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# Laser synthesis: a solvent-free approach for preparation of phenylthiazolo[5,4-*b*]pyridine derivatives

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**Materials and methods**

All reagents were purchased from commercial suppliers and were used without further purification except for DMF, which was stored under argon and activated molecular sieves. The reactions were monitored by thin-layer chromatography (TLC) analysis using silica gel (60 F254) plates. Compounds were visualized by UV irradiation. Flash column chromatography was performed on silica gel 60 (230–400 mesh, 0.040–0.063 mm). Melting points (m.p. [◦C]) were taken on samples in open capillary tubes and are uncorrected. 1H and 13C NMR spectra were recorded on a Bruker DPX 250 (13C, 62.9 MHz) (Bruker, Wissembourg, France), Bruker Avance II 250.13 (13C, 63 MHz), Bruker Avance 400.13 (13C, 101 MHz) (Bruker, Wissembourg, France), or on a Bruker Avance III HD nanobay 400.13 (13C, 101 MHz) (Bruker, Wissembourg, France). Chemical shifts are given in parts per million from tetramethylsilane (TMS) as internal standard. The following abbreviations are used for the proton spectra multiplicities: b: broad, s: singlet, d: doublet, t: triplet, q: quartet, p: pentuplet, m: multiplet. Coupling constants (J) are reported in hertz (Hz). Multiplicities were determined by the DEPT 135 sequence. Attributions of protons and carbons were made with the help of HSQC and HMBC 2D NMRs. Eudesmane numbering of carbons was used instead of the IUPAC numbering. Microwaves-assisted reactions were carried out in a Biotage Initiator microwave synthesis instrument and temperatures were measured by IR-sensor (Biotage, Uppsala, Sweden), High-resolution mass spectra (HRMS) were performed on a Maxis UHR-q-TOF mass spectrometer Bruker 4G (Bruker, Wissembourg, France), with an electrospray ionisation (ESI) mode.

**General procedure**

In a sealed tube, the 3-amino-2-chloropyridine (200 mg, 1,55 mmol) was mixed with the isothiocyanate (1 eq). The tube was irradiating with an Nd-YAG nanosecond laser (λ= 355 nm). The formed product was purified with a chromatography column, $CH_2Cl_2$/MeOH (90:10).

N-phenylthiazolo[5,4-*b*]pyridin-2-amine (**1**) this compound has been synthesized with general procedure. White yellow solid. (315 mg, 90%), m.p : 178-180 °C. $^1$H NMR (400 MHz, DMSO) δ 7.04 (t, *J* = 7.4 Hz, 1H), 7.31 – 7.41 (m, 3H), 7.80 – 7.91 (m, 3H), 8.23 (dd, *J* = 4.8, 1.4 Hz, 1H), 11.05 (s, 1H) ppm. $^{13}$C NMR (101 MHz, DMSO) δ 118.7 (2CH), 121.9 (CH), 123.0 (CH), 125.6 (CH), 129.4 (2CH), 140.7 (Cq), 143.6 (CH), 146.3 (Cq), 155.0 (Cq), 161.2 (Cq) ppm.[1]

N-(4-methoxyphenyl)thiazolo[5,4-*b*]pyridin-2-amine (**3**) this compound has been synthesized with general procedure. white yellow solid. 242.78 mg, 61%), m.p 159-161 °C. $^1$H NMR (400 MHz, DMSO) δ 3.74 (s, 3H), 6.96 (d, *J* = 9.0 Hz, 2H), 7.32 (dd, *J* = 8.1, 4.8 Hz, 1H), 7.67 (d, *J* = 9.0 Hz, 2H), 7.82 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.20 (dd, *J* = 4.7, 1.1 Hz, 1H), 10.48 (s, 1H) ppm. $^{13}$C NMR (101 MHz, DMSO) δ 55.7 ($CH_3$), 114.7 (2CH), 120.8 (2CH), 121.9 (CH), 125.2 (CH), 133.7 (C), 143.2 (CH), 146.6 (C), 154.9 (C), 155.6 (C), 161.7 (C) ppm.[2]

N-(4-chlorophenyl)thiazolo[5,4-*b*]pyridin-2-amine (**4**) this compound has been synthesized with general procedure. Yellow solid. (267.03 mg, 66%), m.p 261-263 °C.$^1$H NMR (400 MHz, DMSO) δ 7.35 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.41 (d, *J* = 8.7 Hz, 2H), 7.84 – 7.94 (m, 3H), 8.25 (d, *J* = 4.3 Hz, 1H), 11.24 (s, 1H) ppm. $^{13}$C NMR (101 MHz, DMSO) δ 120.2 (2CH) 121.9 (CH), 125.8 (CH), 126.4 (C), 129.2 (2CH), 139.6 (C), 143.8 (CH), 146.1 (C), 155.0 (C),160.9 (C) ppm. [CAS : 444791-31-5]

N-(4-fluorophenyl)thiazolo[5,4-*b*]pyridin-2-amine (**5**) this compound has been synthesized with general procedure. White yellow solid. (353 mg, 92%), m.p 210-212 °C. $^1$H NMR (400 MHz, DMSO) δ 7.16 – 7.27 (m, 2H), 7.35 (dd, *J* = 8.1, 4.8 Hz, 1H), 7.83 – 7.86 (m, 3H), 8.23 (dd, *J* = 4.8, 1.4 Hz, 1H), 10.97 (s, 1H) ppm. $^{13}$C NMR (101 MHz, DMSO) δ 115.9 (CH), 116.1 (CH), 120.4 (CH), 120.5 (CH), 121.9 (CH), 125.6 (CH), 137.0 (Cq), 143.6 (CH), 146.2 (Cq), 154.9 (Cq), 158.0 (C-F), 161.2 (Cq) ppm. $^{19}$F NMR (376 MHz, DMSO) δ -120.06 ppm.[3]

*N*-(3,5-bis(trifluoromethyl)phenyl)thiazolo[5,4-*b*]pyridin-2-amine (**7**) this compound has been synthesized with general procedure. White solid. (439 mg, 78%), m.p: 262-264 °C. $^{1}$H NMR (400 MHz, DMSO) δ 7.40 (dd, *J* = 8.1, 4.8 Hz, 1H), 7.69 (s, 1H), 7.99 (dd, *J* = 8.1, 1.4 Hz, 1H), 8.32 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.42 (s, 2H), 11.34 (s, 1H) ppm. $^{13}$C NMR (101 MHz, DMSO) δ 115.4 (CH), 118.1 (CH), 122.2 (CH), 123.7 ($CF_3$), 126.8 (CH), 131.4 ($CF_3$), 142.1 (2C), 144.7 (CH), 145.5 (C), 154.7 (C), 160.6 (2C), ppm. $^{19}$F NMR (376 MHz, DMSO) δ -61.71 ppm. HRMS: calcd for $C_{14}H_8F_6N_3S$ $[M + H]^+$ 364.0337, found 364.0335.

*N*-(2-chloro-5-trifluoromethylphenyl)thiazolo[5,4-*b*]pyridin-2-amine, (**8**) this compound has been synthesized with general procedure. white yellow solid. (408 mg, 80%), m.p 160-162 °C. $^{1}$H NMR (250 MHz, DMSO) δ 7.37 (dd, *J* = 8.1, 4.8 Hz, 1H), 7.49 (ddd, *J* = 8.4, 2.2, 0.6 Hz, 1H), 7.77 (dd, *J* = 8.4, 0.6 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 8.40 – 8.22 (m, 1H), 8.85 (s, 1H),10.50 (s, 1H) ppm. $^{13}$C NMR (63 MHz, DMSO) δ 119.8 (CH), 121.6 (CH), 122.0 (CH), 126.3 (CH), 128.3 (C), 128.6 (C), 130.7 (C) 131.4 (CH), 137.7 (C), 144.4 (CH), 145.1 (C), 155.4 (C), 161.9 (C) ppm. $^{19}$F NMR (376 MHz, DMSO) δ -61.23 ppm. HRMS: calcd for $C_{13}H_8ClF_3N_3S$ $[M + H]^+$ 330.0074, found 330.0068.

*N*-(2,6-difluorophenyl)thiazolo[5,4-*b*]pyridin-2-amine (**9**) this compound has been synthesized with general procedure. white yellow solid. (250 mg, 61%), m.p 192-194 °C. $^{1}$H NMR (400 MHz, DMSO) δ 7.18– 7.47 (m, 4H), 7.77 (dd, *J* = 8.1, 1.5 Hz, 1H),8.22 (dd, *J* = 4.8, 1.5 Hz, 1H), 10.26 (s, 1H) ppm. $^{13}$C NMR (101 MHz, DMSO) δ () 163.5 (2C), 159.4 (C), 156.90(C), 155.2 (C), 145.6 (C), 143.5 (CH), 128.5 (CH), 125.5 (CH), 121.9 (CH), 112.8 (CH), 112.6 (CH) ppm. $^{19}$F NMR (376 MHz, DMSO) δ -118.17 ppm. HRMS: calcd for $C_{12}H_8F_2N_3S$ $[M + H]^+$ 264.0401, found 264.0397.

## NMR spectra

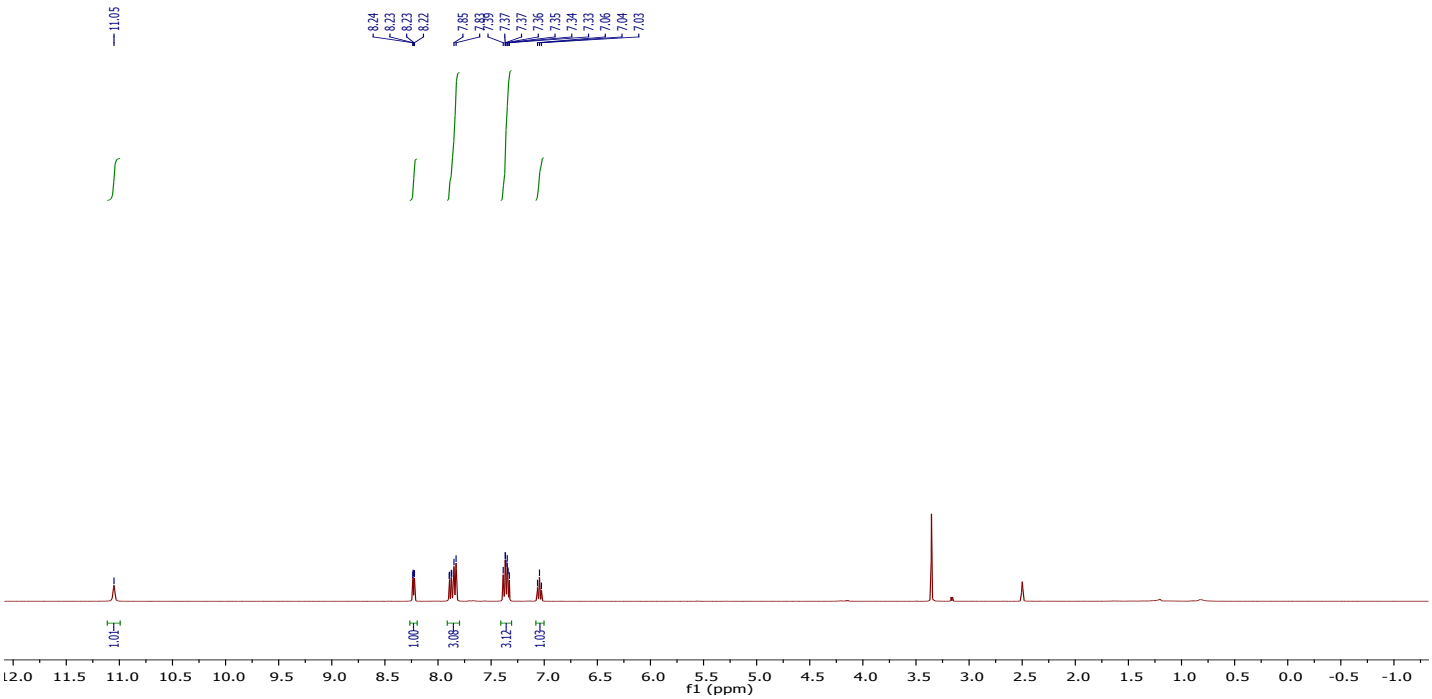


**Figure 1.** $^{1}$H NMR spectrum of *N*-phenylthiazolo[5,4-*b*]pyridin-2-amine (**1**) in DMSO.

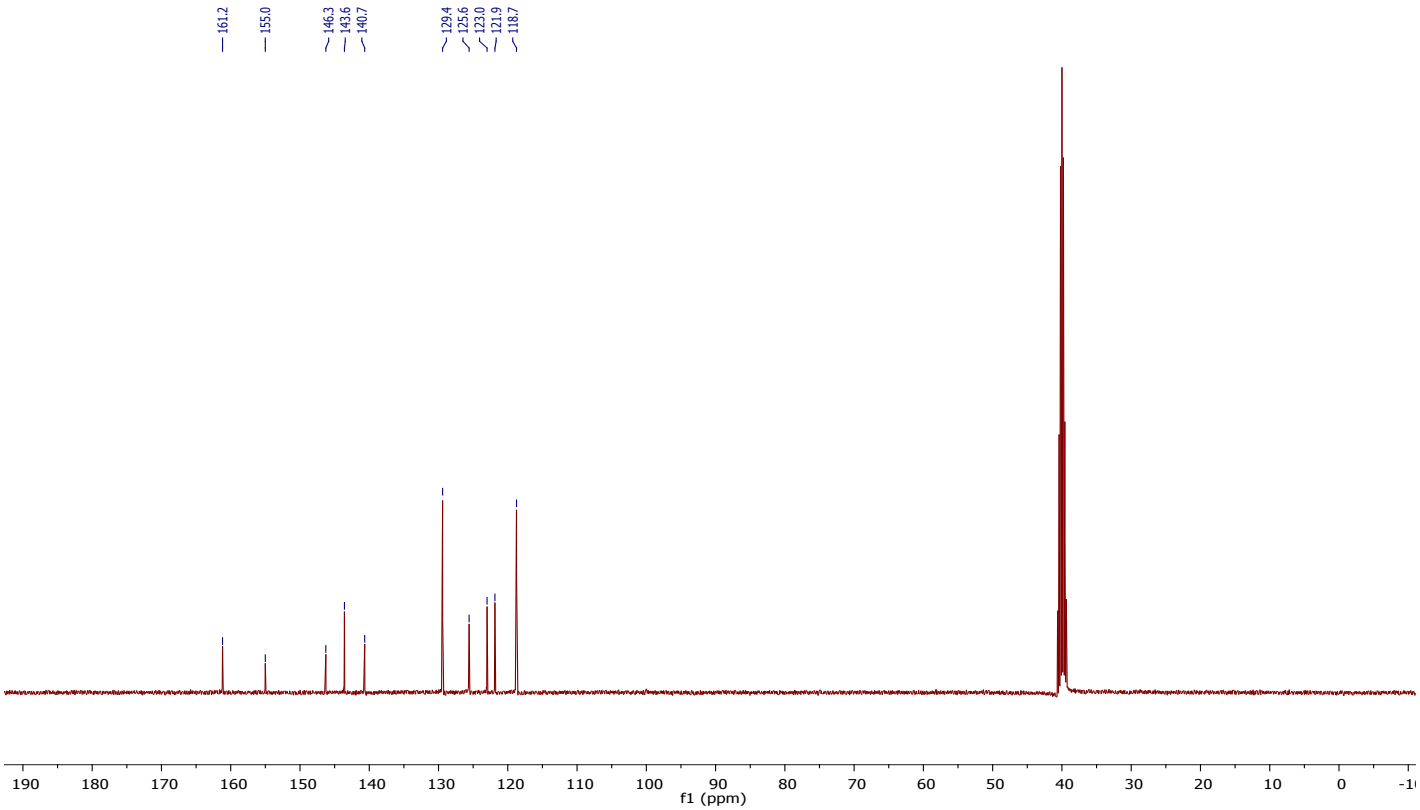


**Figure 2.** $^{13}$C NMR spectrum of *N*-phenylthiazolo[5,4-*b*]pyridin-2-amine (**1**) in DMSO.

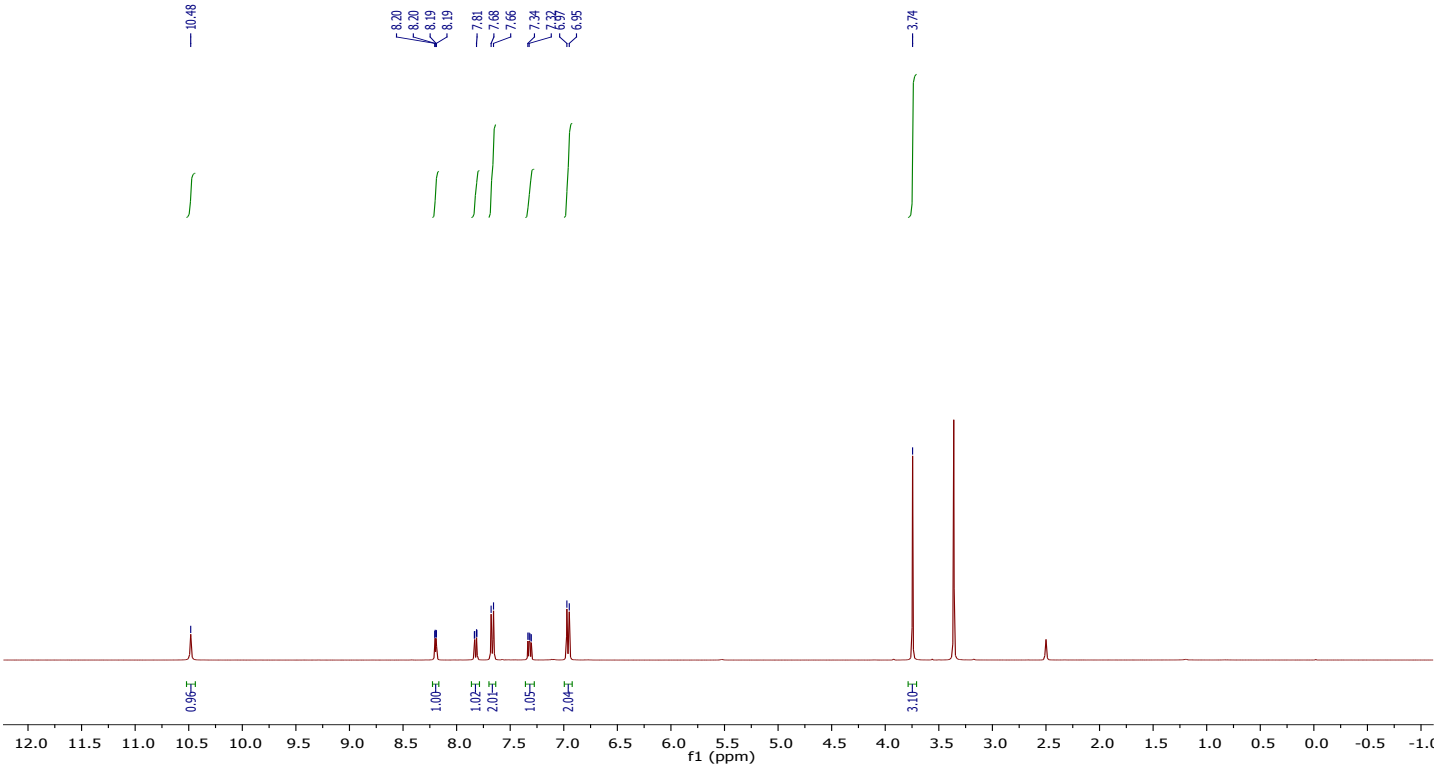


**Figure 3.** $^{1}$H NMR spectrum of *N*-(4-methoxyphenyl)thiazolo[5,4-*b*]pyridin-2-amine (**3**) in DMSO.

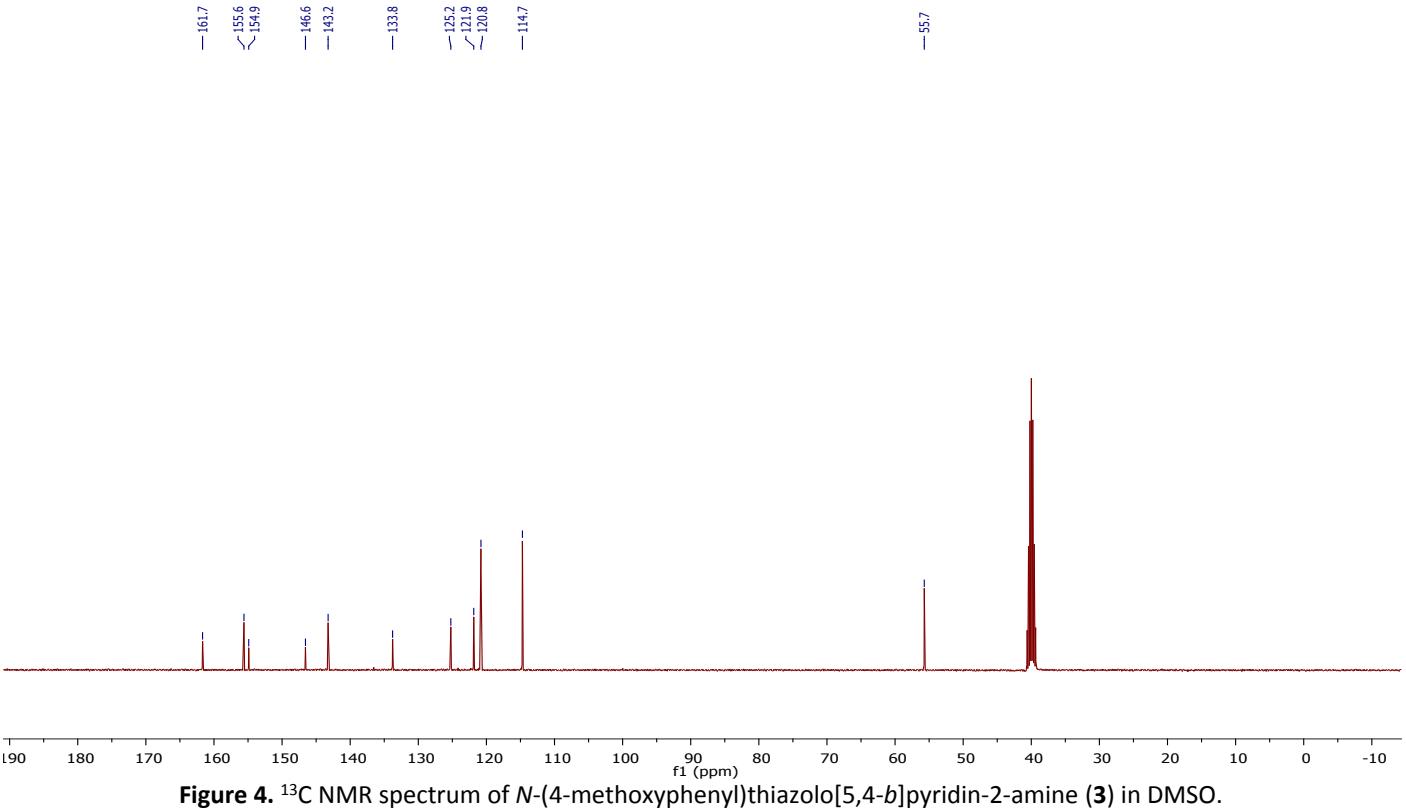


**Figure 4.** $^{13}$C NMR spectrum of *N*-(4-methoxyphenyl)thiazolo[5,4-*b*]pyridin-2-amine (**3**) in DMSO.

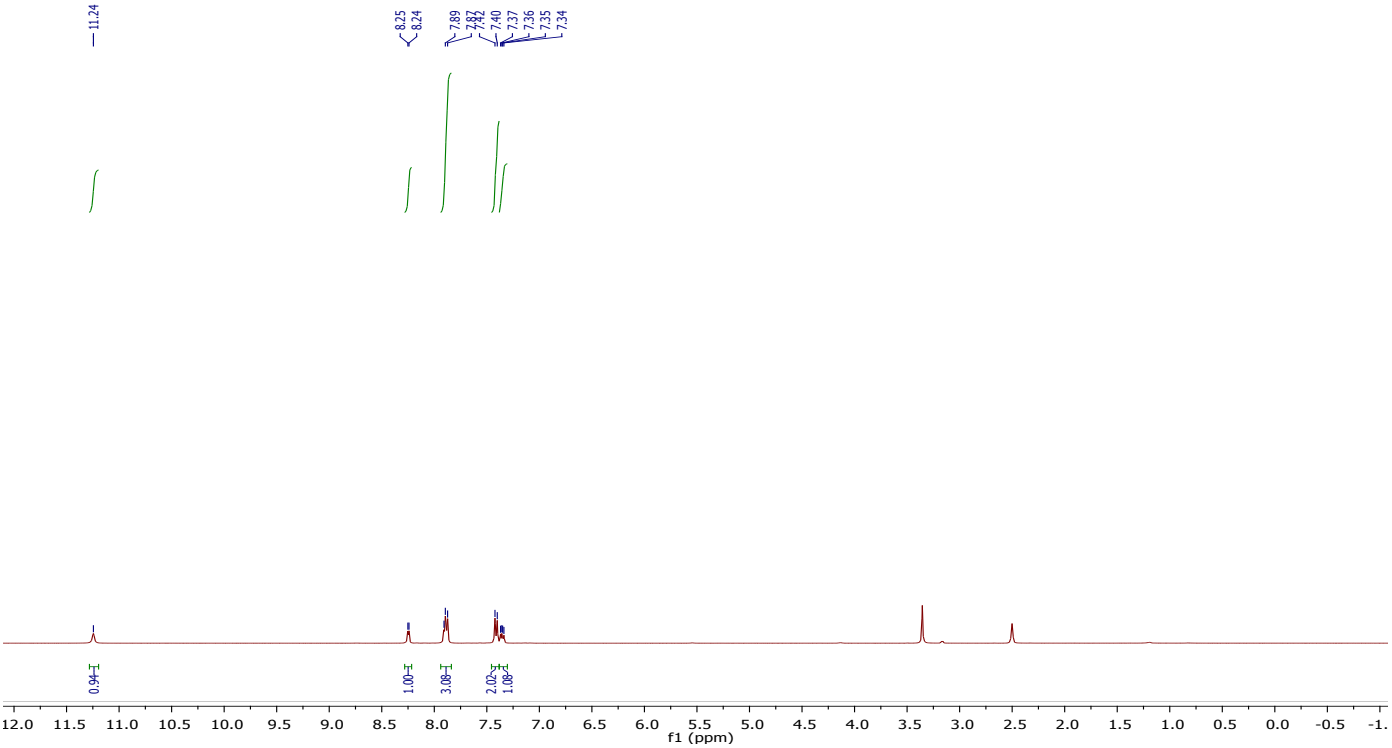


**Figure 5.** [1]H NMR spectrum of *N*-(4-chlorophenyl)thiazolo[5,4-*b*]pyridin-2-amine (**4**) in DMSO.

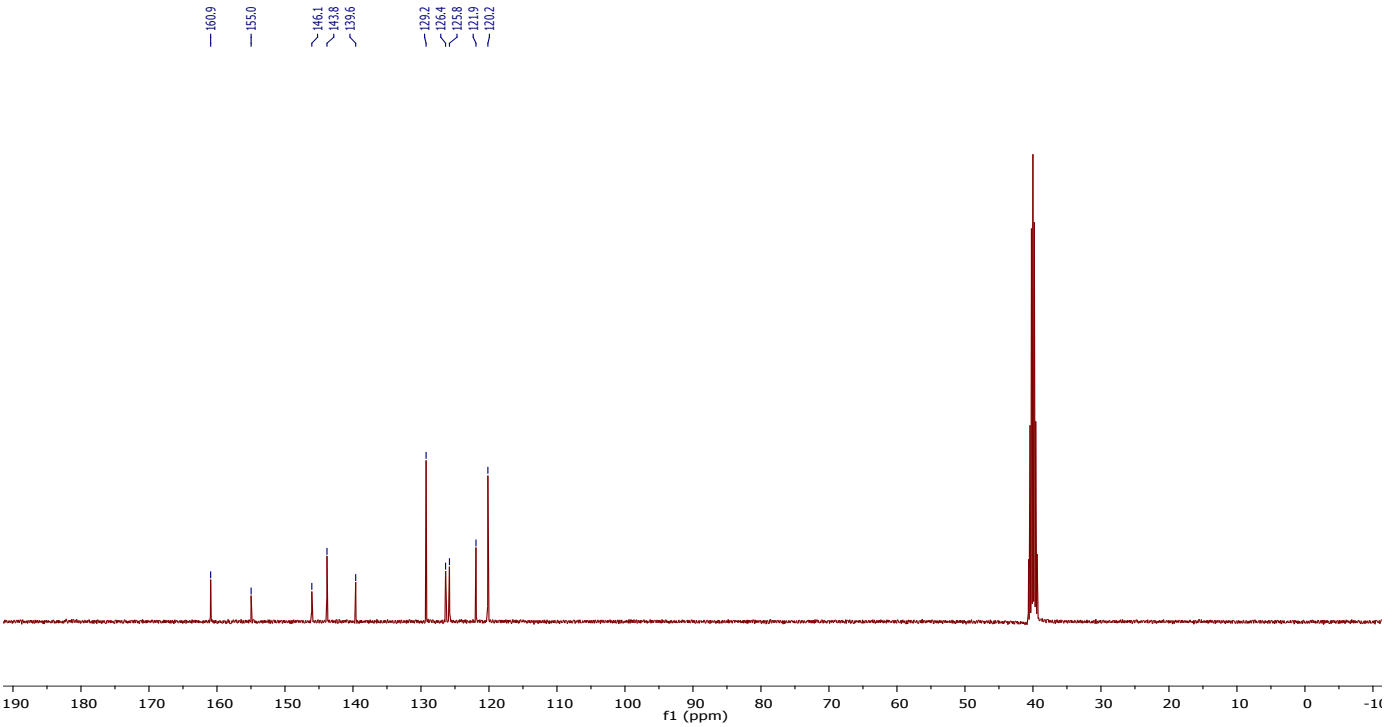


**Figure 6.** [13]C NMR spectrum of *N*-(4-chlorophenyl)thiazolo[5,4-*b*]pyridin-2-amine (**4**) in DMSO.

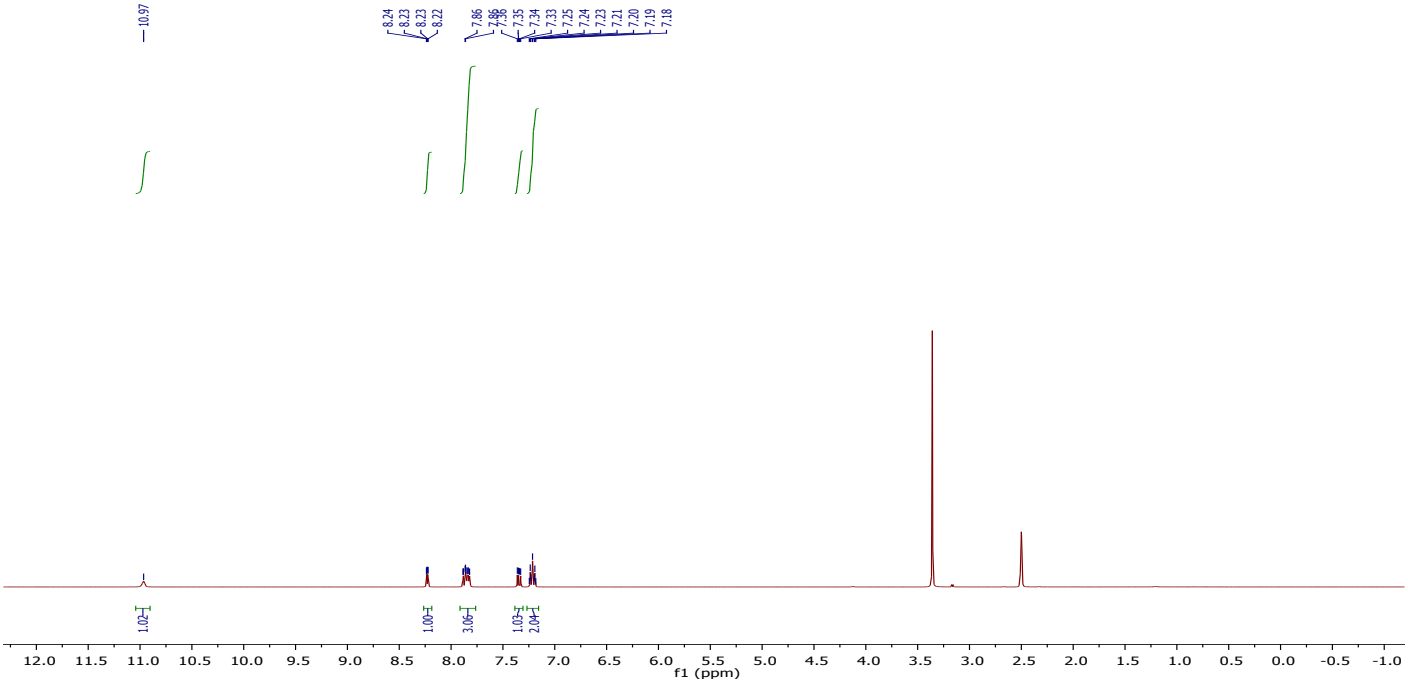


**Figure 7.** $^{1}$H NMR spectrum of *N*-(4-fluorophenyl)thiazolo[5,4-*b*]pyridin-2-amine (**5**) in DMSO.

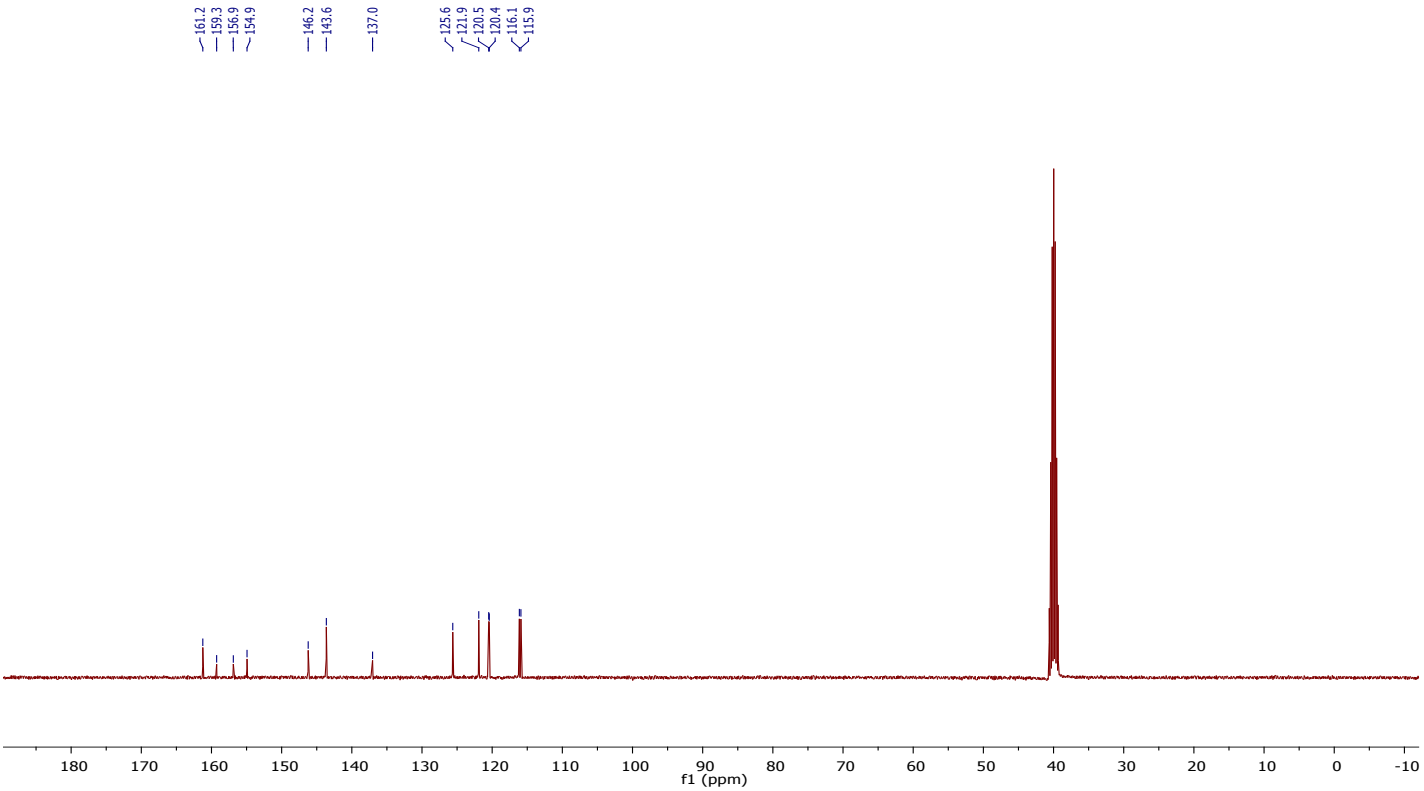


**Figure 8.** $^{13}$C NMR spectrum of *N*-(4-fluorophenyl)thiazolo[5,4-*b*]pyridin-2-amine (**5**) in DMSO.

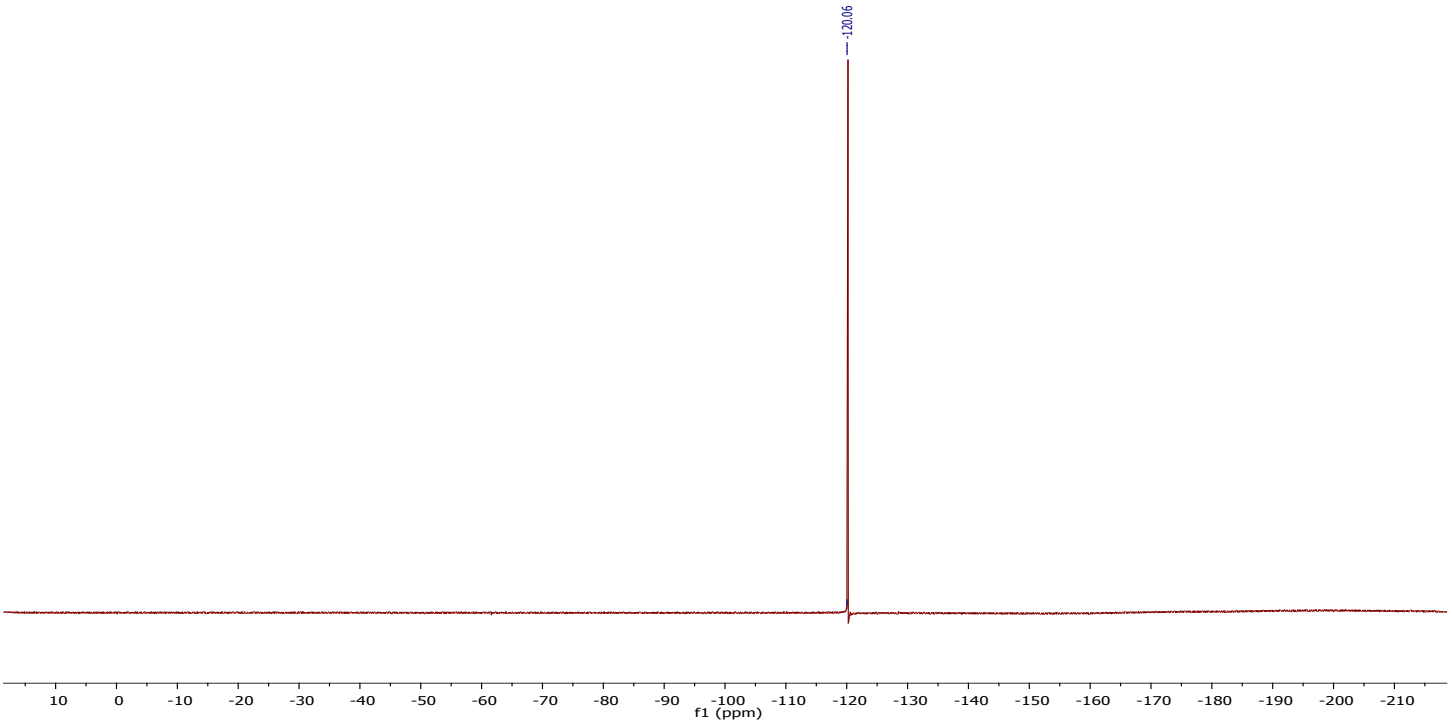


**Figure 9.** $^{19}$F NMR spectrum of *N*-(4-fluorophenyl)thiazolo[5,4-*b*]pyridin-2-amine (**5**) in DMSO.

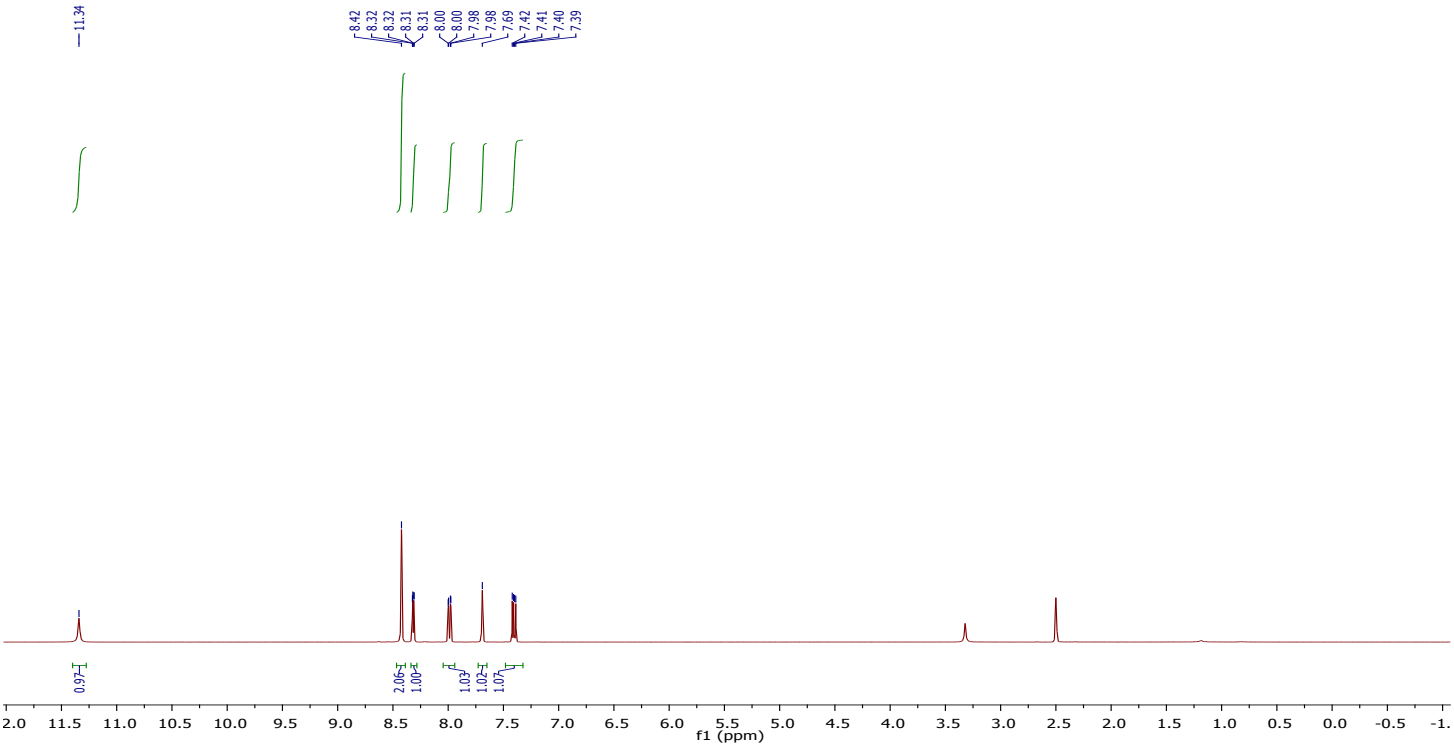


**Figure 10.** $^{1}$H NMR spectrum of *N*-(3,5-bis(trifluoromethyl)phenyl)thiazolo[5,4-*b*]pyridin-2-amine (**7**) in DMSO.

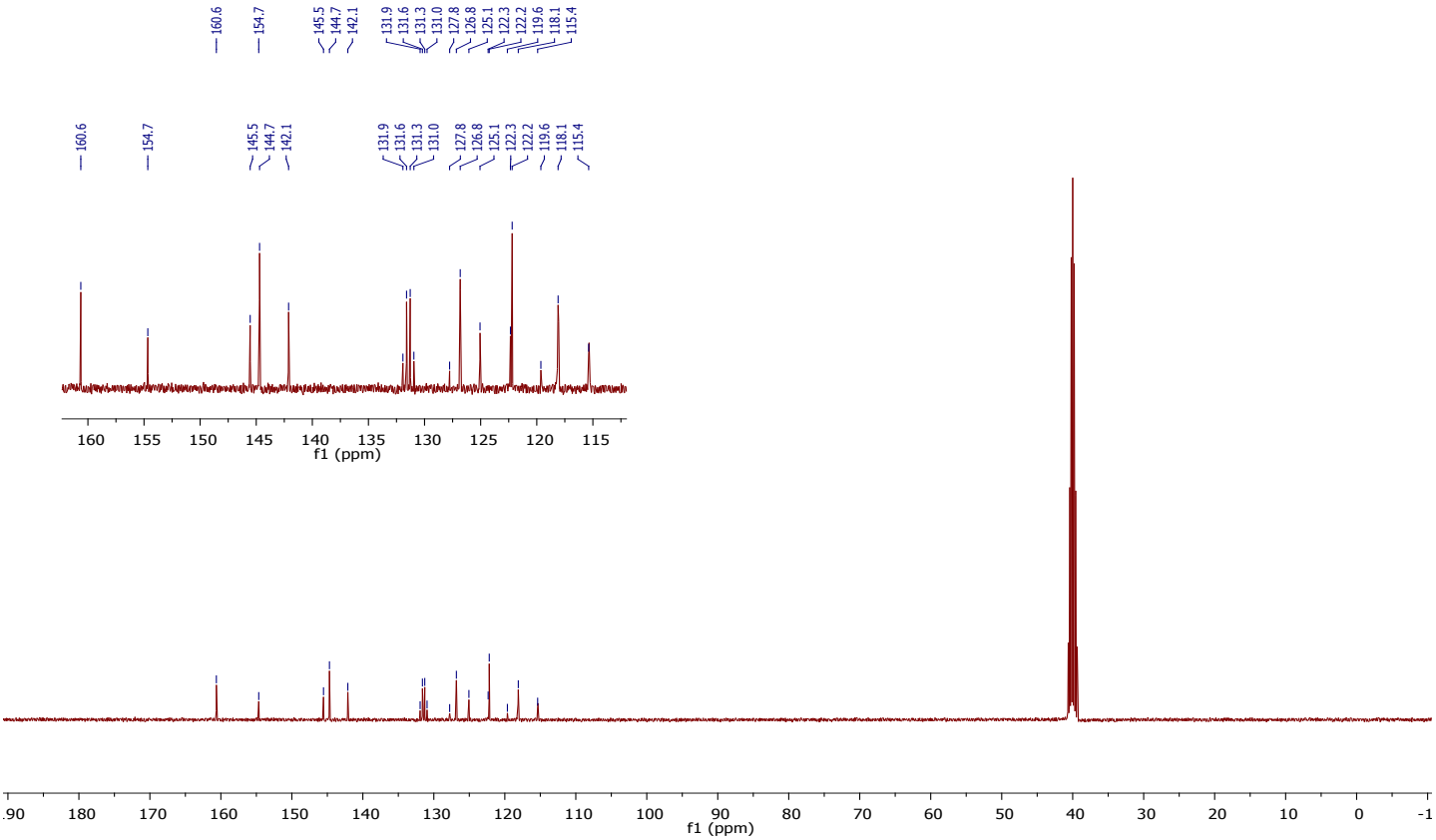


**Figure 11.** $^{13}$C NMR spectrum of *N*-(3,5-bis(trifluoromethyl)phenyl)thiazolo[5,4-*b*]pyridin-2-amine (**7**) in DMSO.

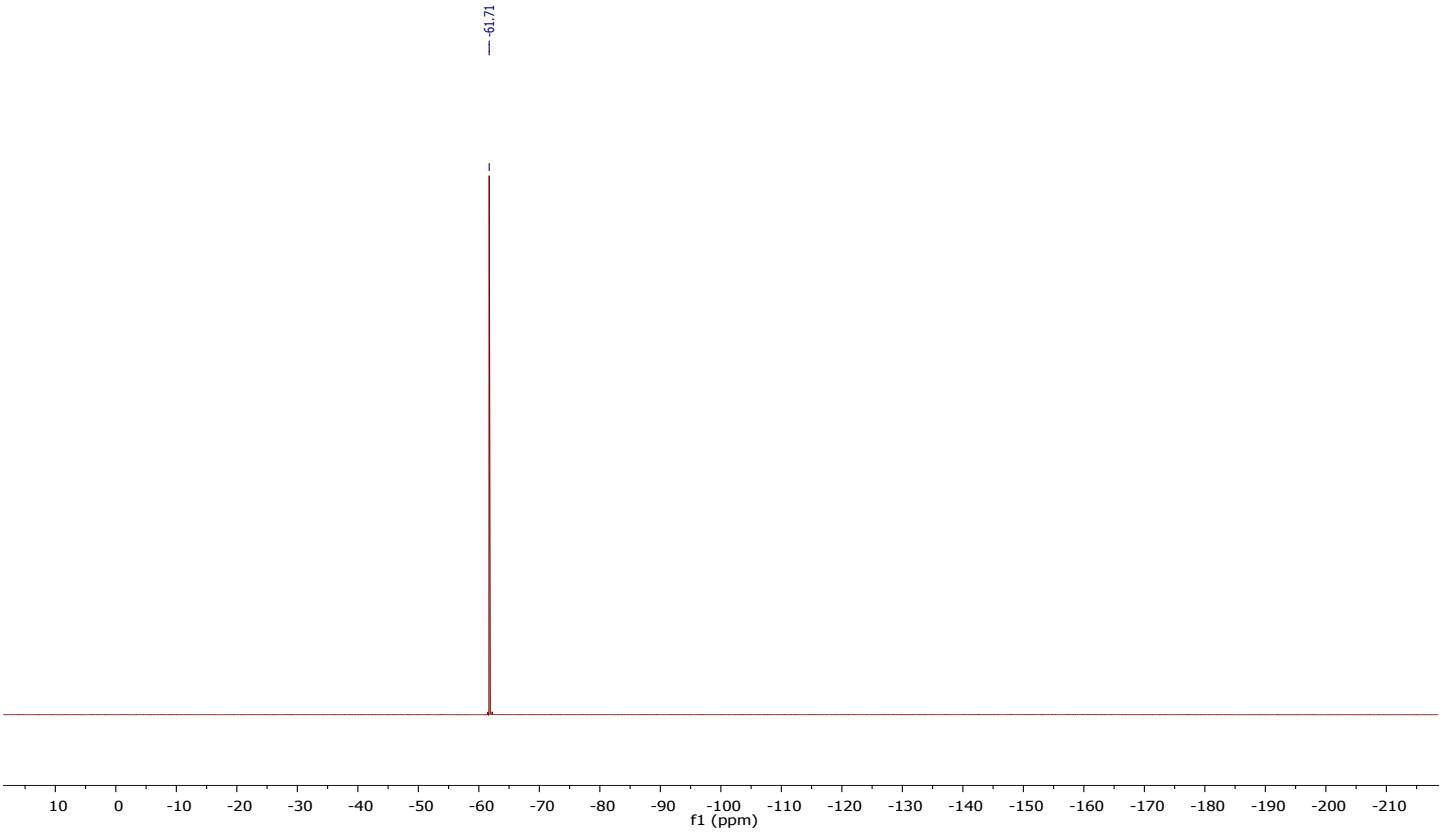


**Figure 12.** $^{19}$F NMR spectrum of *N*-(3,5-bis(trifluoromethyl)phenyl)thiazolo[5,4-*b*]pyridin-2-amine (**7**) in DMSO.

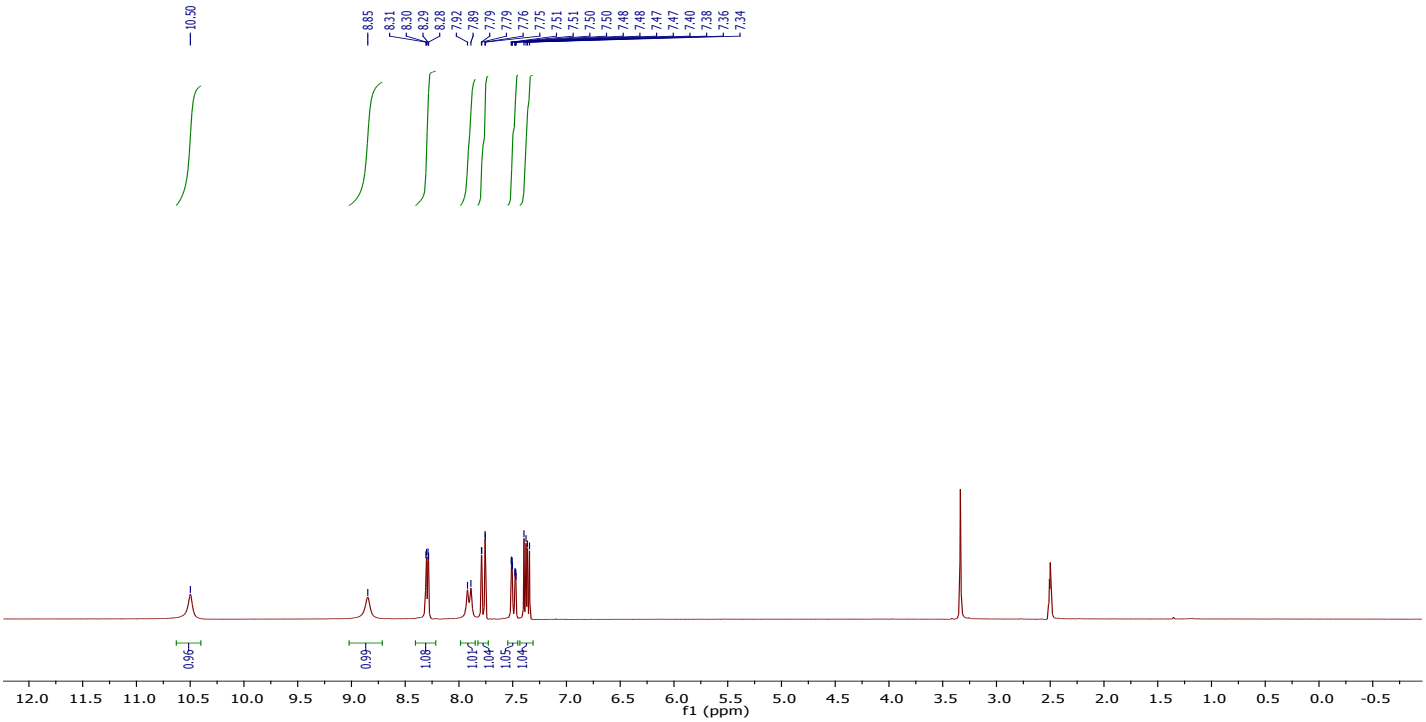


**Figure 13.** $^{1}$H NMR spectrum of *N*-(2-chloro-5-trifluoromethylphenyl)thiazolo[5,4-*b*]pyridin-2-amine, (**8**) in DMSO.

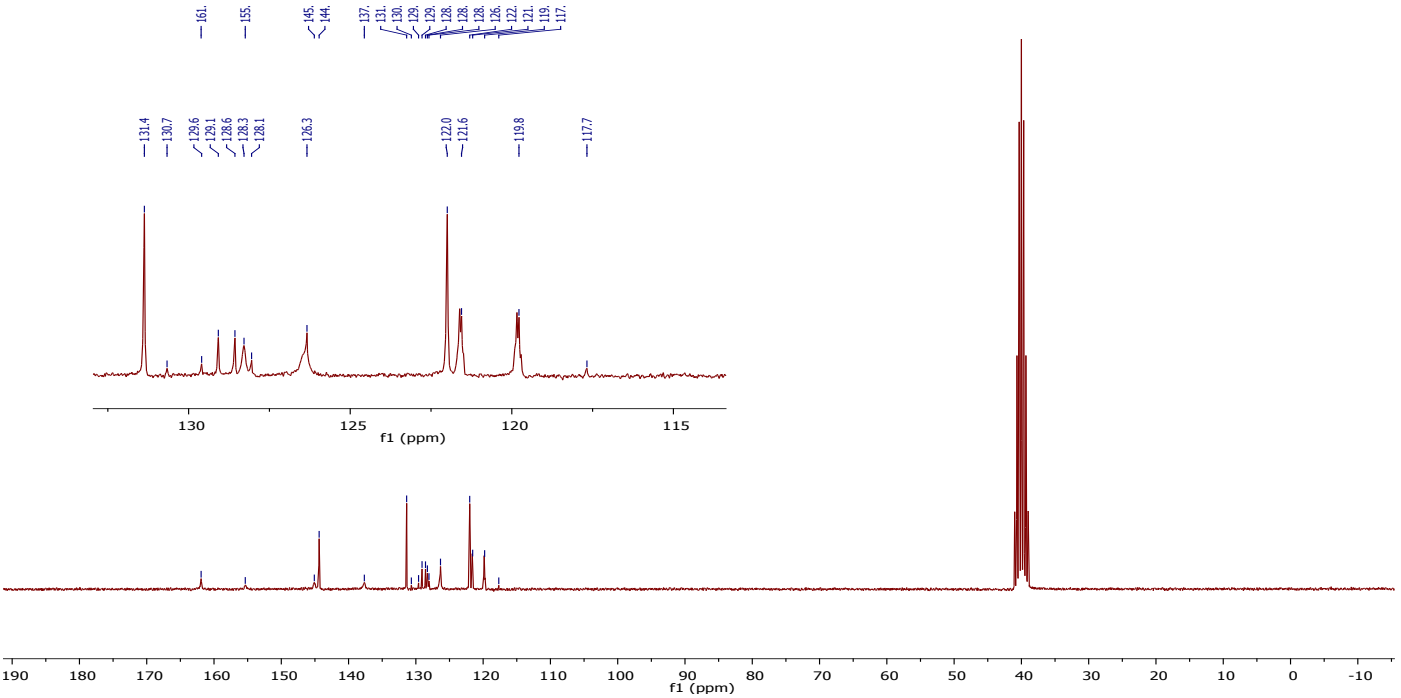


**Figure 14.** $^{13}$C NMR spectrum of *N*-(2-chloro-5-trifluoromethylphenyl)thiazolo[5,4-*b*]pyridin-2-amine, (**8**) in DMSO.

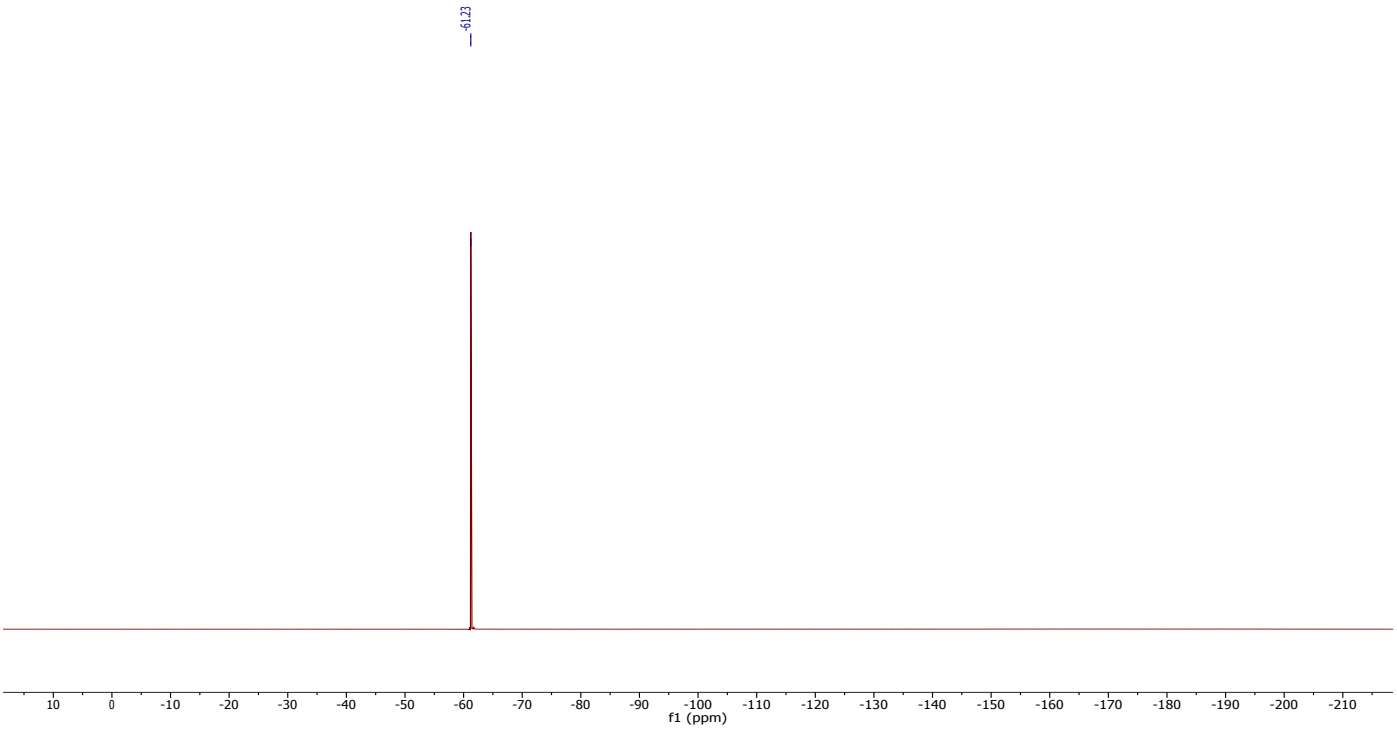


**Figure 15.** $^{19}F$ NMR spectrum of *N*-(2-chloro-5-trifluoromethylphenyl)thiazolo[5,4-*b*]pyridin-2-amine, (**8**) in DMSO.

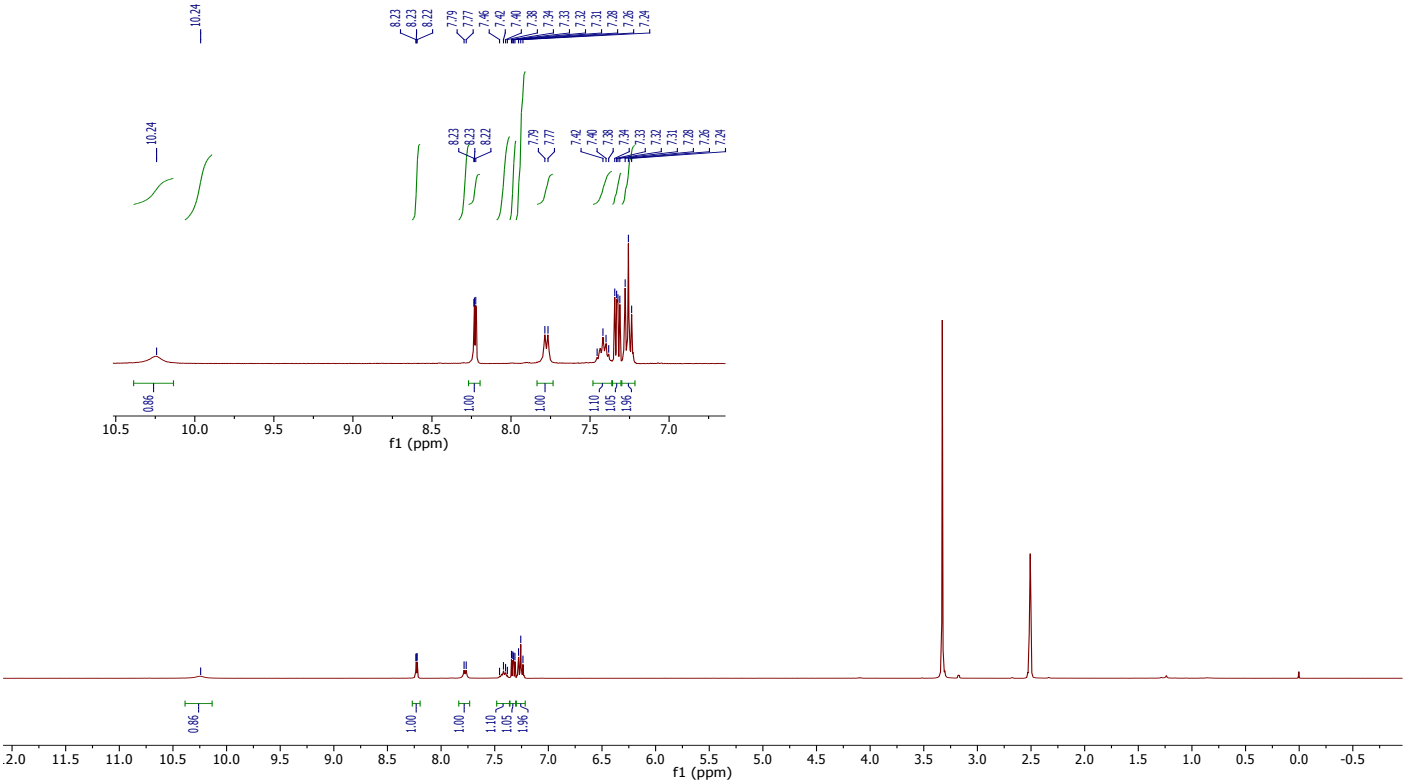


**Figure 16.** $^{1}H$ NMR spectrum of N-(2,6-difluorophenyl)thiazolo[5,4-b]pyridin-2-amine (**9**) in DMSO.

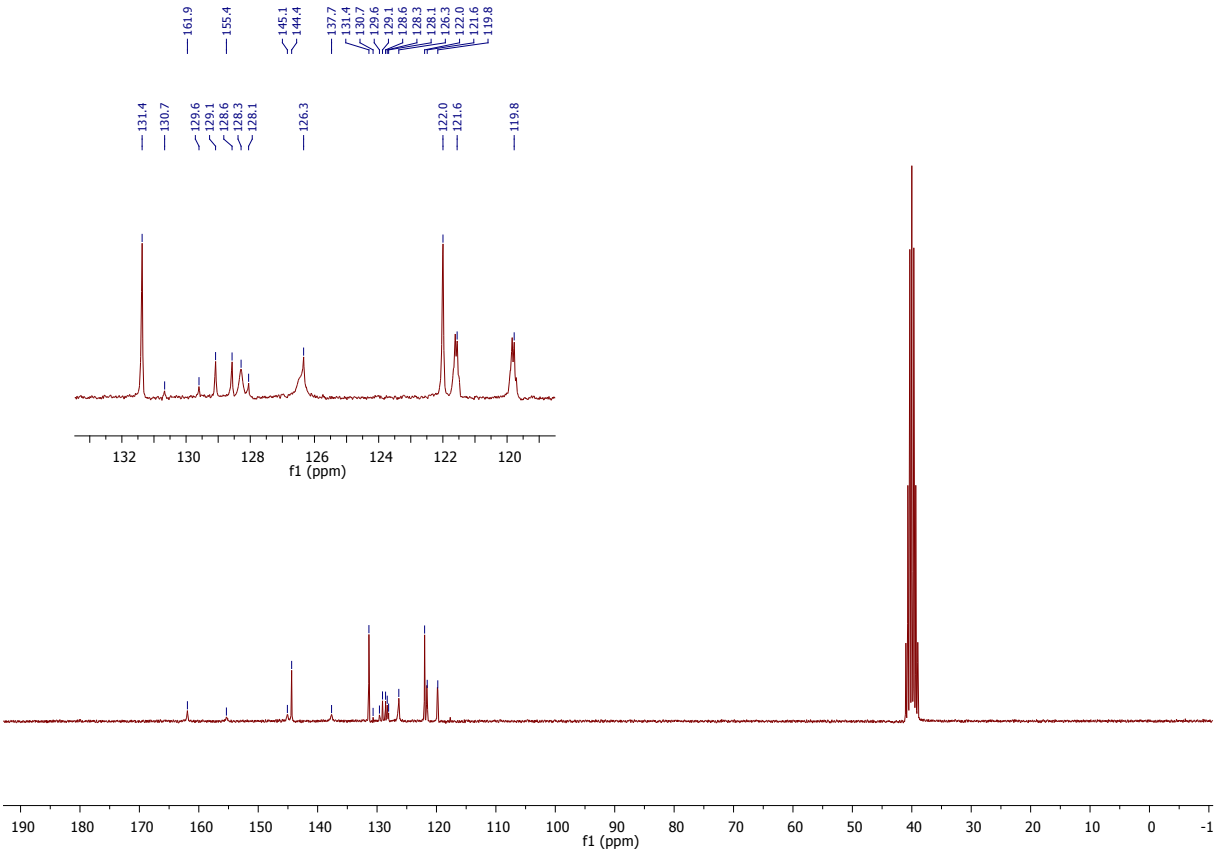


**Figure 17.** $^{13}$C NMR spectrum of *N*-(2,6-difluorophenyl)thiazolo[5,4-*b*]pyridin-2-amine (**9**) in DMSO.

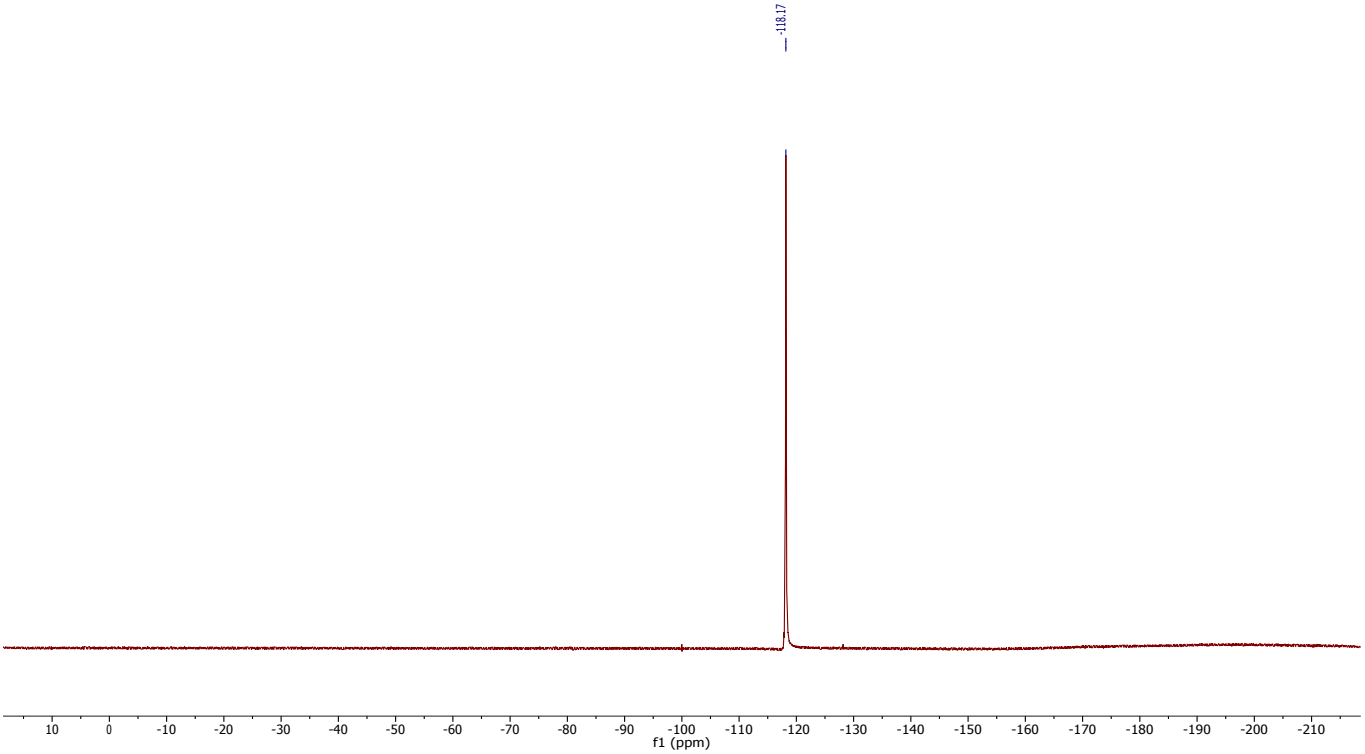


**Figure 18.** $^{19}$F NMR spectrum of *N*-(2,6-difluorophenyl)thiazolo[5,4-*b*]pyridin-2-amine (**9**) in DMSO.

## References

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