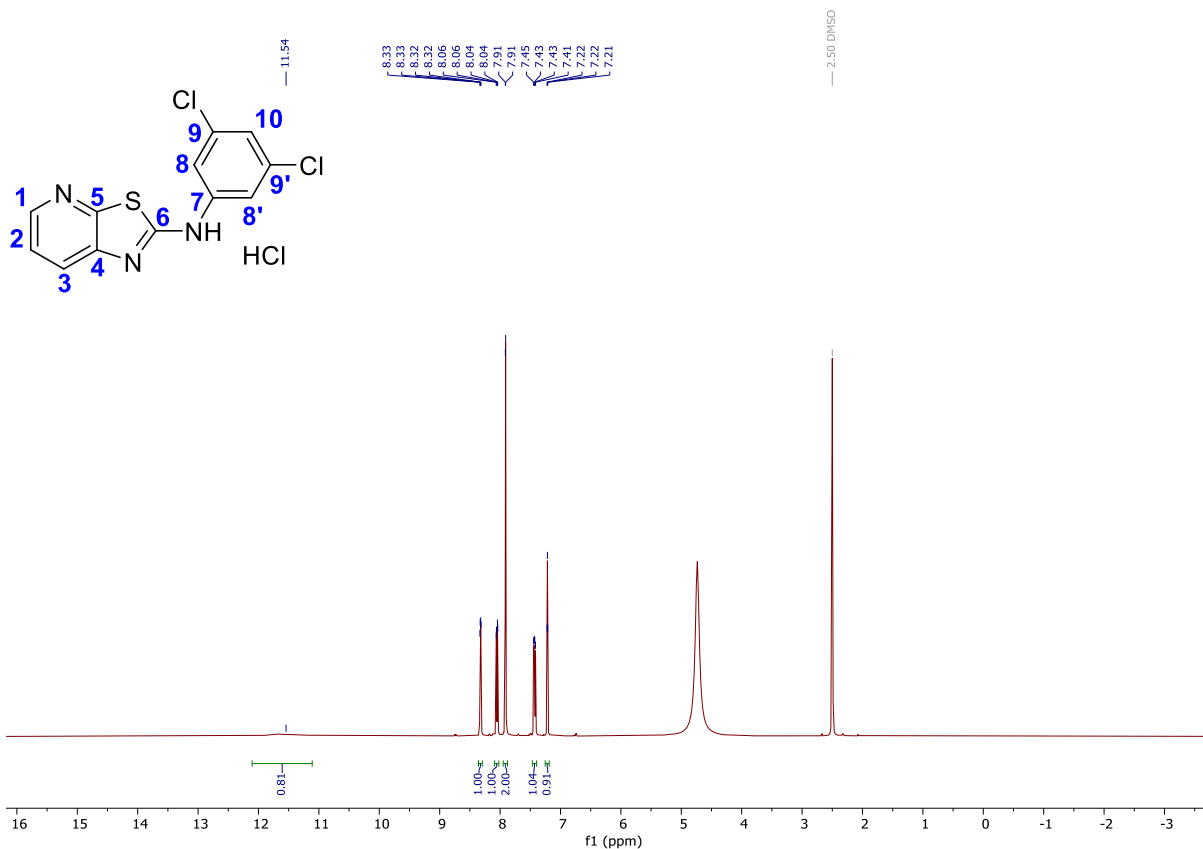
Aspect : beige powder

Melting point : 265°C (decomposition)

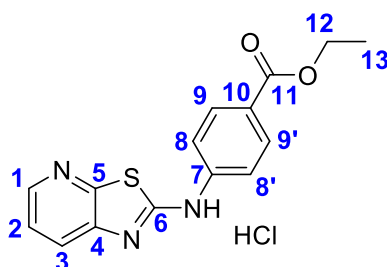
HRMS (ESI+): m/z calculated for $C_{12}H_8Cl_2N_3S$ [$M + H^+$] = 295.9811 ; found = 295.9810

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 7.22 (t, J = 1.8 Hz, 1H, $^{10}H_{Ar}$), 7.43 (dd, J = 8.2, 4.9 Hz, 1H, $^2H_{Ar}$), 7.91 (d, J = 1.8 Hz, 2H, $^8H_{Ar}$ and $^8'H_{Ar}$), 8.05 (dd, J = 8.2, 1.6 Hz, 1H, $^3H_{Ar}$), 8.33 (dd, J = 4.9, 1.6 Hz, 1H, $^1H_{Ar}$), 11.54 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 116.2 ($^8CH_{Ar}$ and $^8'CH_{Ar}$), 121.5 ($^{10}CH_{Ar}$), 121.8 ($^2CH_{Ar}$), 126.6 ($^3CH_{Ar}$), 134.3 ($^9C^{IV}$ and $^9'C^{IV}$), 142.2 ($^7C^{IV}$), 143.2 ($^1CH_{Ar}$), 145.6 ($^4C^{IV}$), 153.7 ($^5C^{IV}$) and 160.3 ($^6C^{IV}$).



N-(ethyl 4-aminobenzoate)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 3 was applied to ethyl 4-isothiocyanatobenzoate and 3-amino-2-chloropyridine to give *N*-(ethyl 4-aminobenzoate)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 55% yield.

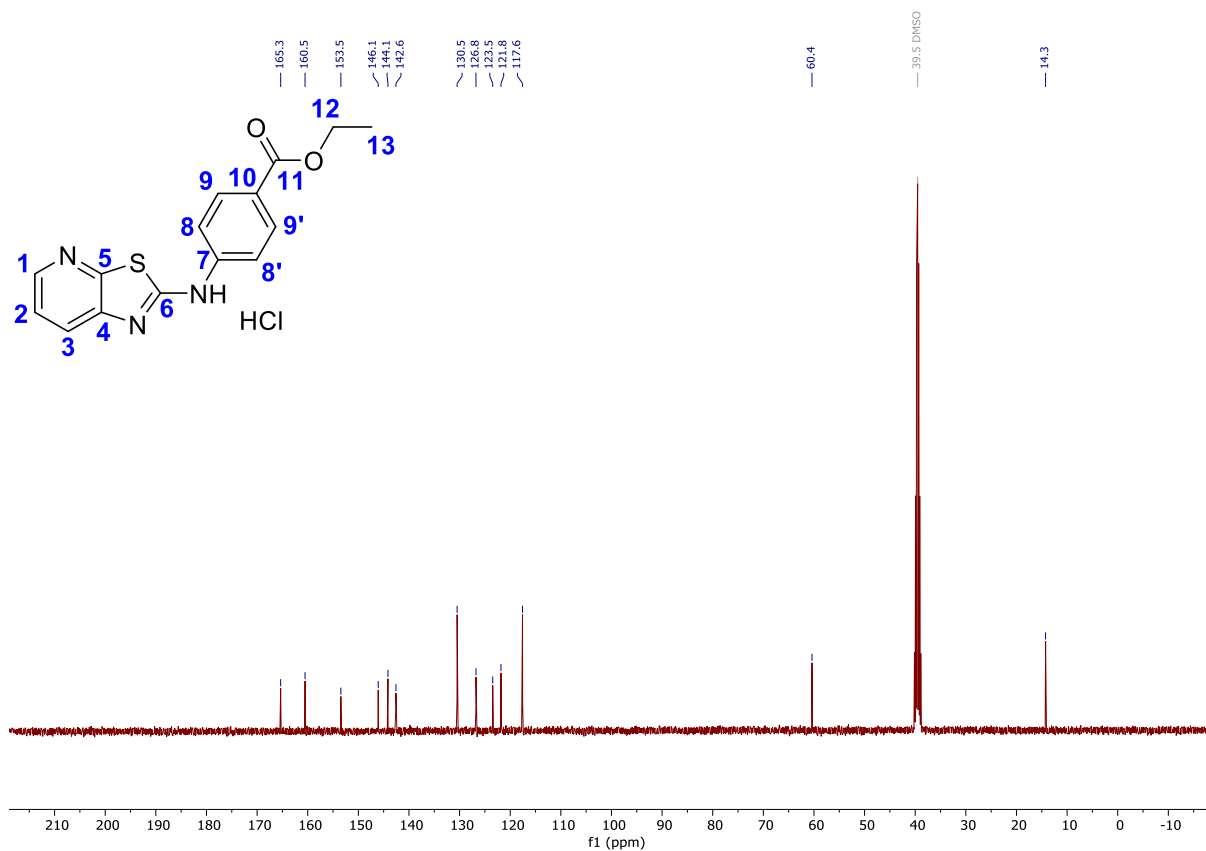
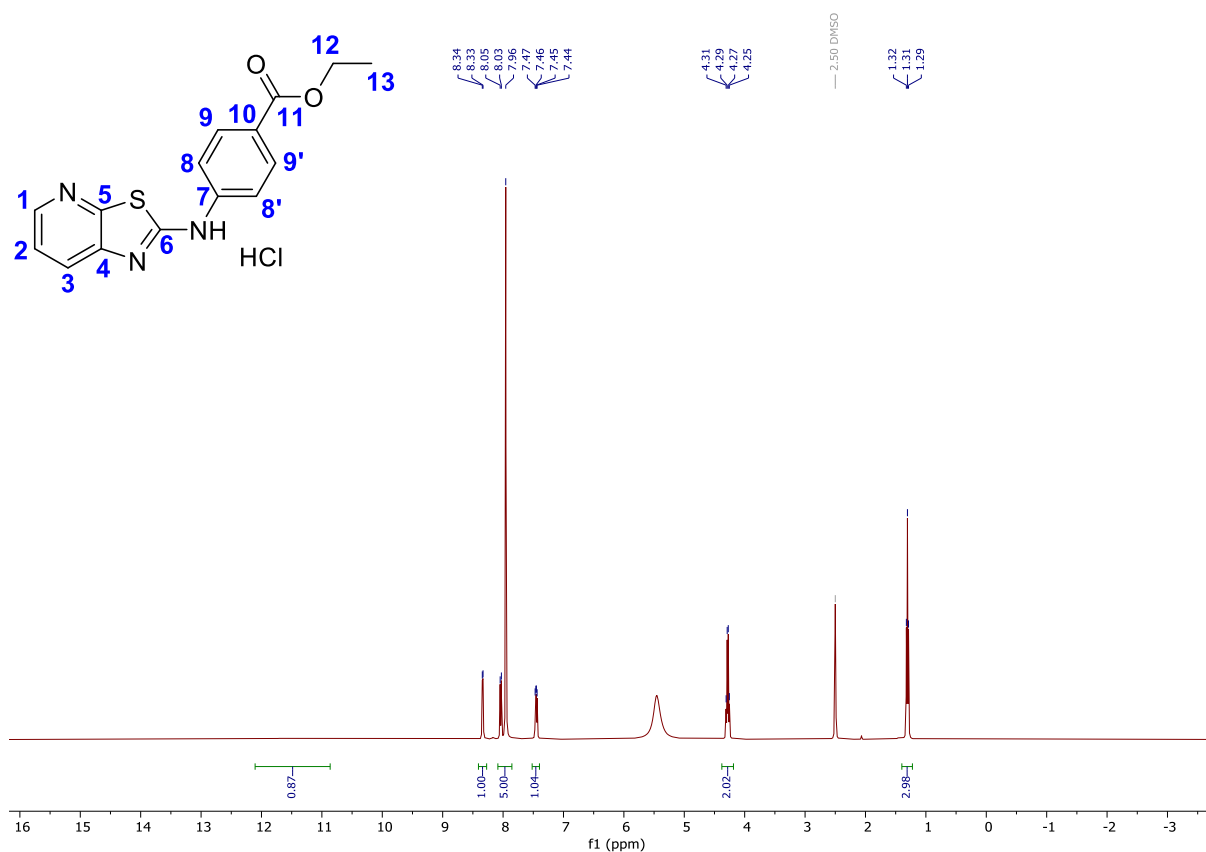
Aspect : beige powder

Melting point : 230°C.

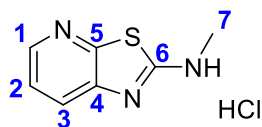
HRMS (ESI+): m/z calculated for $C_{15}H_{14}N_3O_2S$ [$M + H^+$] = 300.0801 ; found = 300.0801

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 1.31 (t, J = 7.1 Hz, 3H, $^{13}CH_3$), 4.28 (q, J = 7.1 Hz, 2H, $^{12}CH_2$), 7.45 (dd, J = 8.1, 4.9 Hz, 1H, $^2H_{Ar}$), 7.96 (s, 4H, H_{Ar}), 8.04 (d, J = 8.3 Hz, 1H, $^3H_{Ar}$), 8.34 (d, J = 4.9 Hz, 1H, $^1H_{Ar}$), 11.48 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 14.3 ($^{13}CH_3$), 60.4 ($^{12}CH_2$), 117.6 (2x CH_{Ar}), 121.8 (2CH), 123.5 ($^{10}C^{IV}$), 126.8 (3CH), 130.5 (2x CH_{Ar}), 142.6 (1CH), 144.2 ($^7C^{IV}$), 146.1 ($^4C^{IV}$), 153.5 ($^5C^{IV}$), 160.5 ($^6C^{IV}$) and 165.3 ($^{11}C^{IV}=O$).



N-methylthiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 1 was applied to methyl isothiocyanate and 3-amino-2-chloropyridine to give *N*-methylthiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 50% yield.

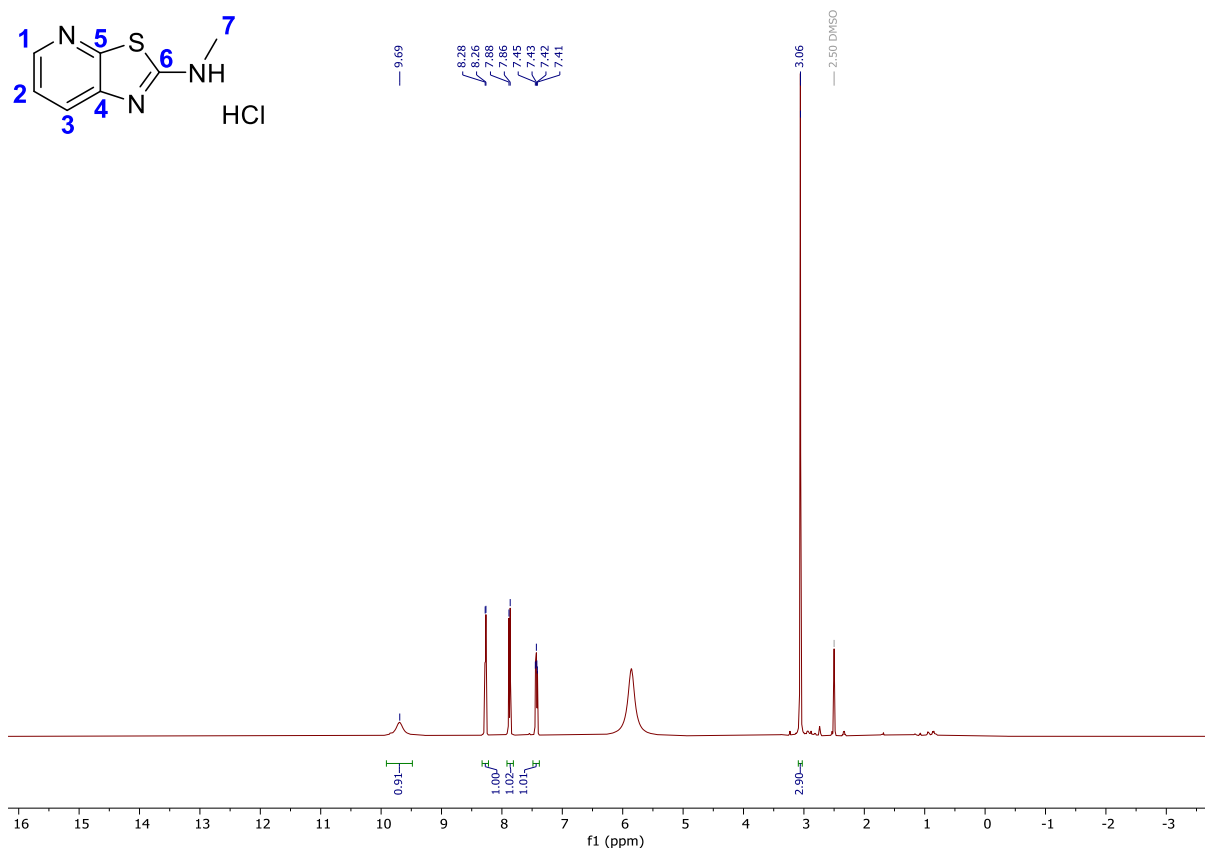
Aspect : beige powder

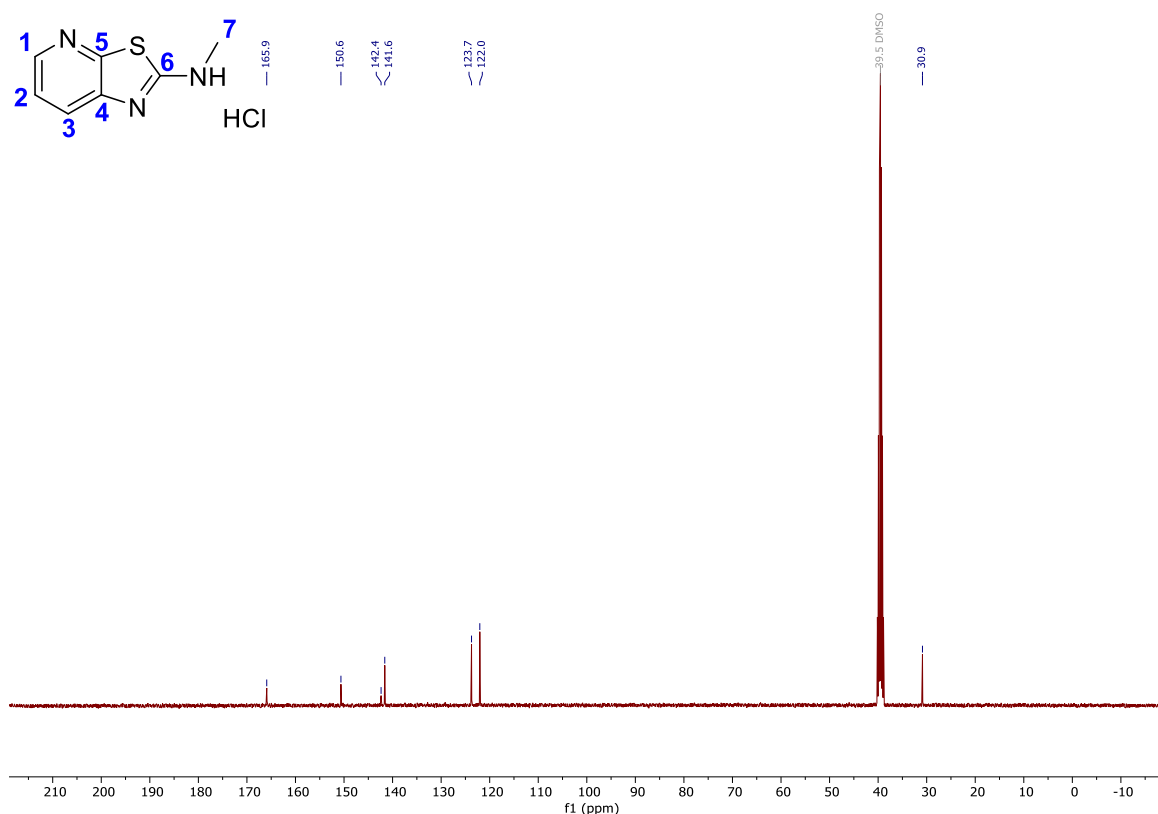
Melting point : 239°C (lit. 264-265) [40]

HRMS (ESI+): m/z calculated for $C_7H_8N_3S$ $[M + H^+]$ = 166.0433 ; found = 166.0438

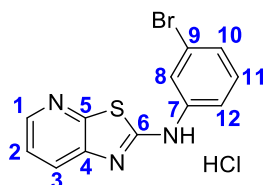
1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 3.06 (s, 3H, 7CH_3), 7.43 (dd, J = 8.1, 5.0 Hz, 1H, $^2H_{Ar}$), 7.88 (d, J = 8.1 Hz, $^3H_{Ar}$), 8.27 (d, J = 5.0 Hz, 1H, $^1H_{Ar}$), 9.69 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 30.9 (7CH_3), 122.0 ($^2CH_{Ar}$), 123.7 ($^3CH_{Ar}$), 141.6 ($^1CH_{Ar}$), 142.4 ($^4C^{IV}$), 150.6 ($^5C^{IV}$) and 165.9 ($^6C^{IV}$).





N-(3-bromophenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride



General procedure 1 was applied to 3-bromophenyl isothiocyanate and 3-amino-2-chloropyridine to give *N*-(3-bromophenyl)thiazolo[5,4-*b*]pyridin-2-amine hydrochloride in 58% yield.

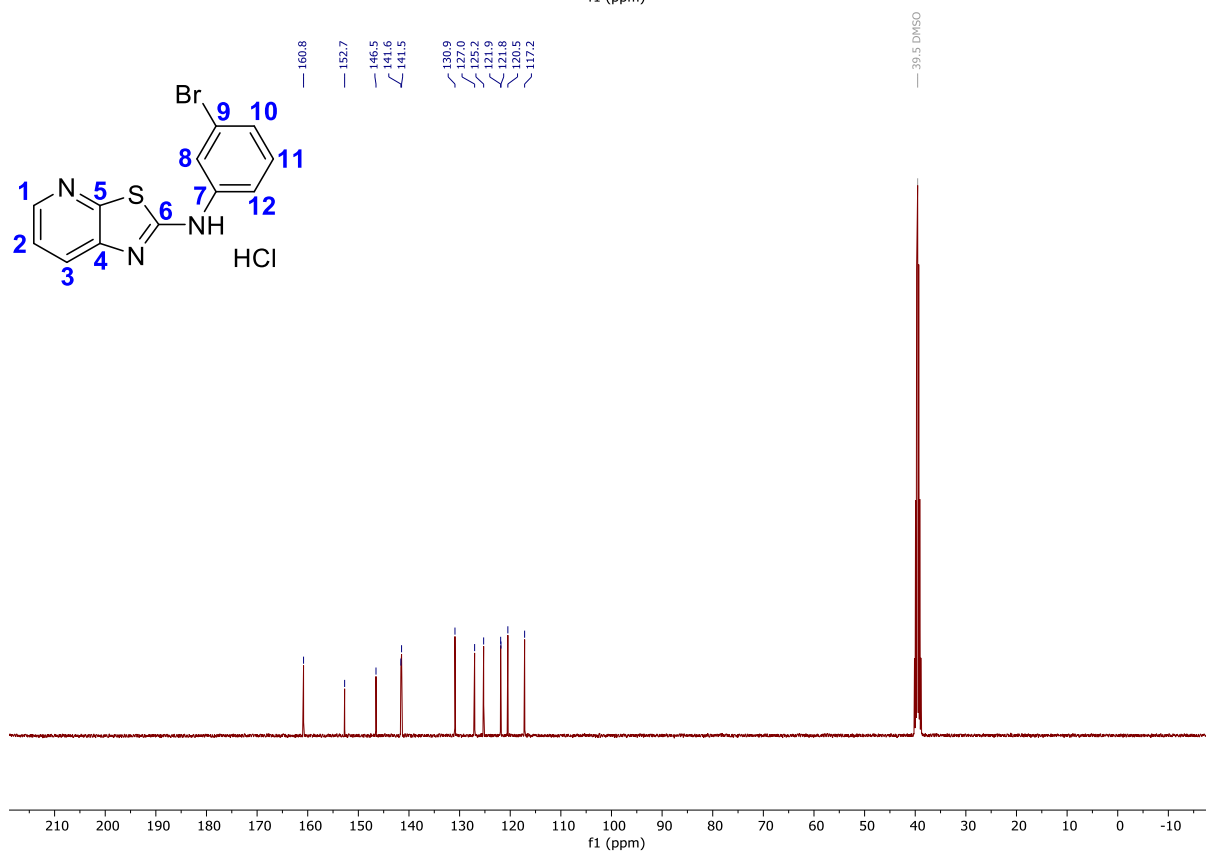
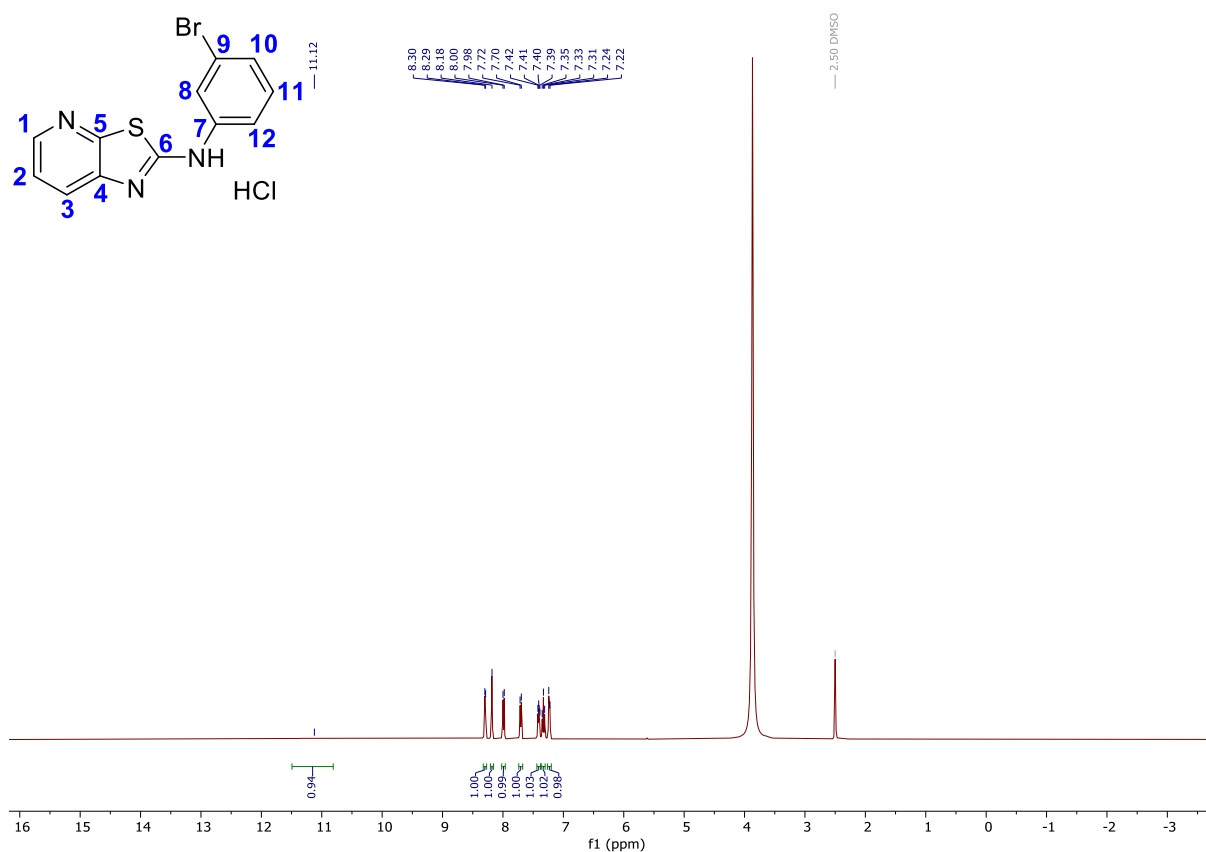
Aspect : yellowish powder

Melting point : 231°C

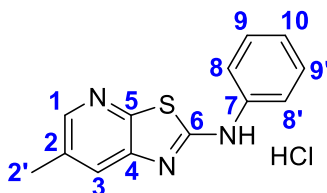
HRMS (ESI+) : calculated for C₁₂H₉BrN₃S [M + H⁺] = 305.9695 ; found = 305.9689

¹H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 7.23 (d, J = 8.1 Hz, 1H, ¹²H_{Ar}), 7.33 (t, J = 8.1 Hz, 1H, ¹¹H_{Ar}), 7.41 (dd, J = 8.4, 5.2 Hz, 1H, ²H_{Ar}), 7.71 (d, J = 8.2 Hz, 1H, ¹⁰H_{Ar}), 7.99 (d, J = 8.1 Hz, 1H, ³H_{Ar}), 8.18 (s, 1H, ⁸H_{Ar}), 8.29 (d, J = 5.3 Hz, 1H, ¹H_{Ar}), 11.12 (bs, 1H, N-H).

¹³C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 117.2 (¹⁰CH_{Ar}), 120.5 (⁸CH_{Ar}), 121.8 (²CH_{Ar}), 121.9 (⁹C^{IV}), 125.2 (¹²CH_{Ar}), 127.0 (³CH_{Ar}), 130.9 (¹¹CH_{Ar}), 141.5 (¹CH_{Ar}), 141.6 (⁷C^{IV}), 146.5 (⁴C^{IV}), 152.7 (⁵C^{IV}) and 160.8 (⁶C^{IV}).



N-phenylthiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride



General procedure 2 was applied to phenyl isothiocyanate and 3-amino-2-chloro-5-methylpyridine to give *N*-phenylthiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride in 64% yield.

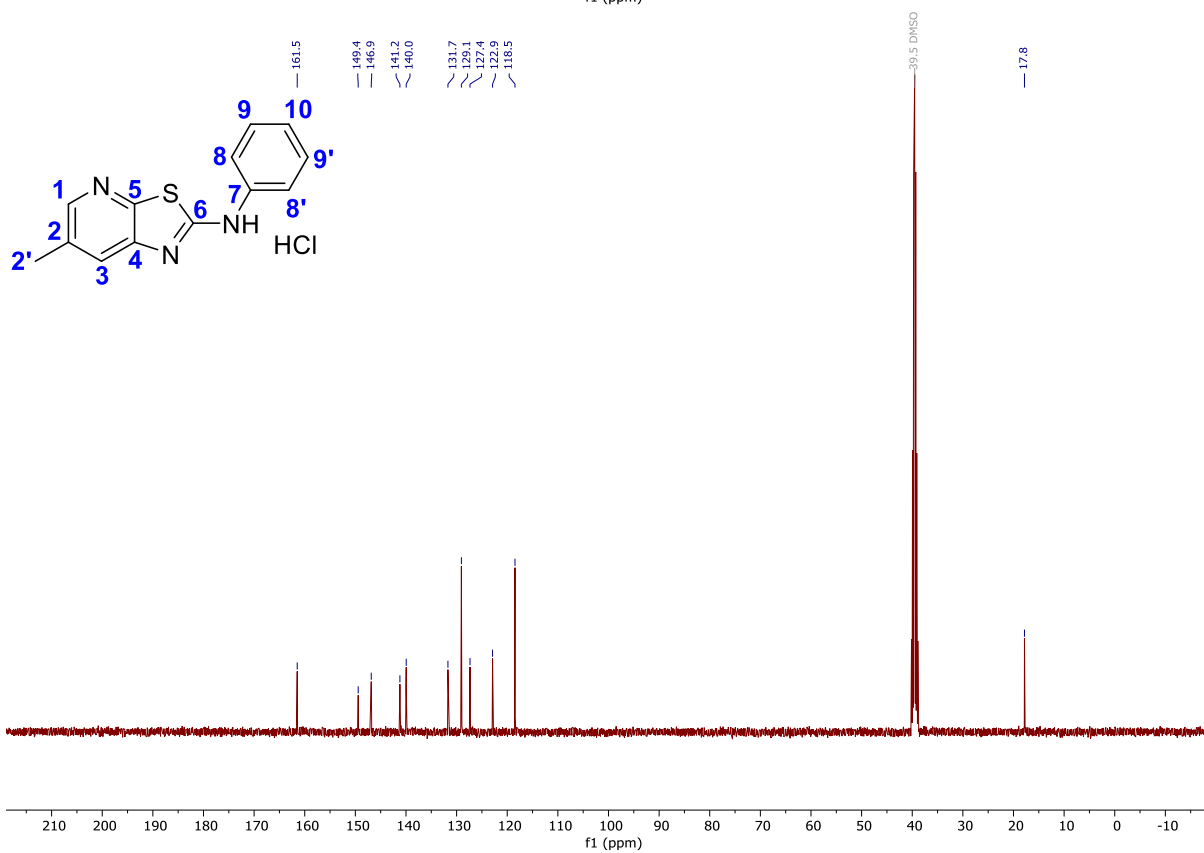
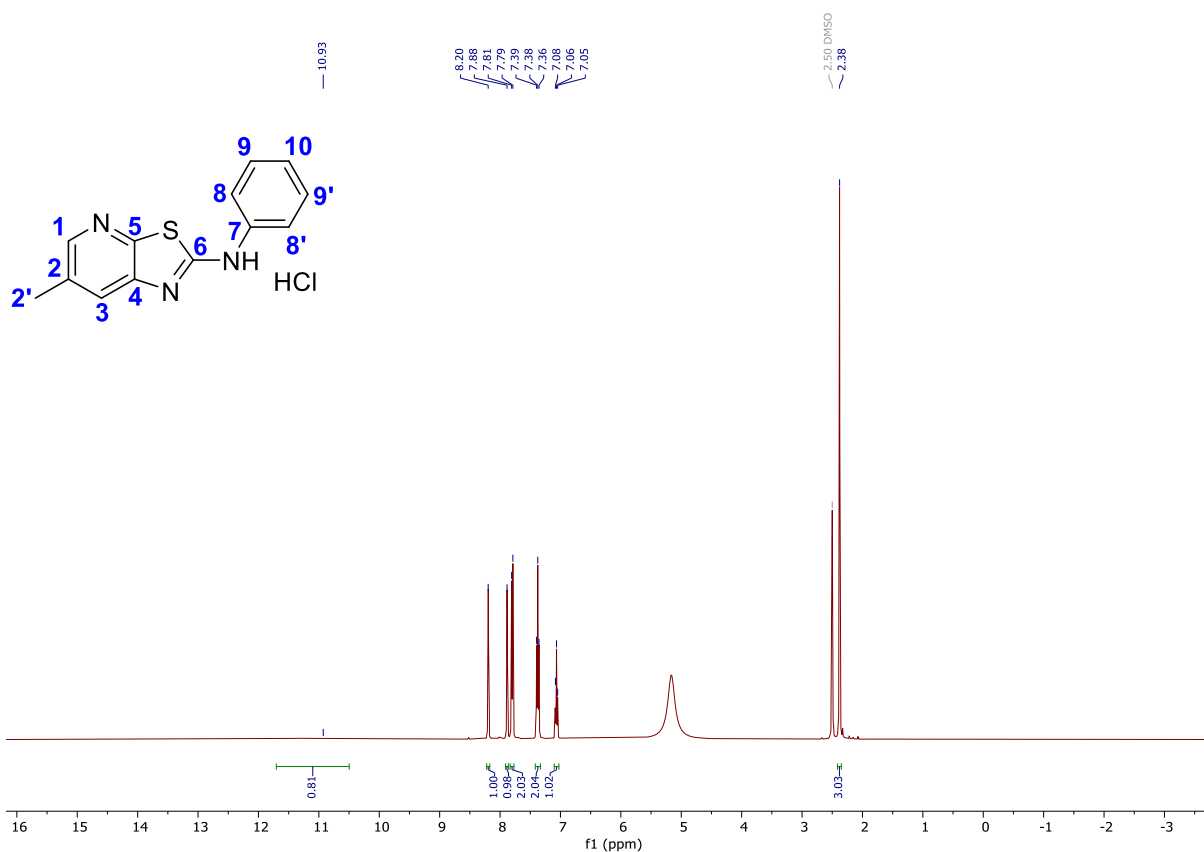
Aspect : beige powder

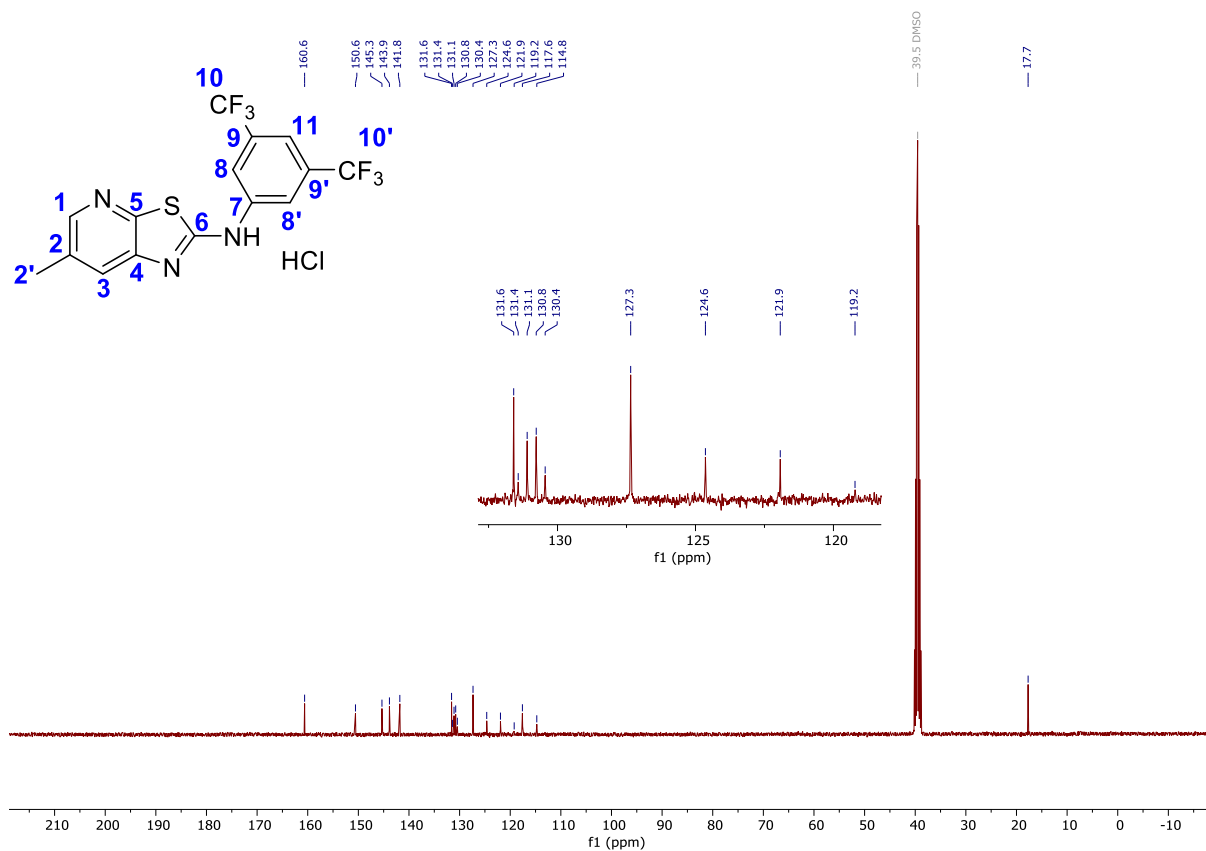
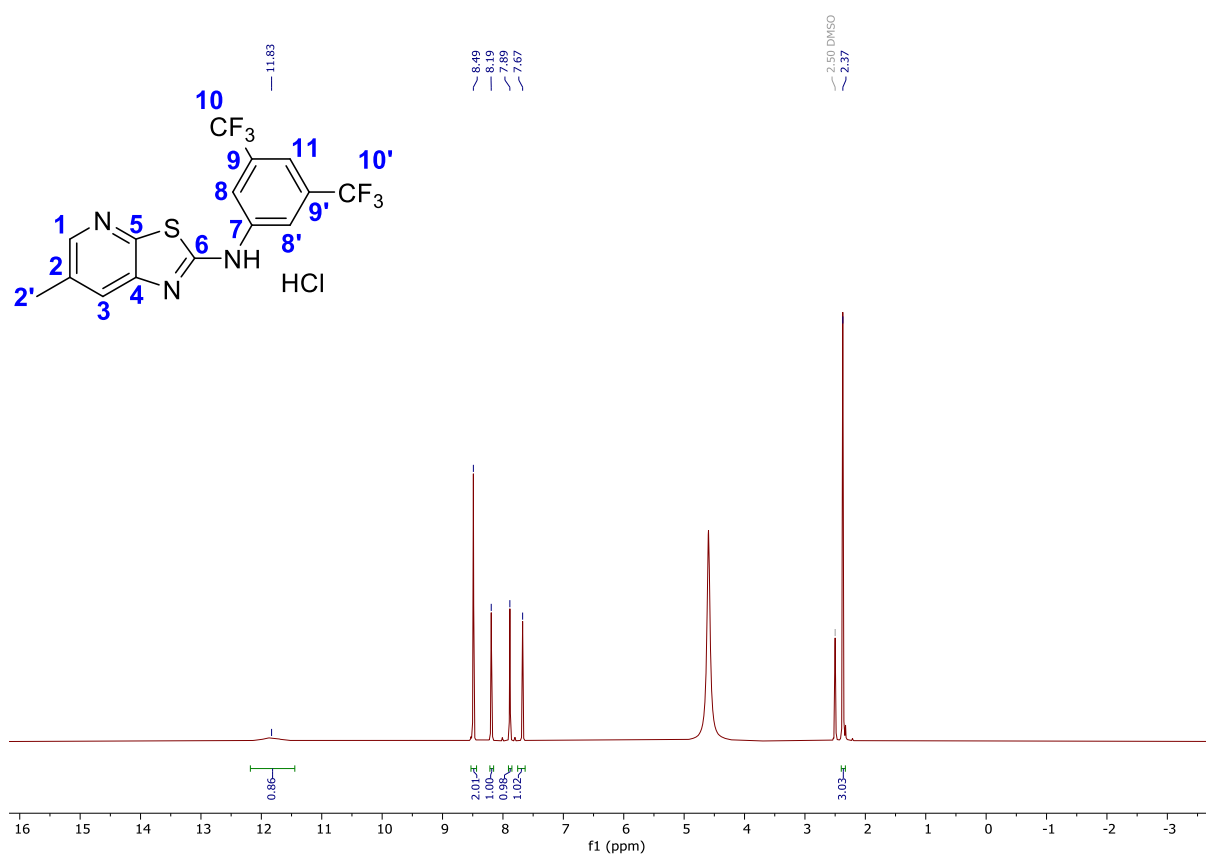
Melting point : 228°C (decomposition)

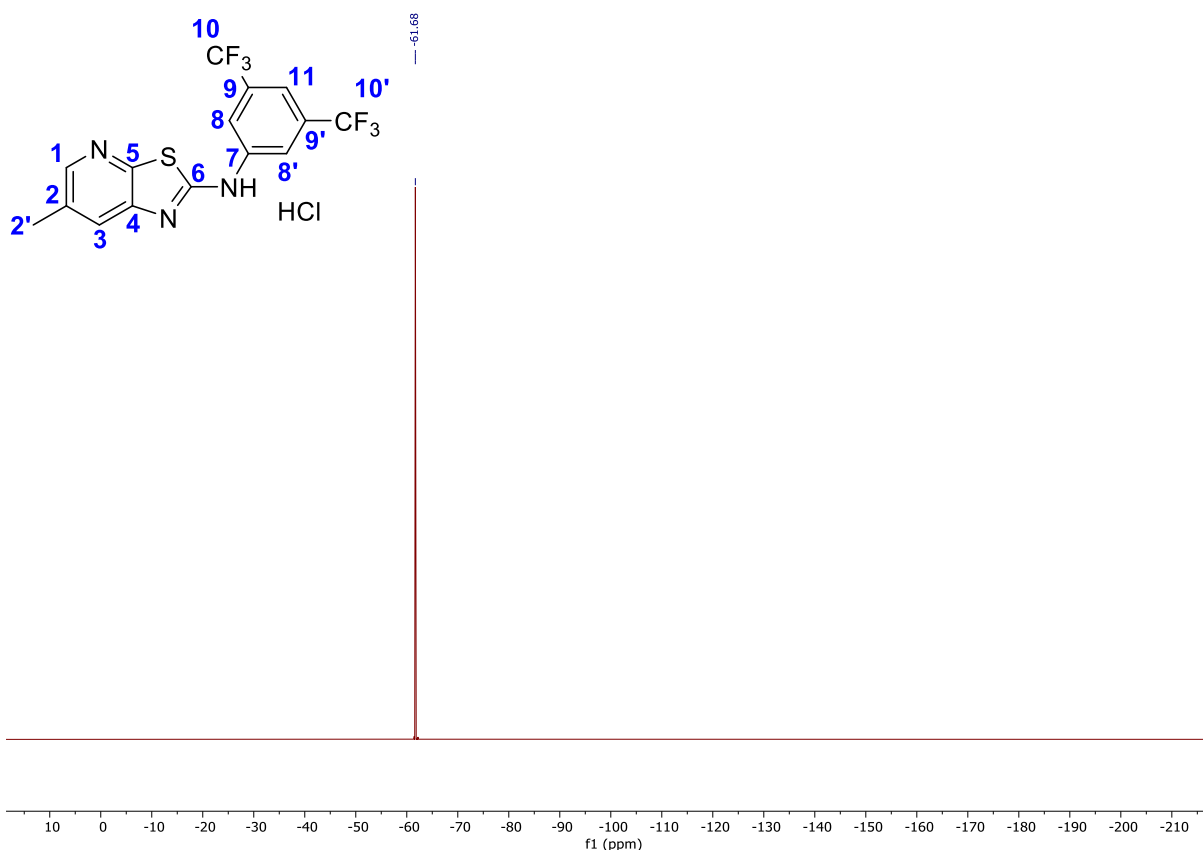
HRMS (ESI+): m/z calculated for $C_{13}H_{12}N_3S$ $[M + H^+] = 242.0746$; found = 242.0749

1H NMR (DMSO-*d*₆, 400 MHz) : $\delta_H = 2.38$ (s, 3H, 2CH_3), 7.06 (t, $J = 7.4$ Hz, 1H, $^{10}H_{Ar}$), 7.38 (t, $J = 7.6$ Hz, 2H, $^9H_{Ar}$ and $^9'H_{Ar}$), 7.80 (d, $J = 8.3$ Hz, 2H, $^8H_{Ar}$ and $^8'H_{Ar}$), 7.88 (s, 1H, $^3H_{Ar}$), 8.20 (s, 1H, $^1H_{Ar}$), 10.93 (bs, 1H, N-H).

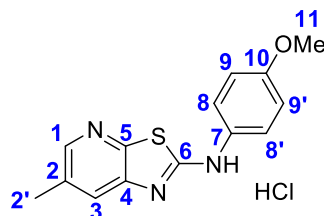
^{13}C NMR (DMSO-*d*₆, 101 MHz) : $\delta_C = 17.8$ (2CH_3), 118.5 ($^8CH_{Ar}$ and $^8'CH_{Ar}$), 122.9 ($^{10}CH_{Ar}$), 127.4 ($^3CH_{Ar}$), 129.1 ($^9CH_{Ar}$ and $^9'CH_{Ar}$), 131.7 ($^2C^{IV}$), 140.0 ($^7C^{IV}$), 141.2 ($^1CH_{Ar}$), 146.9 ($^4C^{IV}$), 149.4 ($^5C^{IV}$) and 161.5 ($^6C^{IV}$).







N-(4-methoxyphenyl)thiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride



General procedure 2 was applied to 4-methoxyphenyl isothiocyanate and 3-amino-2-chloro-5-methylpyridine to give *N*-(4-methoxyphenyl)thiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride in 42% yield.

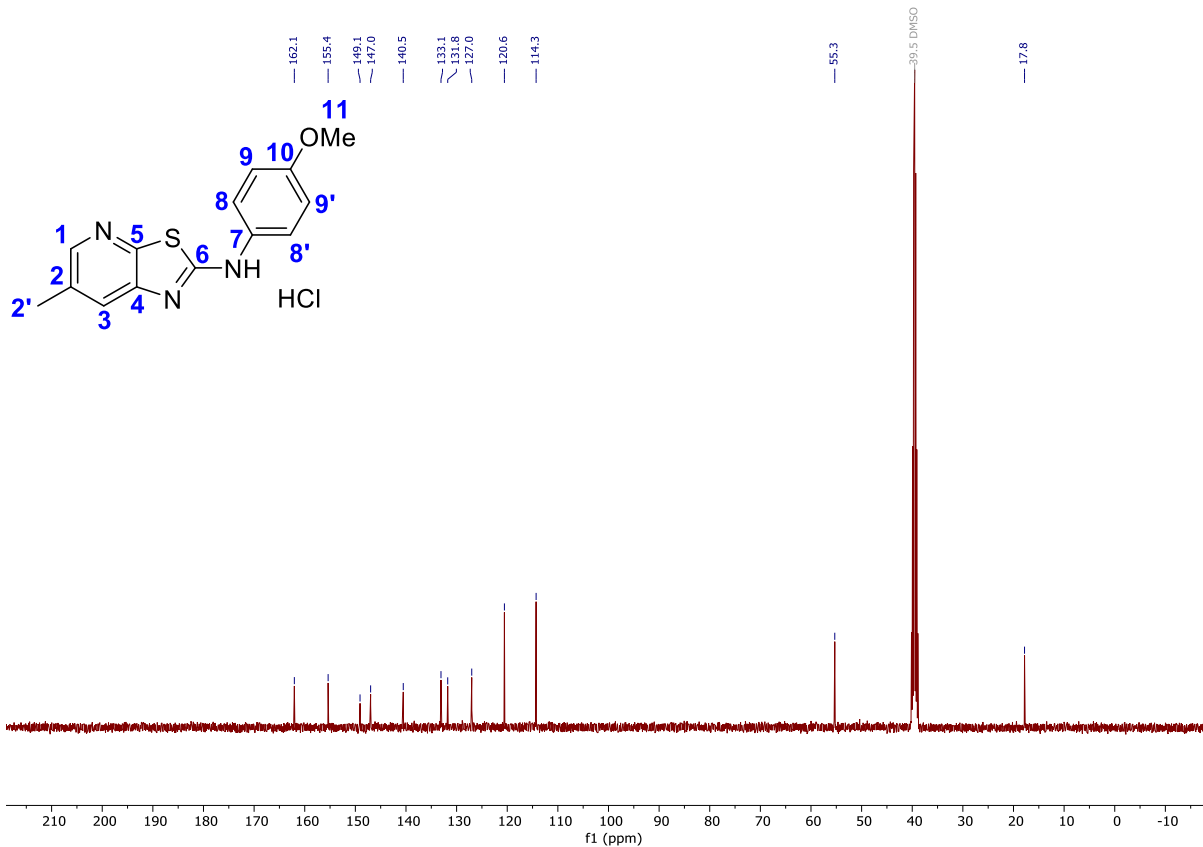
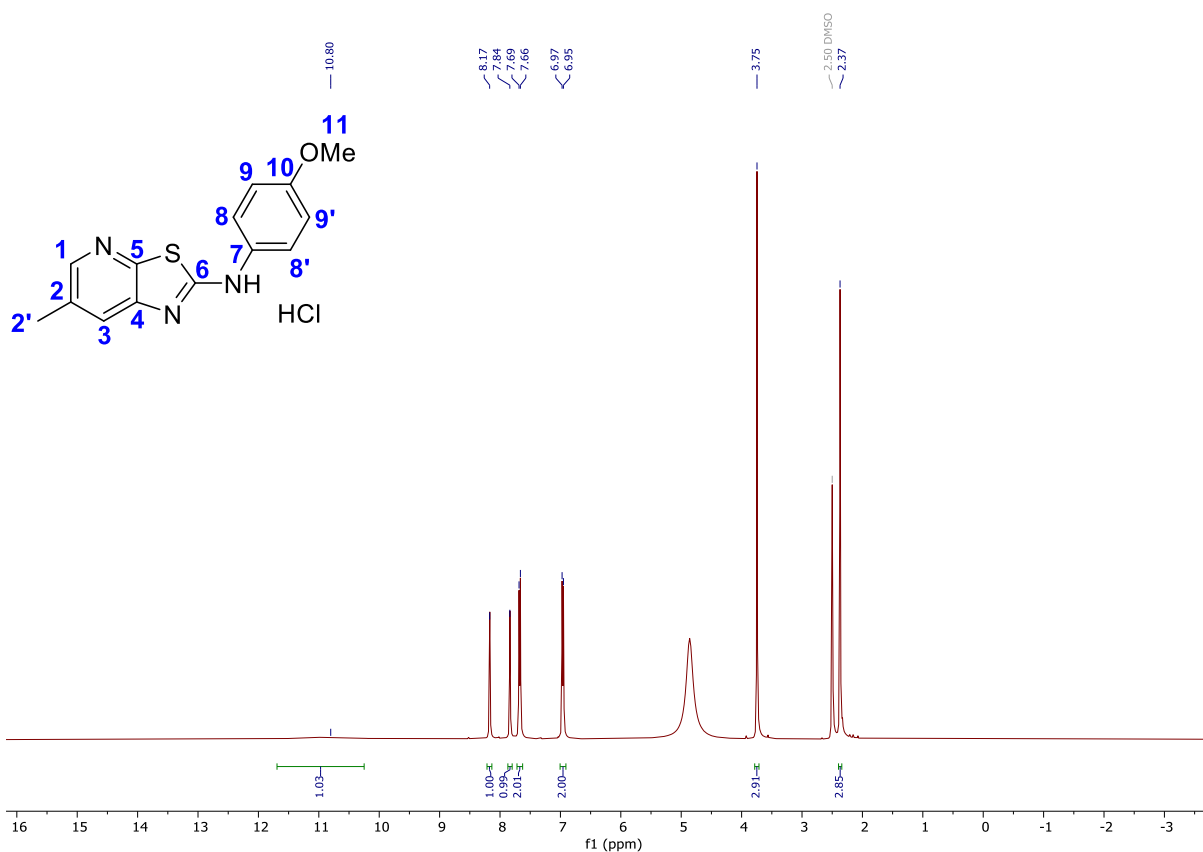
Aspect : yellow powder

Melting point : 212°C (decomposition)

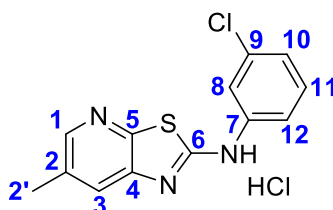
HRMS (ESI+): m/z calculated for $C_{14}H_{14}N_3OS$ $[M + H]^+$ = 272.0852 ; found = 272.0856

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 2.37 (s, 3H, 2CH_3), 3.75 (s, 3H, $^{11}CH_3-O$), 6.96 (d, J = 9.0 Hz, 2H, $^8H_{Ar}$ and $^8'H_{Ar}$), 7.67 (d, J = 9.0 Hz, 2H, $^9H_{Ar}$ and $^9'H_{Ar}$), 7.84 (s, 1H, $^3H_{Ar}$), 8.17 (s, 1H, $^1H_{Ar}$), 10.80 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 17.8 (2CH_3), 55.3 ($^{11}CH_3-O$), 114.3 ($^8CH_{Ar}$ and $^8'CH_{Ar}$), 120.6 ($^9CH_{Ar}$ and $^9'CH_{Ar}$), 127.0 ($^3CH_{Ar}$), 131.8 ($^2C^{IV}$), 133.1 ($^7C^{IV}$), 140.5 ($^1CH_{Ar}$), 147.0 ($^4C^{IV}$), 149.1 ($^5C^{IV}$), 155.4 ($^{10}C^{IV}$) and 162.1 ($^6C^{IV}$).



N-(3-chlorophenyl)thiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride



General procedure 1 was applied to 3-chlorophenyl isothiocyanate and 3-amino-2-chloro-5-methylpyridine to give *N*-(3-chlorophenyl)thiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride in 67% yield.

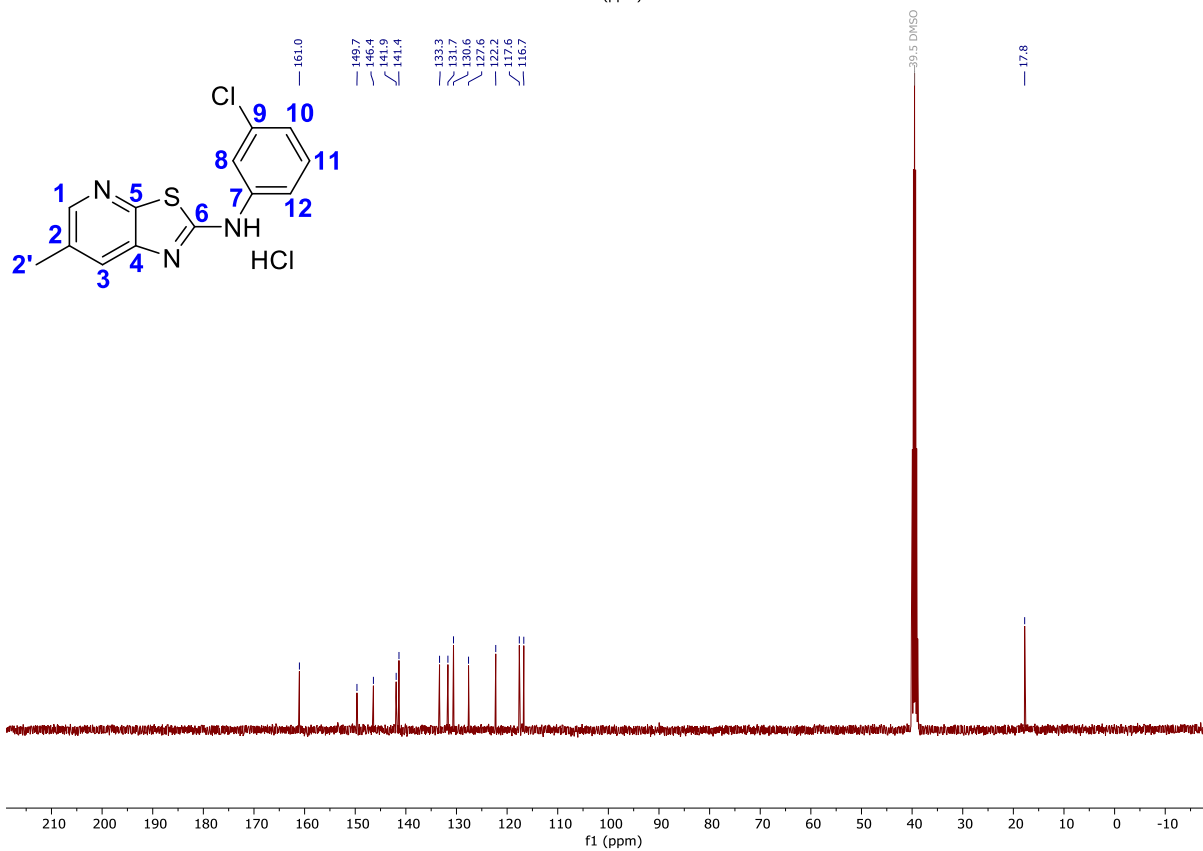
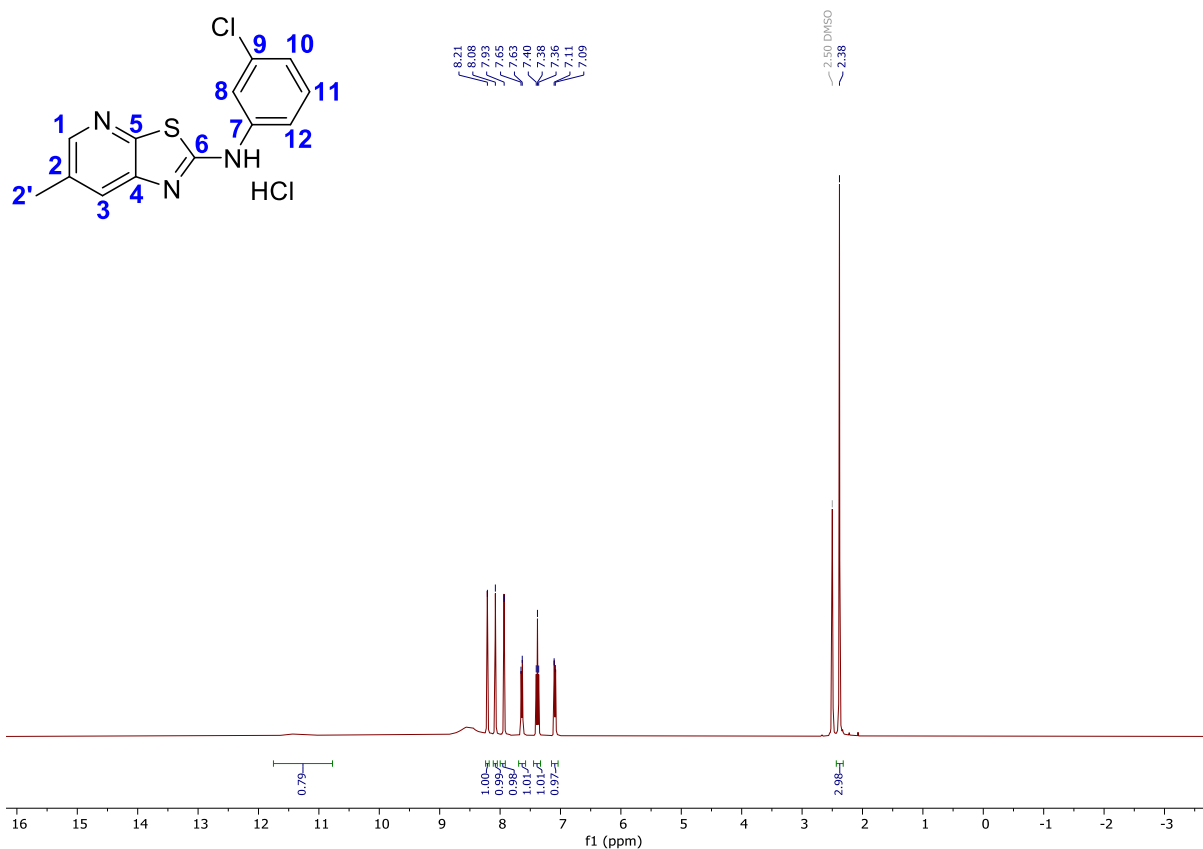
Aspect : colourless powder

Melting point : 214°C.

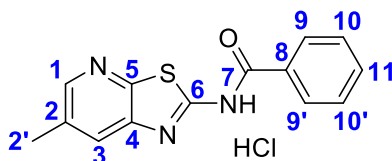
HRMS (ESI+): m/z calculated for $C_{13}H_{11}ClN_3S$ [$M + H^+$] = 276.0357 ; found = 267.0360.

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 2.38 (s, 3H, 2CH_3), 7.09 (dd, J = 8.0, 2.3 Hz, 1H, $^{10}H_{Ar}$), 7.38 (t, J = 8.0 Hz, 1H, $^{11}H_{Ar}$), 7.64 (dd, J = 8.2, 2.3 Hz, 1H, $^{12}H_{Ar}$), 7.93 (s, 1H, $^3H_{Ar}$), 8.08 (s, 1H, $^8H_{Ar}$), 8.21 (s, 1H, $^1H_{Ar}$), 11.34 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 17.8 (2CH_3), 116.7 ($^{12}CH_{Ar}$), 117.6 ($^8CH_{Ar}$), 122.2 ($^{10}CH_{Ar}$), 127.6 ($^3CH_{Ar}$), 130.6 ($^{11}CH_{Ar}$), 131.7 ($^2C^{IV}$), 133.3 ($^3C^{IV}$), 141.4 ($^7C^{IV}$), 141.9 ($^1CH_{Ar}$), 146.4 ($^4C^{IV}$), 149.7 ($^5C^{IV}$) and 161.0 ($^6C^{IV}$).



N-benzamidethiazolo[5,4-*b*]-6-methyl-2-amine hydrochloride



General procedure 1 was applied to benzoyl isothiocyanate and 3-amino-2-chloro-5-methylpyridine to give *N*-benzamidethiazolo[5,4-*b*]-6-methyl-2-amine hydrochloride in 46% yield.

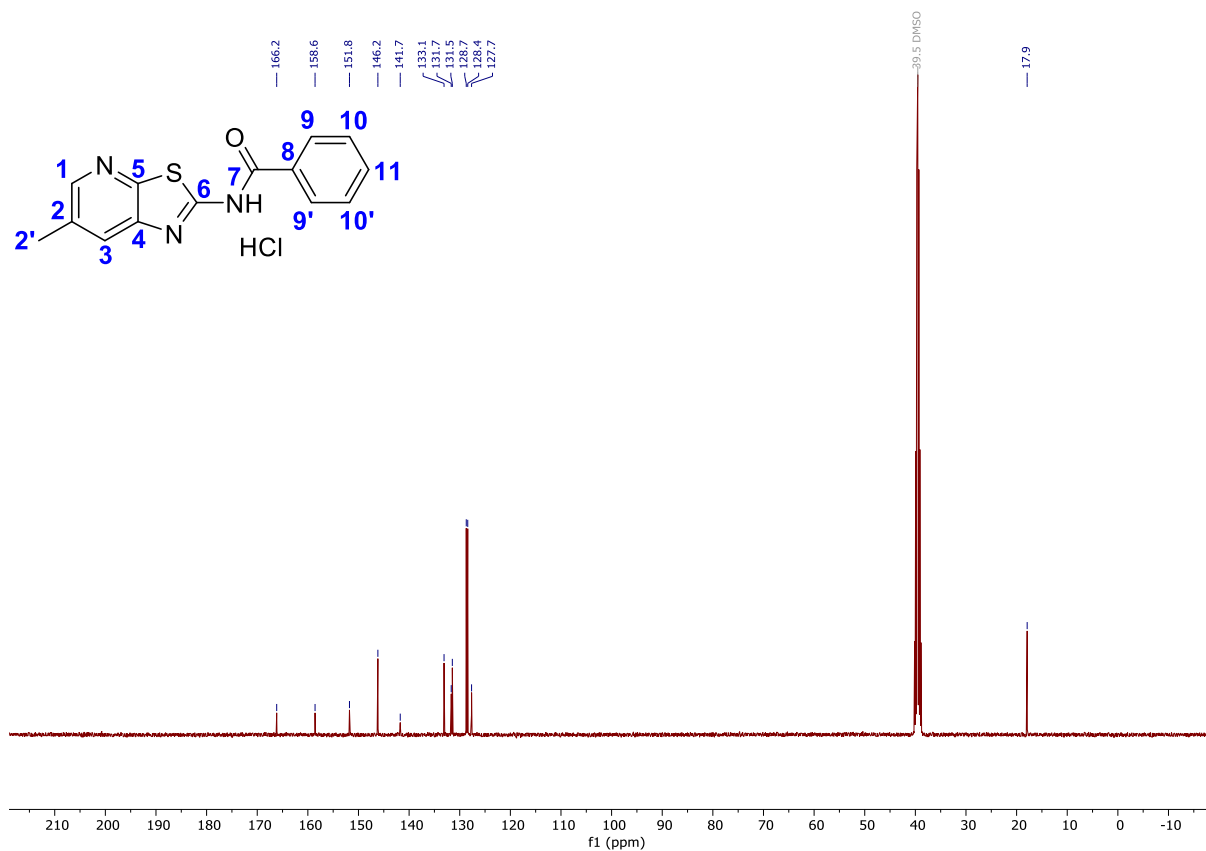
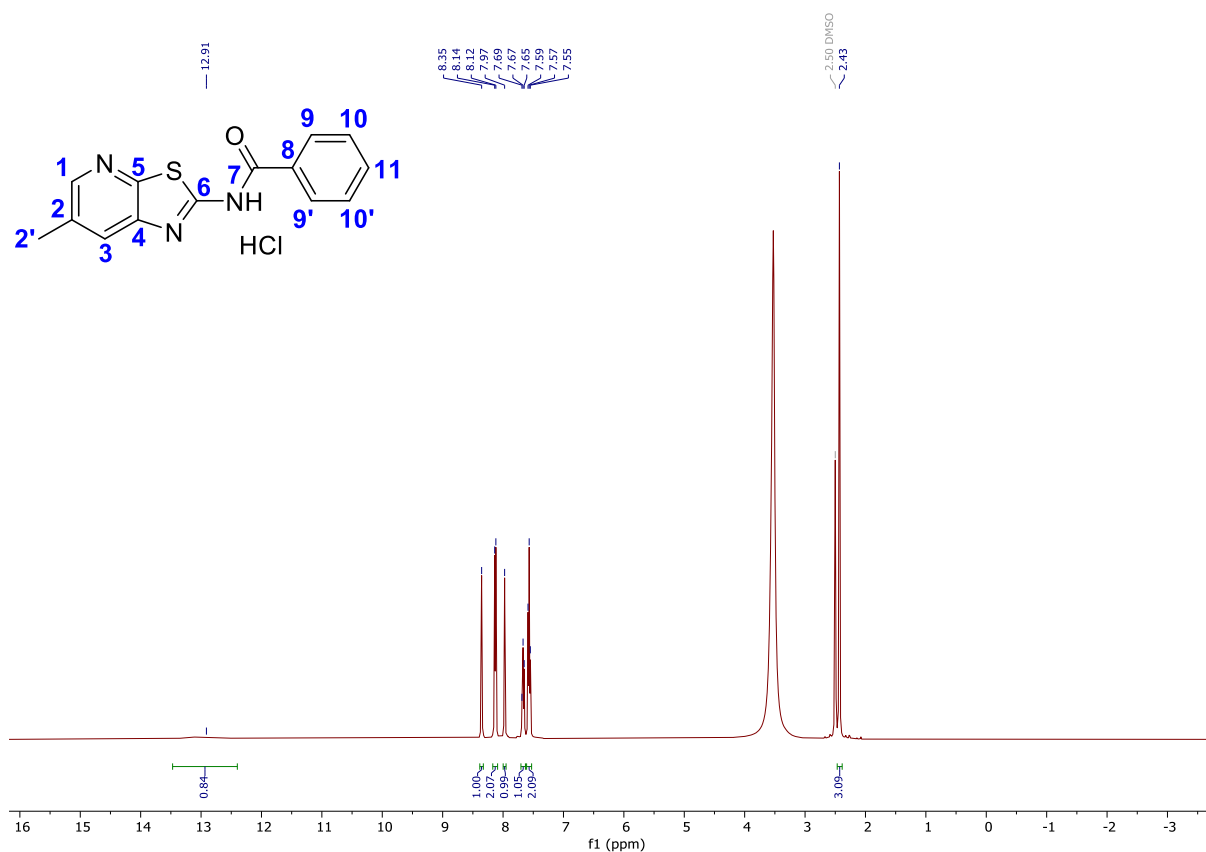
Aspect : colourless powder

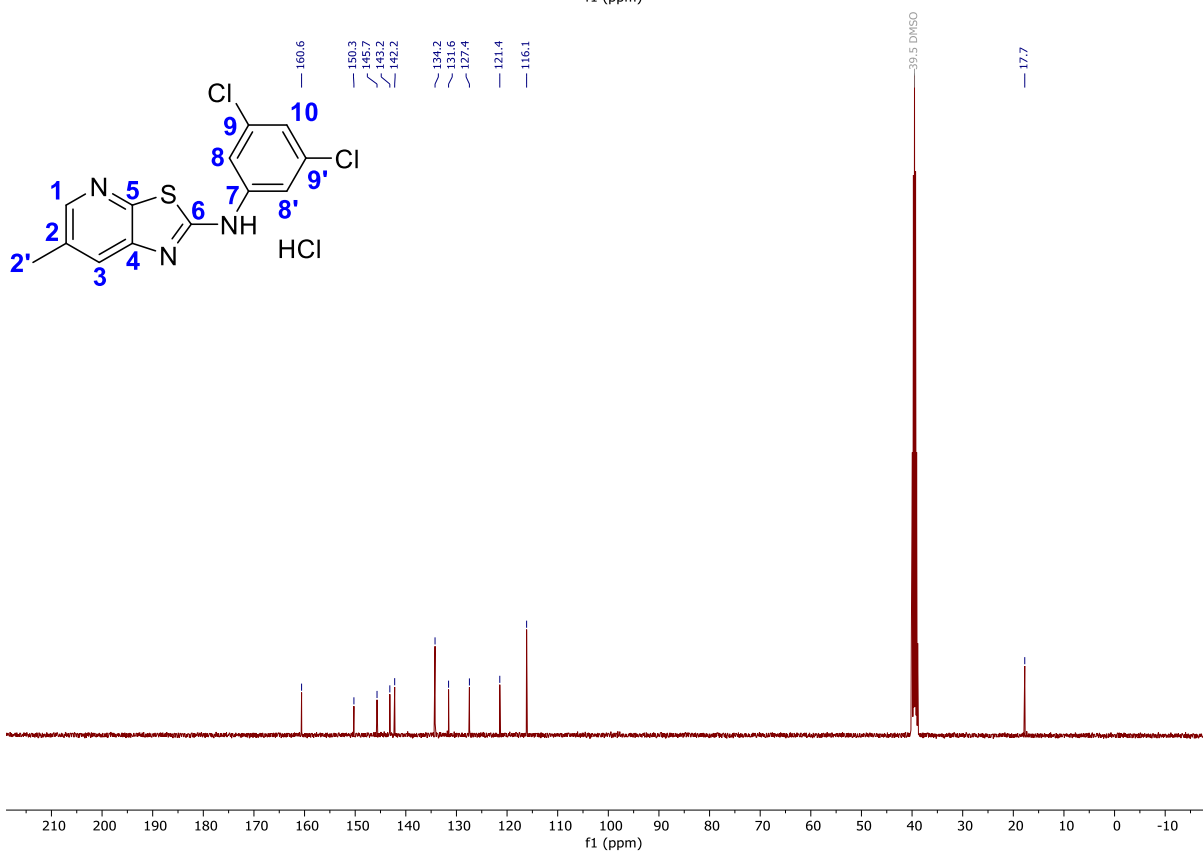
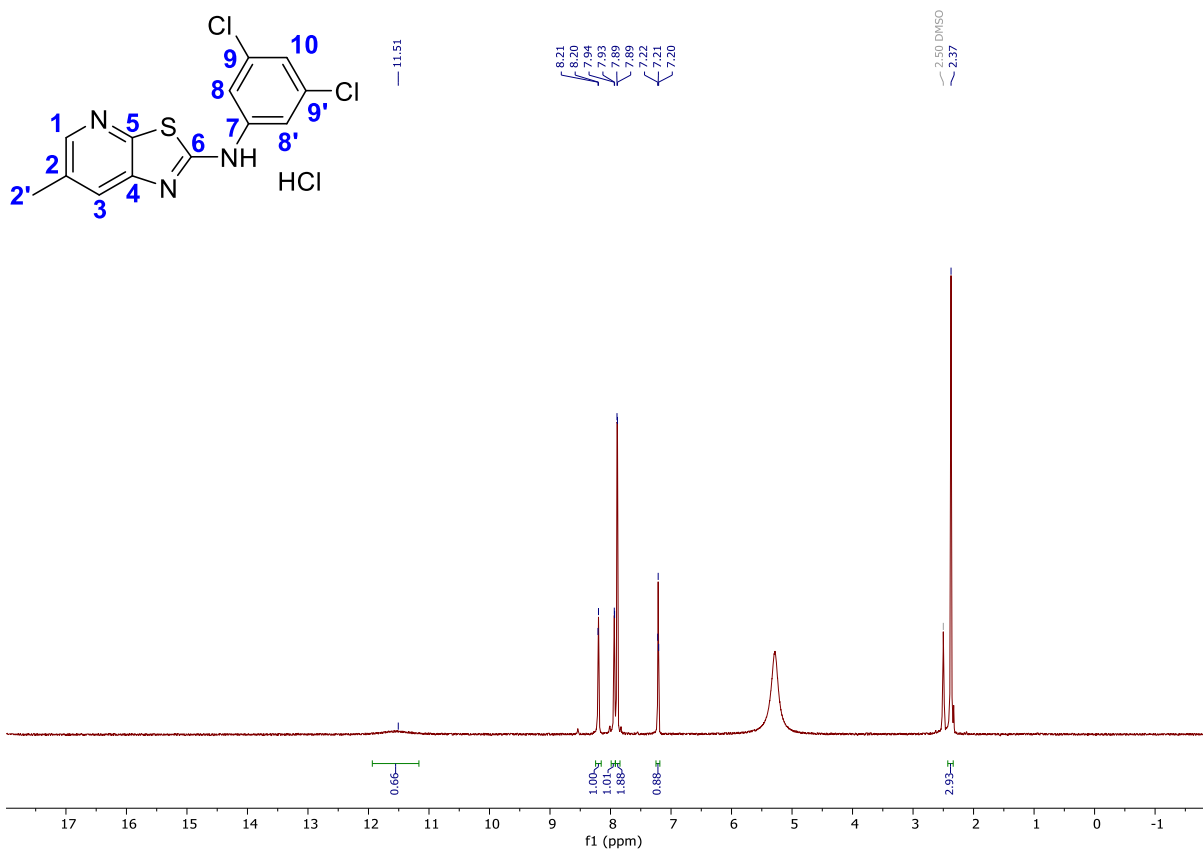
Melting point : 222°C

HRMS (ESI+): m/z calculated for $C_{14}H_{12}N_3OS$ [$M + H^+$] = 270.0696 ; found = 270.0698

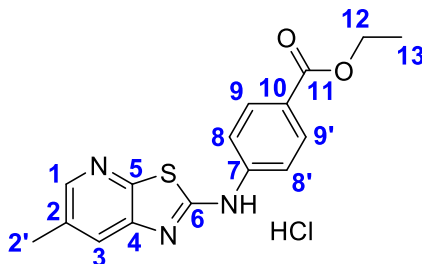
1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 2.43 (s, 3H, 2CH_3), 7.57 (t, $J = 7.7$ Hz, 2H, $^{10}H_{Ar}$ and $^{10'}H_{Ar}$), 7.67 (t, $J = 7.3$ Hz, 1H, $^{11}H_{Ar}$), 7.97 (s, 1H, $^3H_{Ar}$), 8.13 (d, $J = 7.8$ Hz, 2H, $^9H_{Ar}$ and $^9'H_{Ar}$), 8.35 (s, 1H, $^1H_{Ar}$), 12.91 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 17.9 (2CH_3), 127.7 ($^3CH_{Ar}$), 128.4 ($^9CH_{Ar}$ and $^9'CH_{Ar}$), 128.7 ($^{10}CH_{Ar}$ and $^{10'}CH_{Ar}$), 131.5 ($^2C^{IV}$), 131.7 ($^8C^{IV}$), 133.1 ($^{11}CH_{Ar}$), 141.7 ($^4C^{IV}$), 146.2 ($^1CH_{Ar}$), 151.8 ($^5C^{IV}$), 158.6 ($^6C^{IV}$) and 166.2 ($^7C^{IV}=O$).





N-(ethyl 4-aminobenzoate)thiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride



General procedure 1 was applied to ethyl 4-isothiocyanatobenzoate and 3-amino-2-chloro-5-methylpyridine to give *N*-(ethyl 4-aminobenzoate)thiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride in 64% yield.

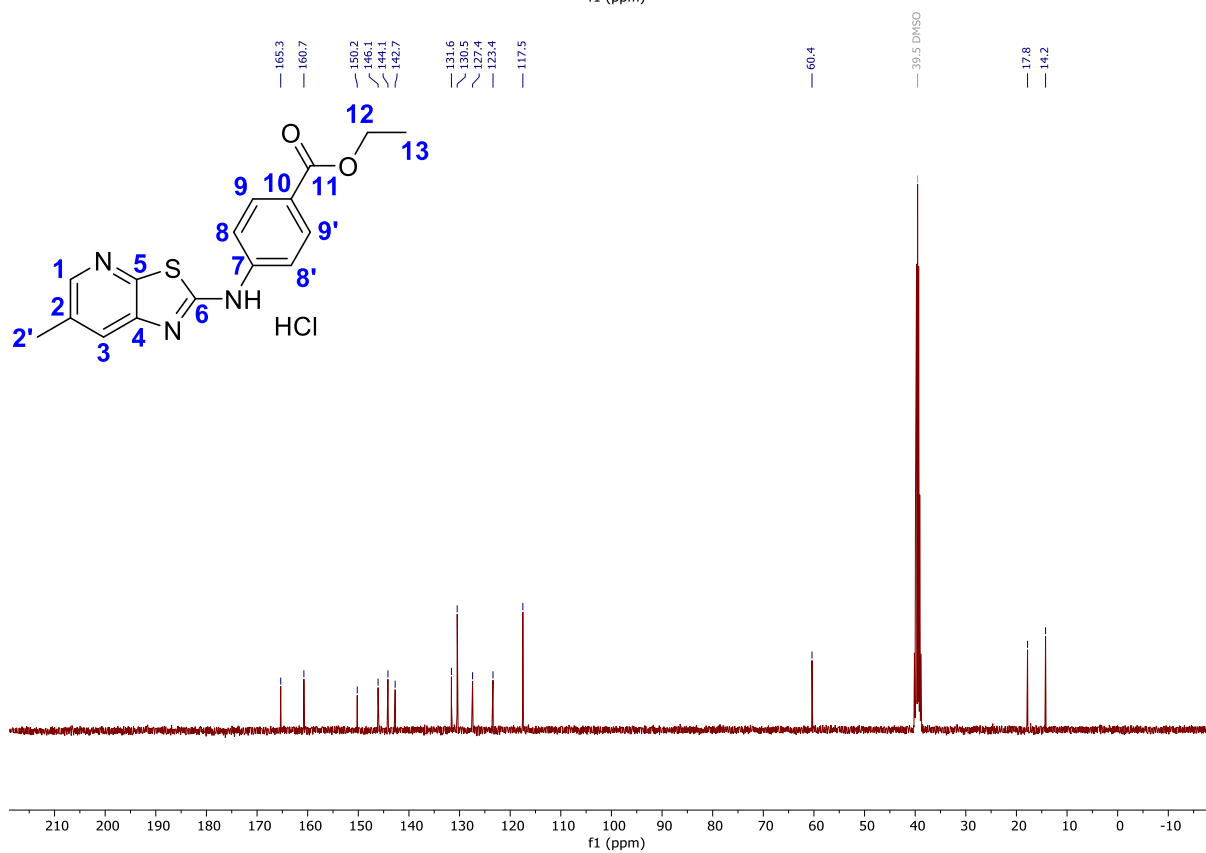
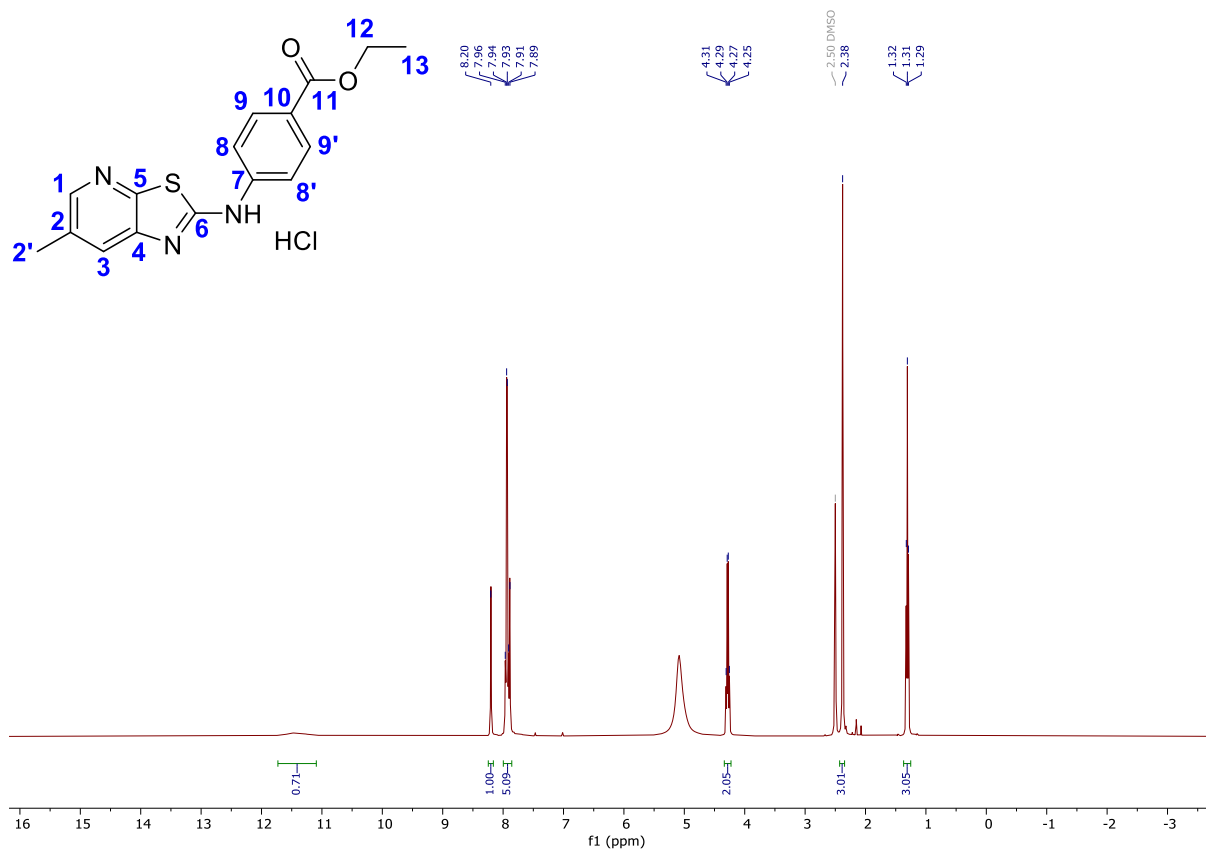
Aspect : beige powder

Melting point : 210°C (decomposition).

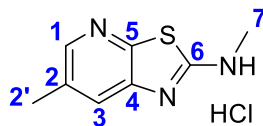
HRMS (ESI+): m/z calculated for $C_{16}H_{16}N_3O_2S$ [$M + H^+$] = 314.0958 ; found = 314.0956.

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 1.31 (t, J = 7.0 Hz, 3H, $^{13}CH_3$), 2.38 (s, 3H, 2CH_3), 4.28 (q, J = 7.0 Hz, 2H, $^{12}CH_2$), 7.89 (s, 1H, $^3H_{Ar}$), 7.89-7.98 (m, 4H, H_{Ar}), 8.20 (s, 1H, $^1H_{Ar}$), 11.41 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 14.2 ($^{13}CH_3$), 17.8 (2CH_3), 60.4 ($^{12}CH_2$), 117.5 (2 × CH_{Ar}), 123.4 ($^{10}C^{IV}$), 127.4 ($^3CH_{Ar}$), 130.5 (2 × CH_{Ar}), 131.6 ($^2C^{IV}$), 142.7 (1CH), 144.2 ($^7C^{IV}$), 146.1 ($^4C^{IV}$), 150.2 ($^5C^{IV}$), 160.8 ($^6C^{IV}$) and 165.3 ($^{11}C^{IV}$).



N-methylthiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride



General procedure 1 was applied to methyl isothiocyanate and 3-amino-2-chloro-5-methylpyridine to give *N*-methylthiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride in 40% yield.

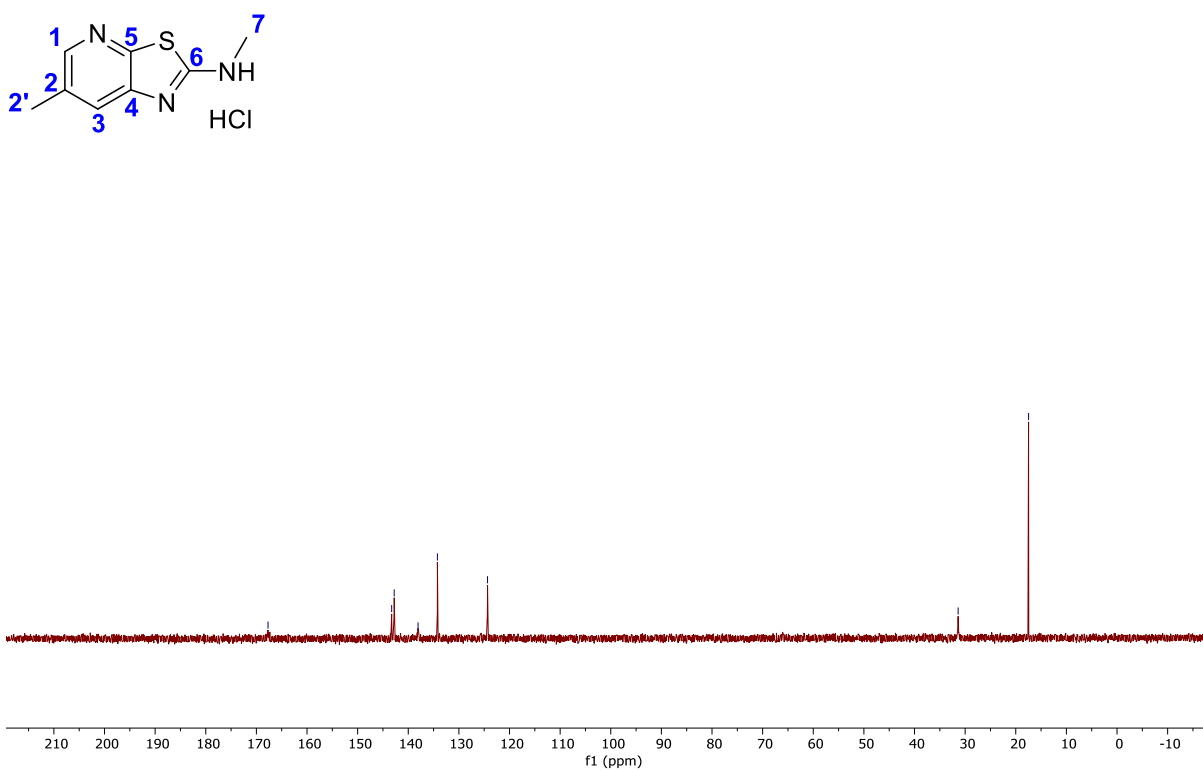
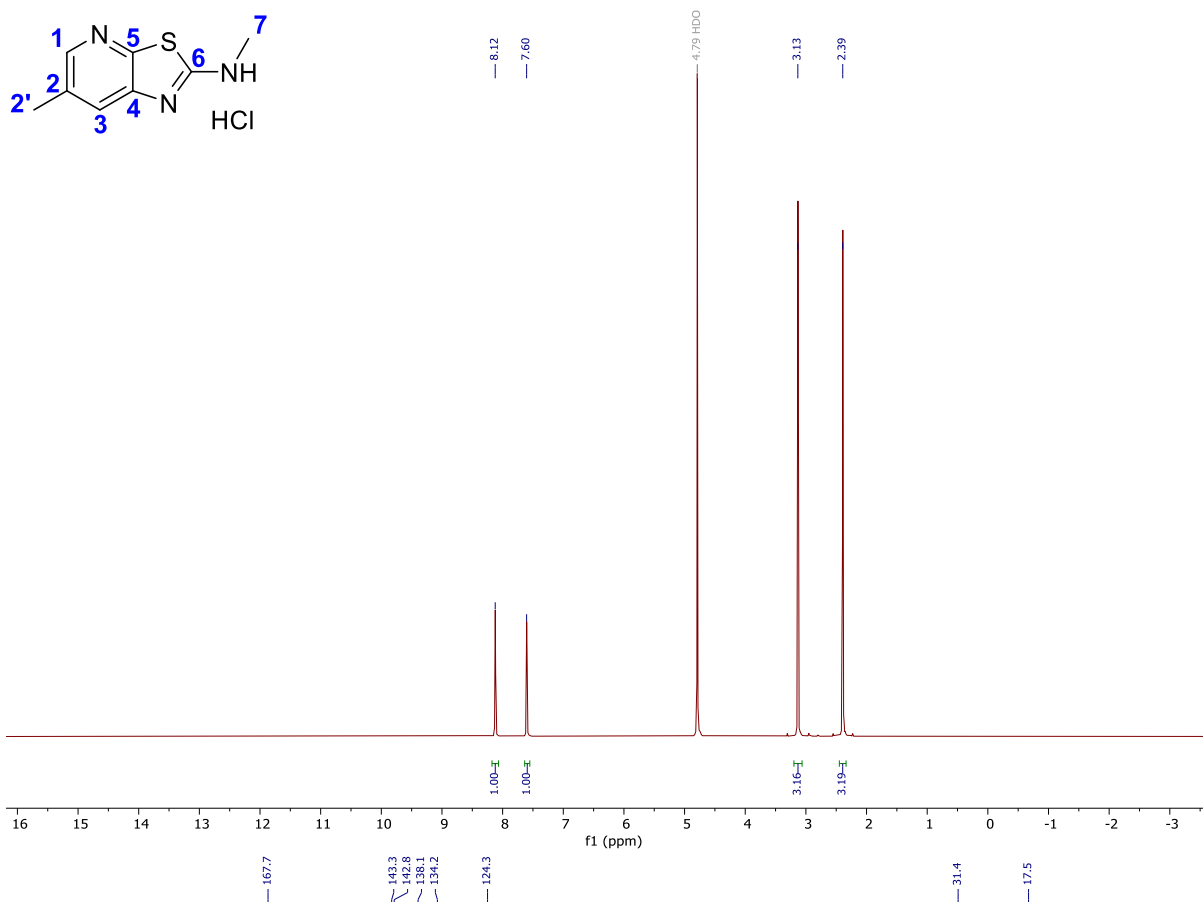
Aspect : colourless powder

Melting point : 186°C (decomposition)

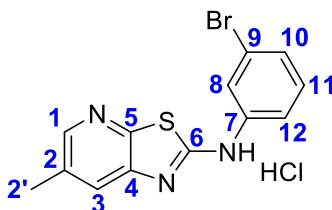
HRMS (ESI+): m/z calculated for $C_8H_{10}N_3S$ [$M + H^+$] = 180.0590 ; found = 180.0587

1H NMR (D_2O , 400 MHz) : δ_H = 2.39 (s, 3H, 2CH_3), 3.13 (s, 3H, 7CH_3), 7.60 (s, 1H, $^3H_{Ar}$), 8.12 (s, 1H, $^1H_{Ar}$).

^{13}C NMR (D_2O , 101 MHz) : δ_C = 17.5 (2CH_3), 31.4 (7CH_3), 124.3 ($^3CH_{Ar}$), 134.2 ($^2C^{IV}$), 138.1 (C^{IV}), 142.8 ($^1CH_{Ar}$), 143.3 (C^{IV}) and 167.7 ($^6C^{IV}$).



N-(3-bromophenyl)thiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride



General procedure 1 was applied to 3-bromophenyl isothiocyanate and 3-amino-2-chloro-5-methylpyridine to give *N*-(3-bromophenyl)thiazolo[5,4-*b*]-6-methylpyridin-2-amine hydrochloride in 62% yield.

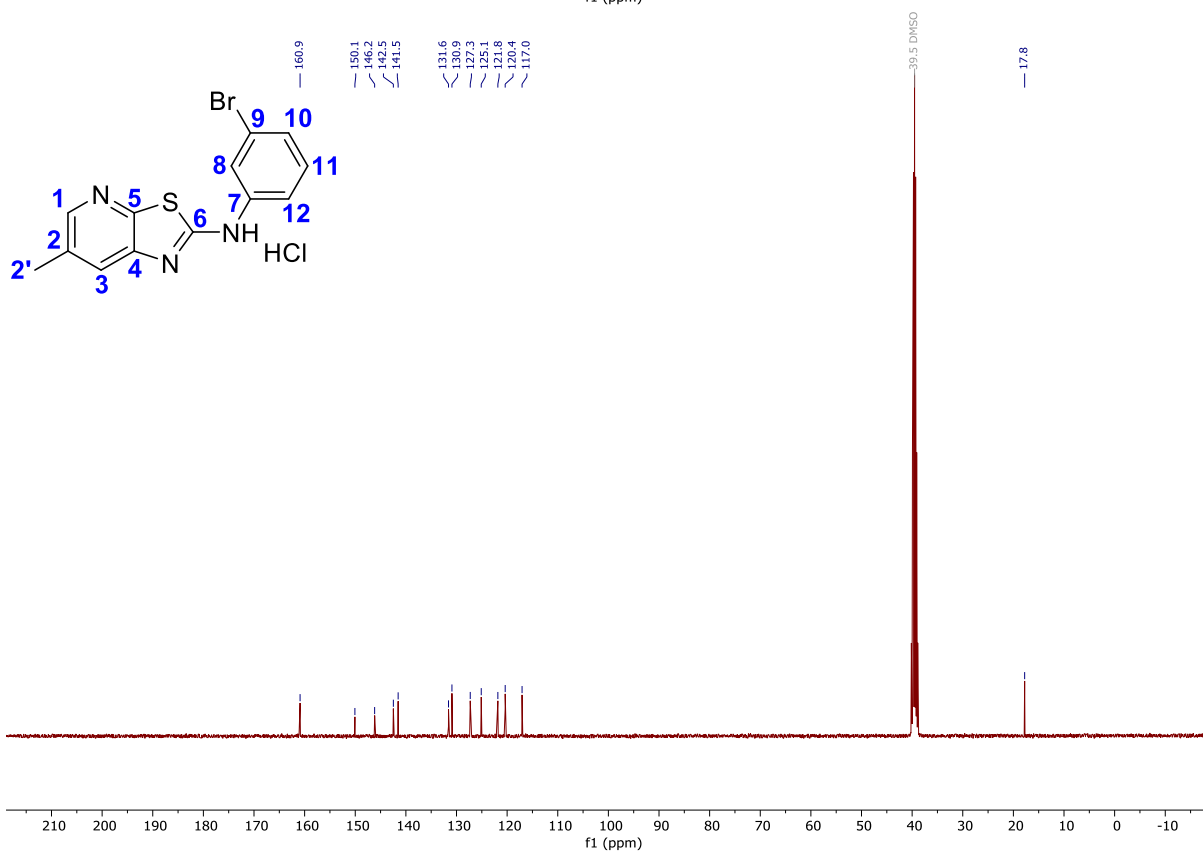
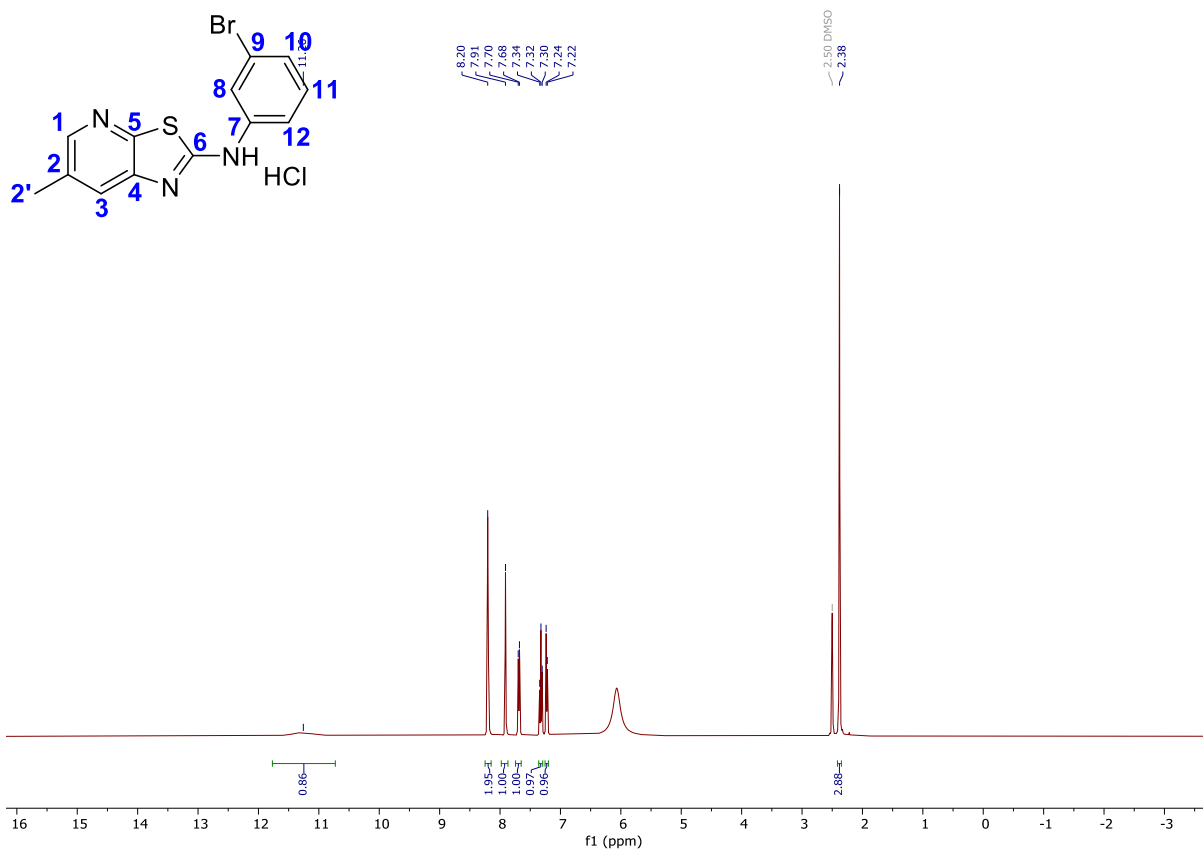
Aspect : beige powder.

Melting point : 247-248°C

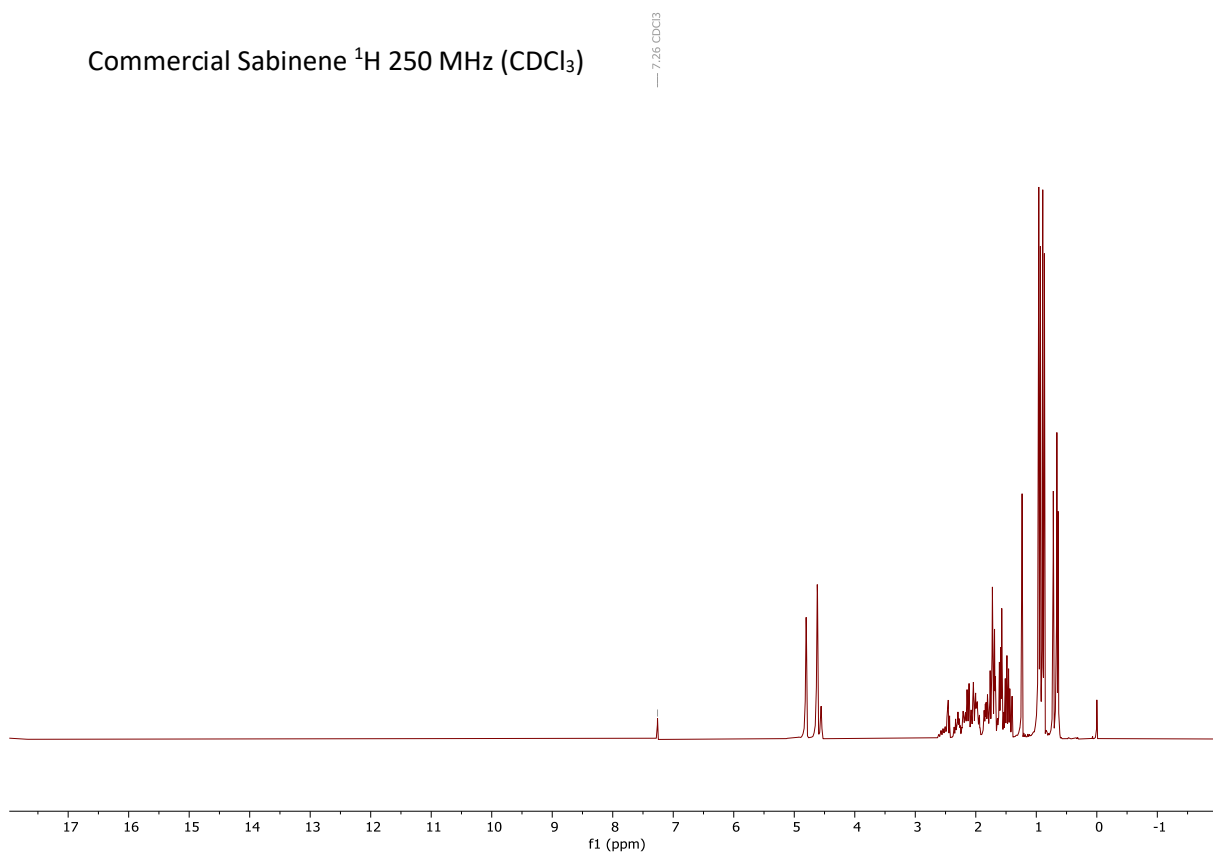
HRMS (ESI+): m/z calculated for $C_{13}H_{11}BrN_3S$ [$M + H^+$] = 319.9852 ; found = 319.9847

1H NMR (DMSO-*d*₆, 400 MHz) : δ_H = 2.38 (s, 3H, 2CH_3), 7.23 (d, J = 7.8 Hz, 1H, $^{12}H_{Ar}$), 7.32 (t, J = 7.9 Hz, 1H, $^{11}H_{Ar}$), 7.69 (d, J = 8.1 Hz, 1H, $^{10}H_{Ar}$), 7.91 (s, 1H, $^3H_{Ar}$), 8.20 (s, 2H, $^1H_{Ar}$ and $^8H_{Ar}$), 11.26 (bs, 1H, N-H).

^{13}C NMR (DMSO-*d*₆, 101 MHz) : δ_C = 17.8 (2CH_3), 117.0 ($^{10}CH_{Ar}$), 120.4 ($^8CH_{Ar}$), 121.8 ($^9C^{IV}$), 125.1 ($^{12}CH_{Ar}$), 127.3 ($^3CH_{Ar}$), 130.9 ($^{11}CH_{Ar}$), 131.6 ($^2C^{IV}$), 141.5 ($^7C^{IV}$), 142.5 ($^1CH_{Ar}$), 146.2 ($^4C^{IV}$), 150.1 ($^5C^{IV}$) and 160.9 ($^6C^{IV}$).



Commercial Sabinene ^1H 250 MHz (CDCl_3)



Distilled Sabinene ^1H 250 MHz (CDCl_3)

