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Ring switching tricomponent synthesis of pyrano[2,3-*b*]pyridine multifunctional derivatives

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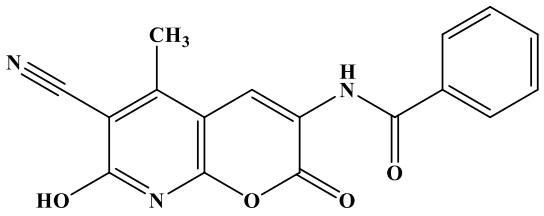
^{1}H and ^{13}C NMR spectra were recorded on an Agilent 400 MR+ spectrometer (400 MHz for ^{1}H NMR spectra and 100 MHz for ^{13}C NMR spectra) in DMSO-d_6, internal standard TMS. The mass spectra were obtained on a Finnigan MAT 4615P instrument using a direct inlet system. The temperature of the ionization chamber was 180 °C, the ionization voltage was 70 eV, and the emission current was 100 μA.

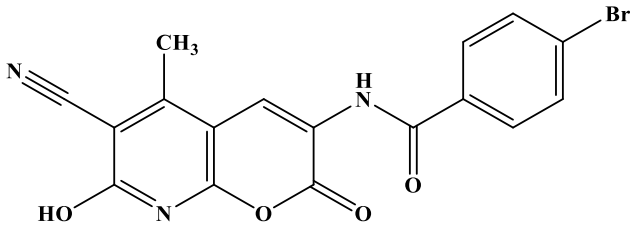
Starting 4-methyl-2,6-dioxo-1,2,5,6-tetrahydropyridine-3-carbonitrile[S1] and hippuric acids [S2] were synthesized according to known recipes from the corresponding literary sources.

General procedure. A mixture of 4-methyl-2,6-dioxo-1,2,5,6-tetrahydropyridine-3-carbonitrile **1** (300 mg, 2 mmol), triethyl orthoformate (385 mg, 2.6 mmol) and hippuric acid **2** (360 mg, 2 mmol) was heated in Ac_2O (1.5 ml) for 1 h. The red intermediate **A** appears and quickly turns into a colorless precipitate. The final product was filtered off and washed with ethyl alcohol to give 550 mg of 3-benzoylamino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3a**.

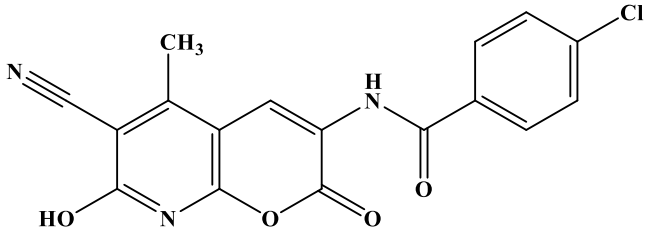
Compounds **3b-g** were prepared similarly.



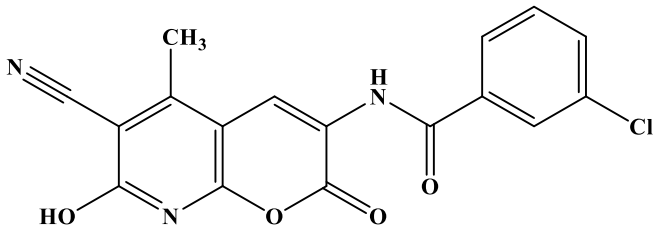
3-Benzoylamino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile 3a. Yield 86%. White solid, mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.61 (s, 3H, Me), 7.52 (t, 2H, H_{Ar}, J 7.3 Hz), 7.61 (t, 1H, H_{Ar}, J 7.3 Hz), 7.93 (d, 2H, H_{Ar}, J 7.3 Hz), 8.55 (s, 1H, CH), 9.78 (s, 1H, NH), 13.56 (b.s, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 17.7, 115.2, 119.5, 122.1, 125.9, 128.1, 129.0, 132.7, 133.8, 155.1, 155.2, 155.6, 156.5, 157.3, 166.4. MS (EI, 70 eV) *m/z*: 321 (M+). Found (%): C, 63.51; H, 3.47; N, 13.04. Calc. for $C_{17}H_{11}N_3O_4$. C, 63.55; H, 3.45; N, 13.08.



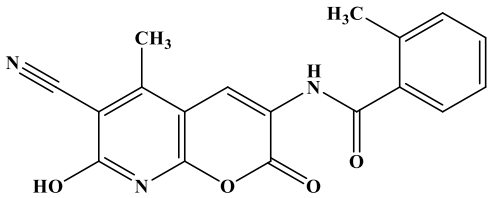
3-(4-Bromobenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile 3b. Yield 90%. White solid, mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d$_6$) δ: 2.58 (s, 3H, Me), 7.71 (d, 2H, H$_{Ar}$, J 8.5 Hz), 7.85 (d, 2H, H$_{Ar}$, J 8.5 Hz), 8.51 (s, 1H, CH), 9.90 (s, 1H, NH), 13.38 (b.s, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d$_6$) δ: 17.7, 115.1, 121.9, 126.0, 126.1, 126.5, 130.3, 132.0, 132.9, 155.5, 156.4, 157.2, 163.7, 165.6, 172,4. MS (EI, 70 eV) *m/z*: 400 (M+). Found (%): C, 51.03; H, 2.56; N, 10.48. Calc. for $C_{17}H_{10}BrN_3O_4$. C, 51.02; H, 2.52; N, 10.50;.



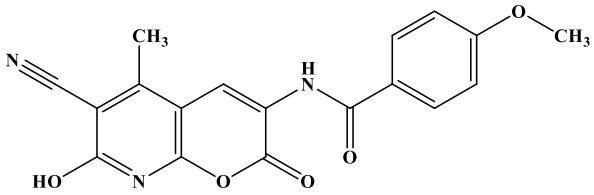
3-(4-Chlorobenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile 3c. Yield 92%. White solid, mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d$_6$) δ: 2.60 (s, 3H, Me), 7.59 (d, 2H, H$_{Ar}$, J 7.9 Hz), 7.95 (d, 2H, H$_{Ar}$, J 7.9 Hz), 8.53 (s, 1H, CH), 9.96 (s, 1H, NH), 13.75 (b.s, 1H, OH). ^{13}C NMR (100 MHz, DMSO-D$_6$) δ: 17.7, 115.2, 121.9, 126.7, 129.1, 130.2, 132.6, 137.5, 155.0, 155.6, 156.6, 157.2, 158.1, 163.7, 165.7. MS (EI, 70 eV) *m/z*: 355 (M+). Found (%): C, 57.44; H, 2.80; N, 11.78. Calc. for $C_{17}H_{10}ClN_3O_4$. C, 57.40; H, 2.83; N, 11.81.



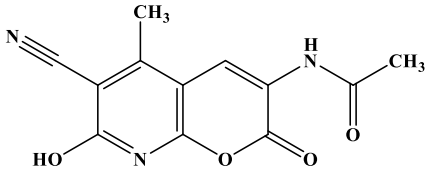
3-(3-Chlorobenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile 3d. Yield 84%. White solid, mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d$_6$) δ: 2.60 (s, 3H, Me), 7.55 (t, 1H, H$_{Ar}$, J 7.9 Hz), 7.66 (d, 1H, H$_{Ar}$, J 7.9 Hz), 7.87 (d, 1H, H$_{Ar}$, J 7.9 Hz), 7.96 (s, 1H, H$_{Ar}$,), 8.52 (s, 1H, CH), 10.02 (s, 1H, NH), 13.58 (b.s, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d$_6$) δ: 17.7, 115.2, 121.8, 127.0, 127.2, 128.1, 131.0, 132.4, 133.7, 135.9, 148.6, 155.7, 157.1, 157.3, 160.6, 163.8, 165.3. MS (EI, 70 eV) *m/z*: 355 (M+). Found (%): C, 57.41; H, 2.86; N, 11.84. Calc. for $C_{17}H_{10}ClN_3O_4$. C, 57.40; H, 2.83; N, 11.81.



3-(2-Methylbenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile 3e. Yield 78%. White solid, mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.40 (s, 3H, Me_{Ar}), 2.62 (s, 3H, Me), 7.26 – 7.30 (m, 2H, H_{Ar}), 7.37 (t, 1H, H_{Ar}, J 7.5 Hz), 7.44 (d, 1H, H_{Ar}, J 7.5 Hz), 8.59 (s, 1H, CH), 9.89 (s, 1H, NH), 13.71 (b.s, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 17.7, 20.0, 115.3, 122.3, 124.9, 126.1, 127.9, 130.6, 131.1, 136.1, 136.2, 154.7, 155.5, 156.4, 157.2, 160.5, 163.7, 169.2. MS (EI, 70 eV) *m/z*: 335 (M+). Found (%): C, 64.45; H, 3.95; N, 12.54. Calc. for $C_{17}H_{11}N_3O_4$. C, 64.48; H, 3.91; N, 12.53.



3-(4-Methoxylbenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile 3f. Yield 82%. White solid, mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.58 (s, 3H, Me), 3.82 (s, 3H, $Me_{Methoxy}$), 7.02 (d, 2H, H_{Ar}, J 8.8 Hz), 7.89 (d, 2H, H_{Ar}, J 8.8 Hz), 8.51 (s, 1H, CH), 9.53 (s, 1H, NH), 12.88 (b.s, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 17.7, 55.9, 114.3, 115.2, 122.3, 125.8, 130.1, 155.4, 156.3, 157.1, 157.4, 157.8, 162.8, 163.6, 165.7, 172.4. MS (EI, 70 eV) *m/z*: 321 (M+). Found (%):MS (EI, 70 eV) *m/z*: 351 (M+). Found (%): C, 61.50; H, 3.73; N, 11.91. Calc. for $C_{18}H_{13}N_3O_5$. C, 61.54; H, 3.73; N, 11.96.



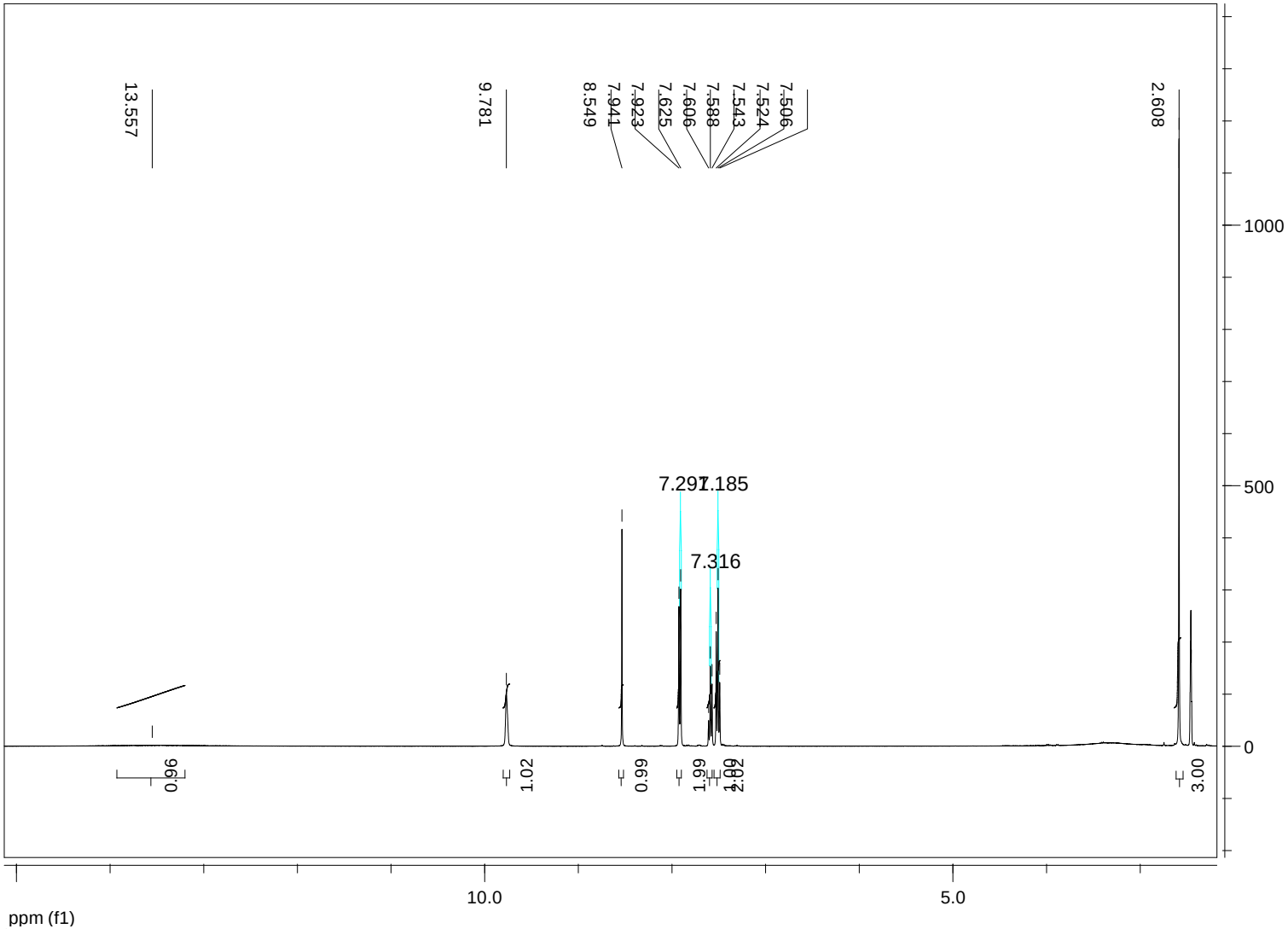
3-Acetylamino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile 3g. Yield 92%. White solid, mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.13 (s, 3H, Me_{Ac}), 2.54 (s, 3H, Me), 8.61 (s, 1H, CH), 9.81 (s, 1H, NH), 13.55 (b.s, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 17.6, 24.3, 115.2, 120.8, 120.8, 122.9, 154.8, 155.1, 155.7, 157.2, 163.5, 170.6. MS (EI, 70 eV) *m/z*: 321 (M+). Found (%):MS (EI, 70 eV) *m/z*: 259 (M+). Found (%): C, 55.64; H, 3.53; N, 16.. Calc. for $C_{12}H_9N_3O_4$. C, 55.60; H, 3.50; N, 16.21.

References

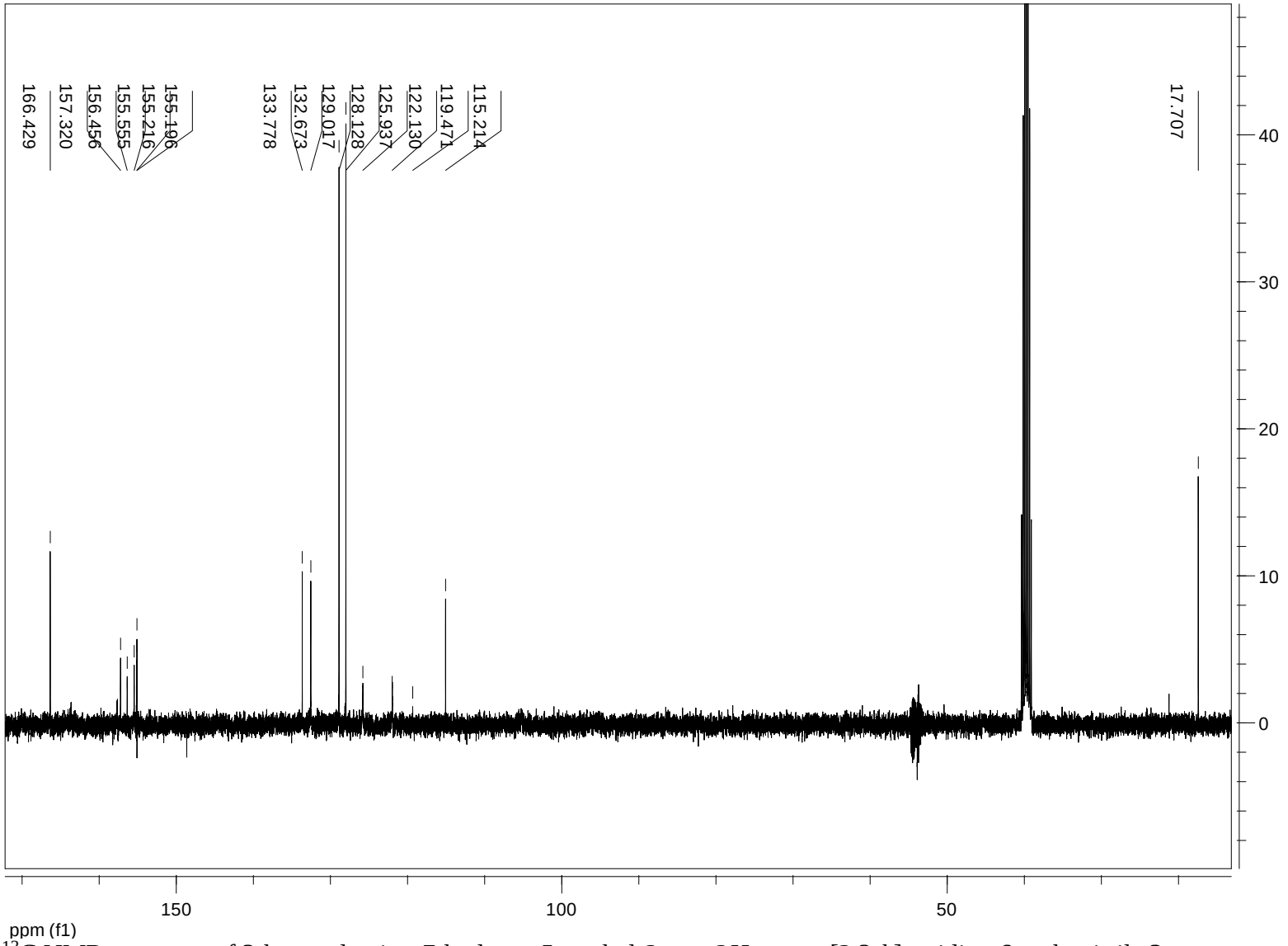
[S1] F. Tietze und Th. Eicher, Reactionen und Synthesen im organischchemischen Praktikum und Forchungslaboratorium, Georg Thieme Verlag, Stuttgart, 1991 (in German).

[S2] Organic Syntheses, Coll. Vol. 2, p.328 (1943); Vol. 12, p.40 (1932) DOI: 10.15227/orgsyn.012.0040

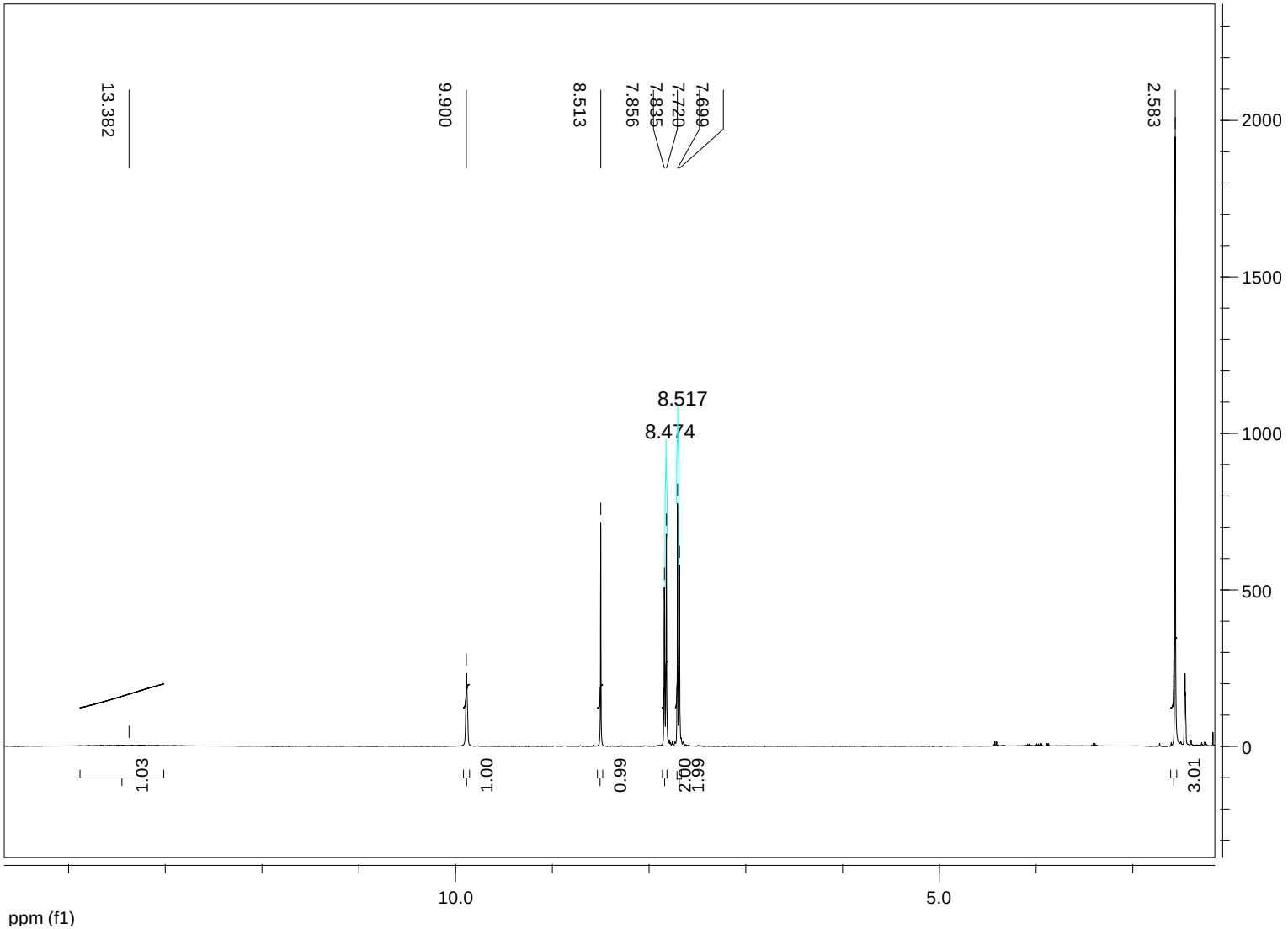
Pictures of ^{1}H and ^{13}C NMR spectra of compounds **3a-g**



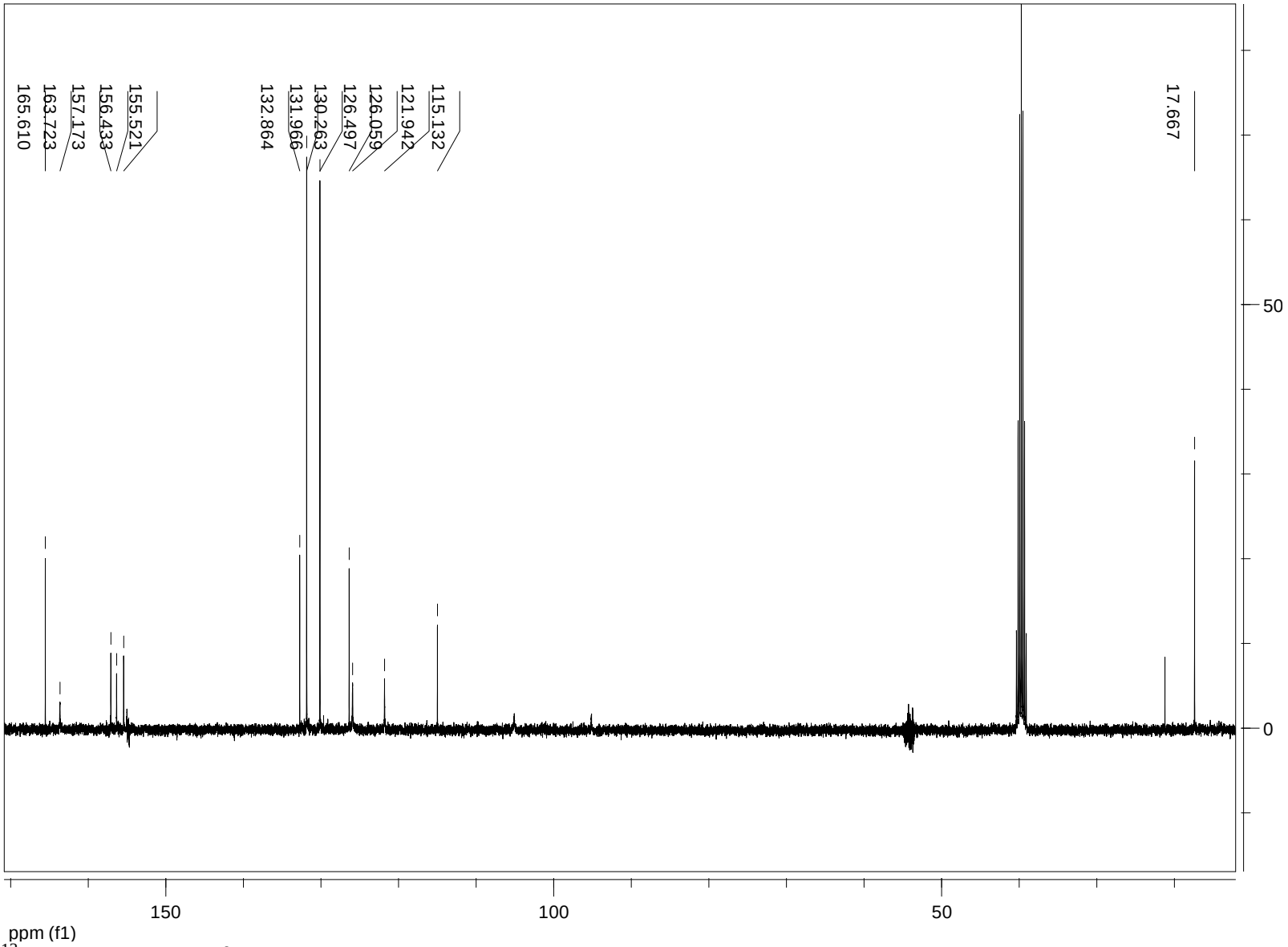
^{1}H NMR spectrum of 3-benzoylamino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3a**.



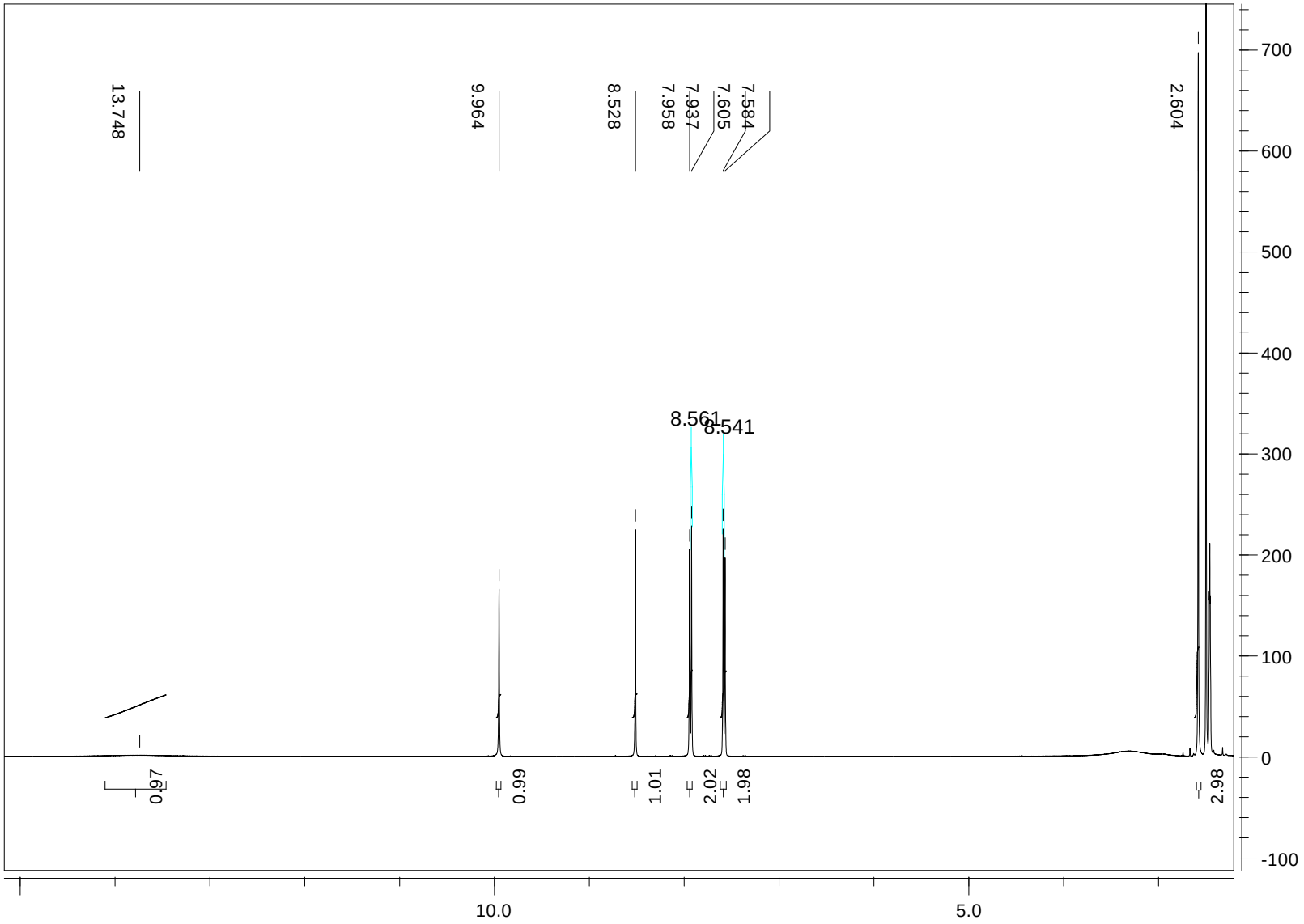
^{13}C NMR spectrum of 3-benzoylamino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3a**.



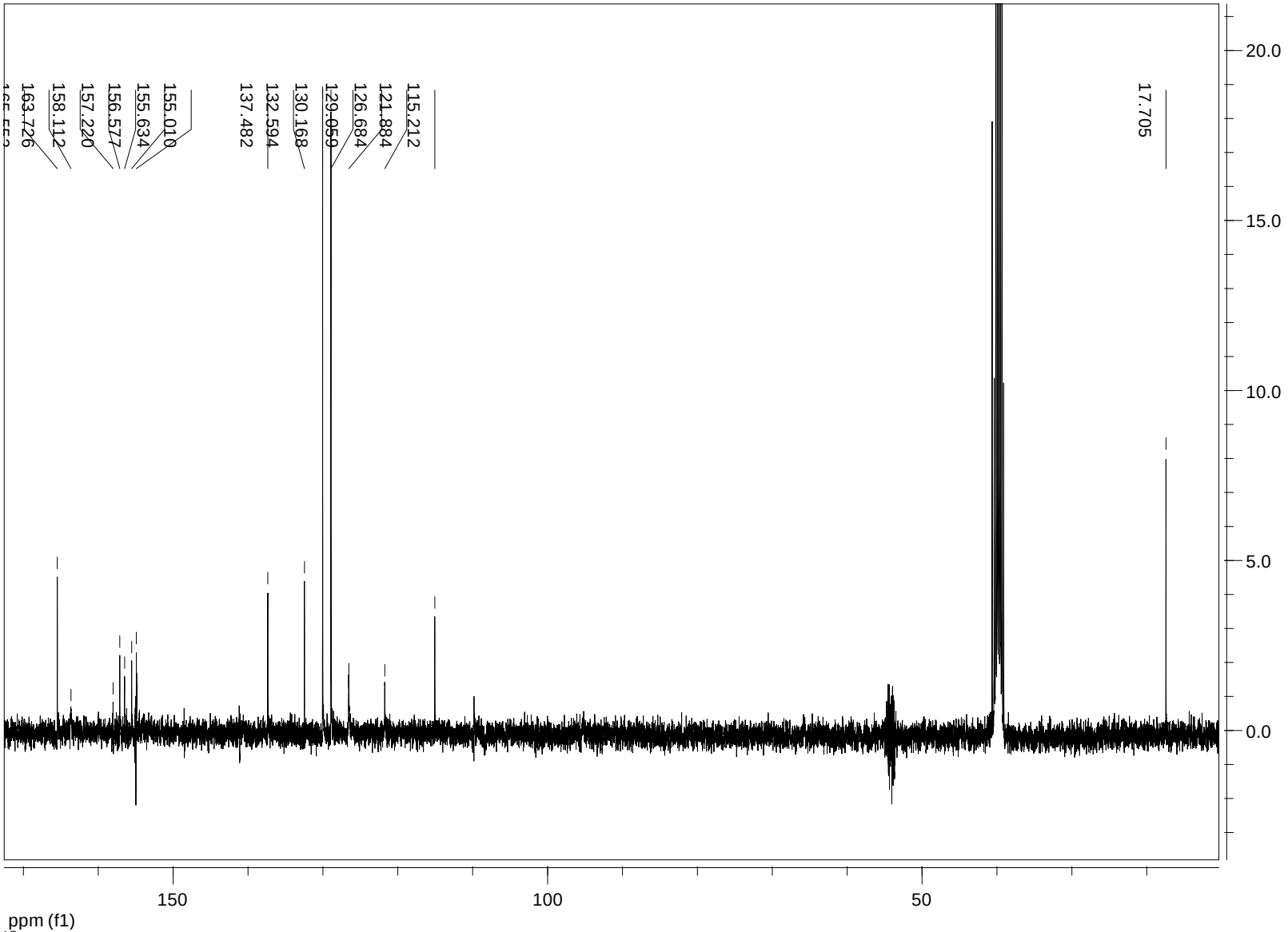
^{1}H NMR spectrum of 3-(4-bromobenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3b**.



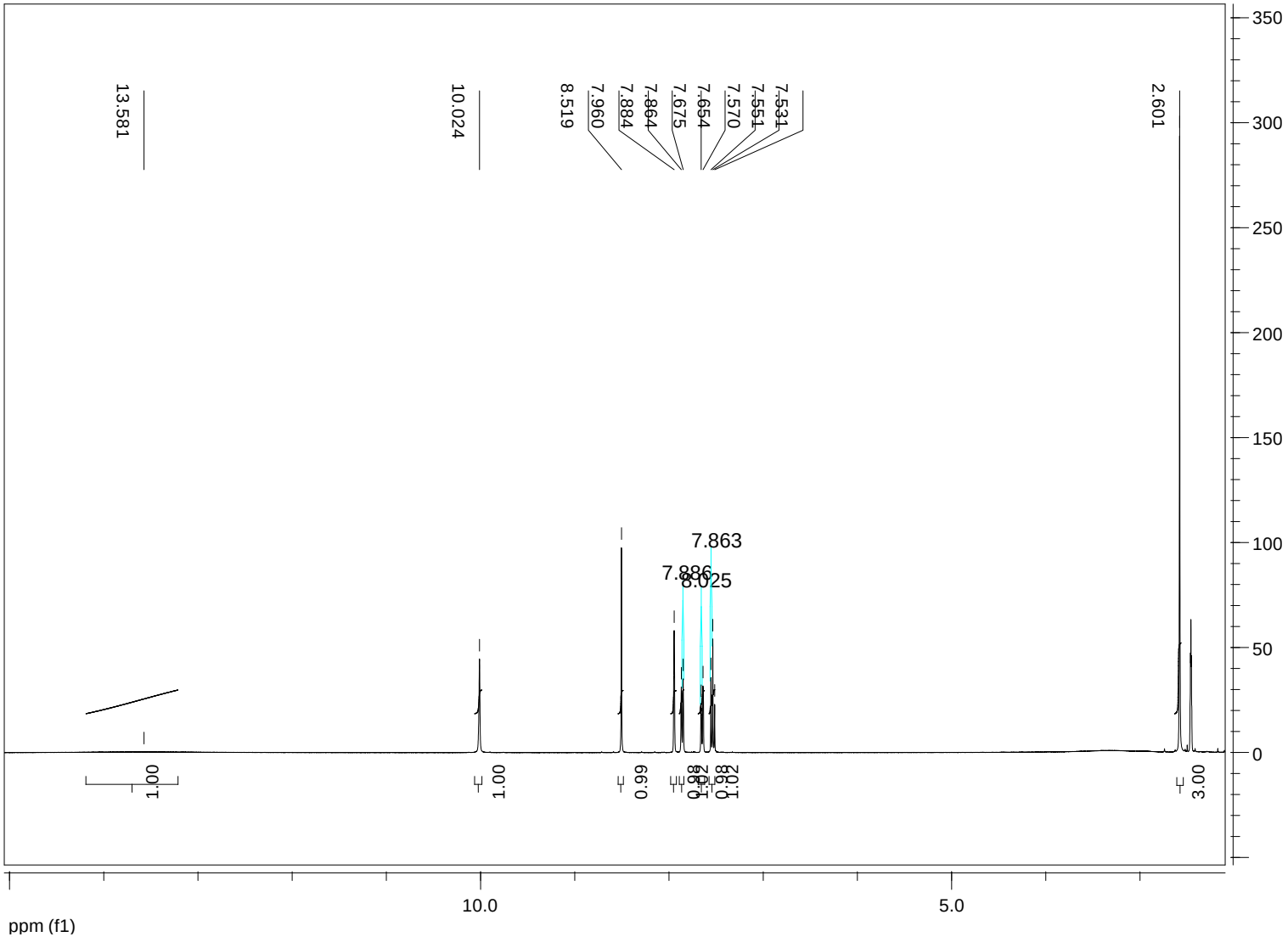
^{13}C NMR spectrum of 3-(4-bromobenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3b**.



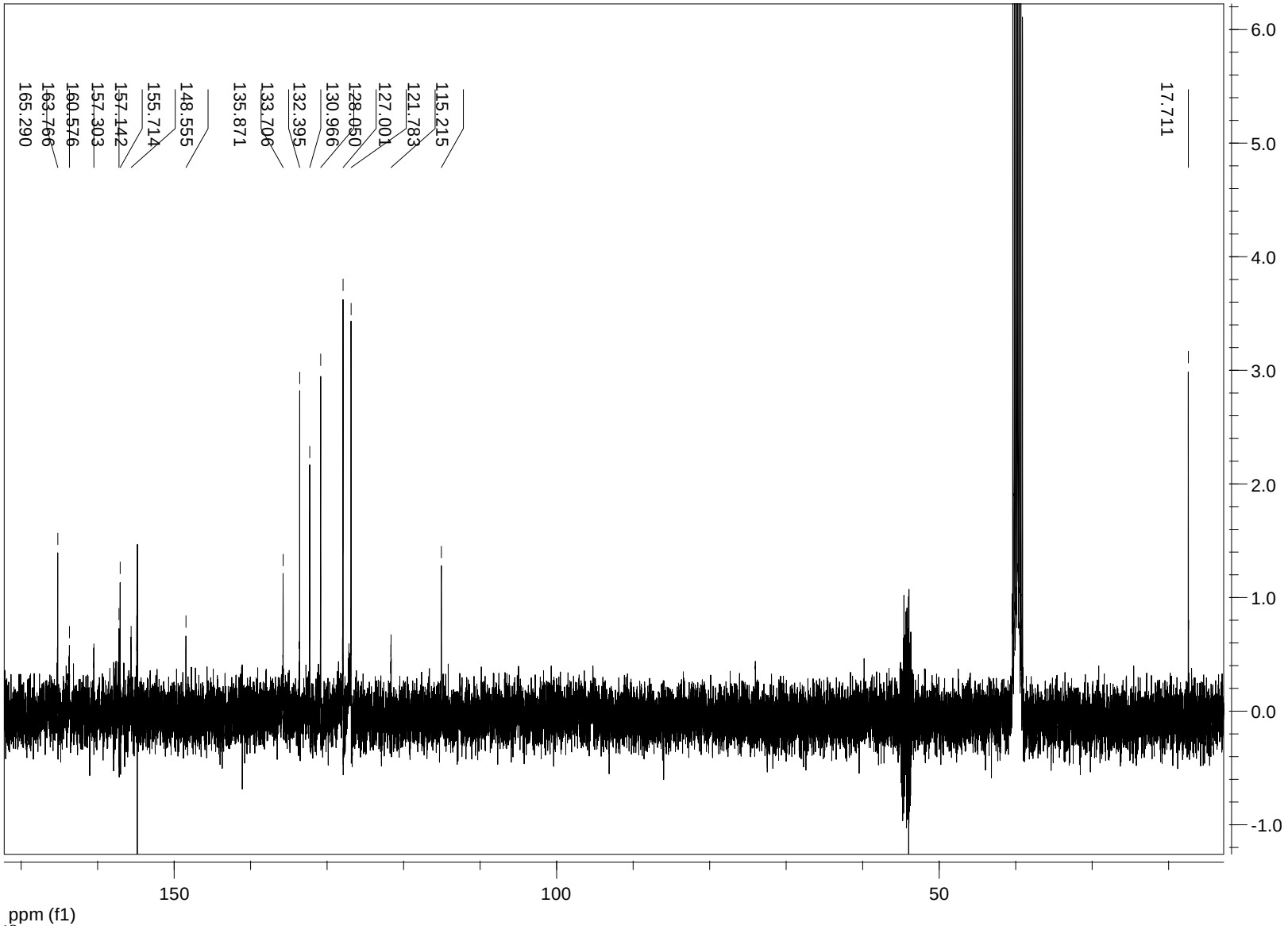
^{1}H NMR spectrum of 3-(4-chlorobenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3c**



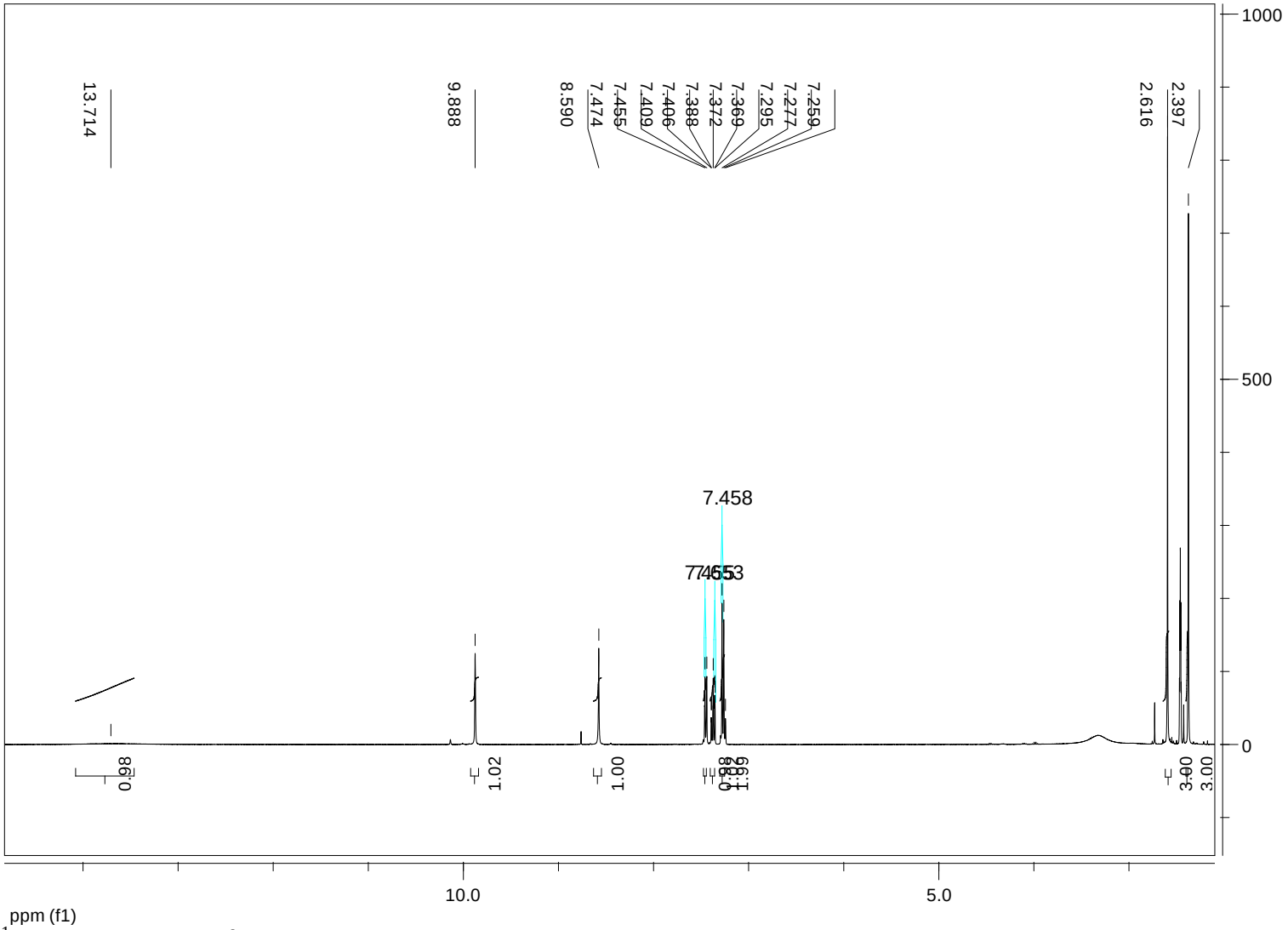
^{13}C NMR spectrum of 3-(4-chlorobenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **4c**



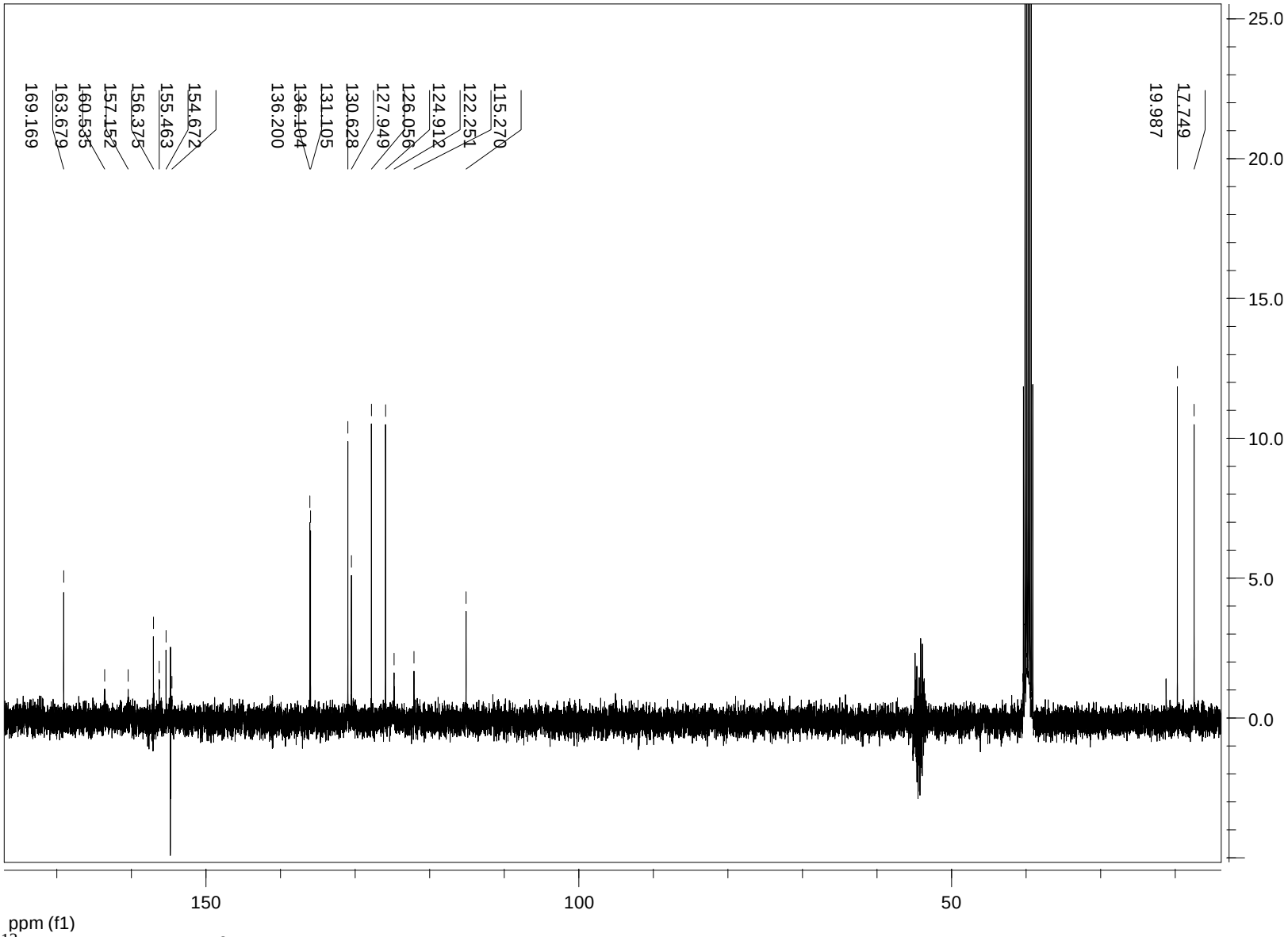
^{1}H NMR spectrum of 3-(3-chlorobenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3d**



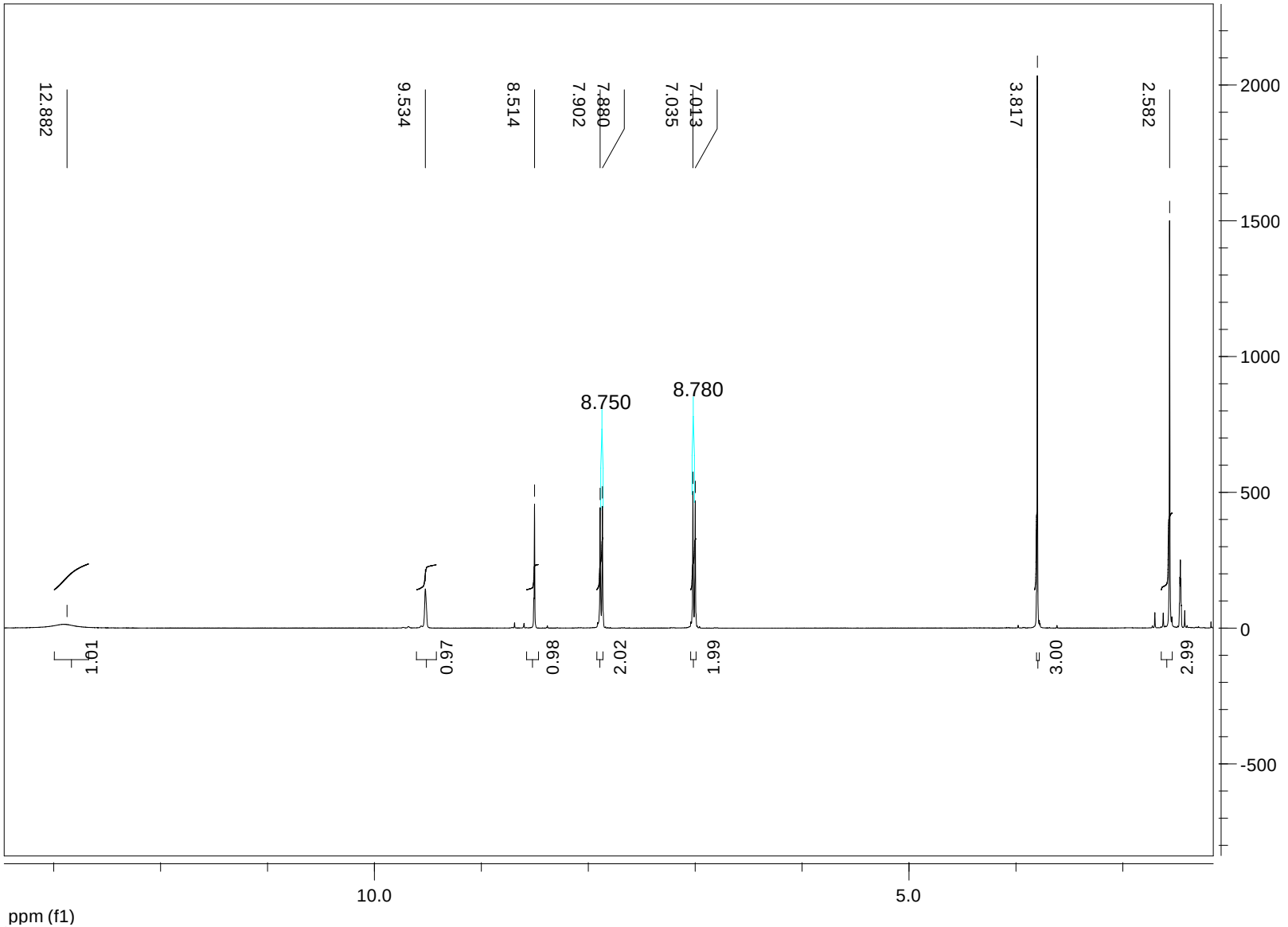
^{13}C NMR spectrum of 3-(3-chlorobenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3d**



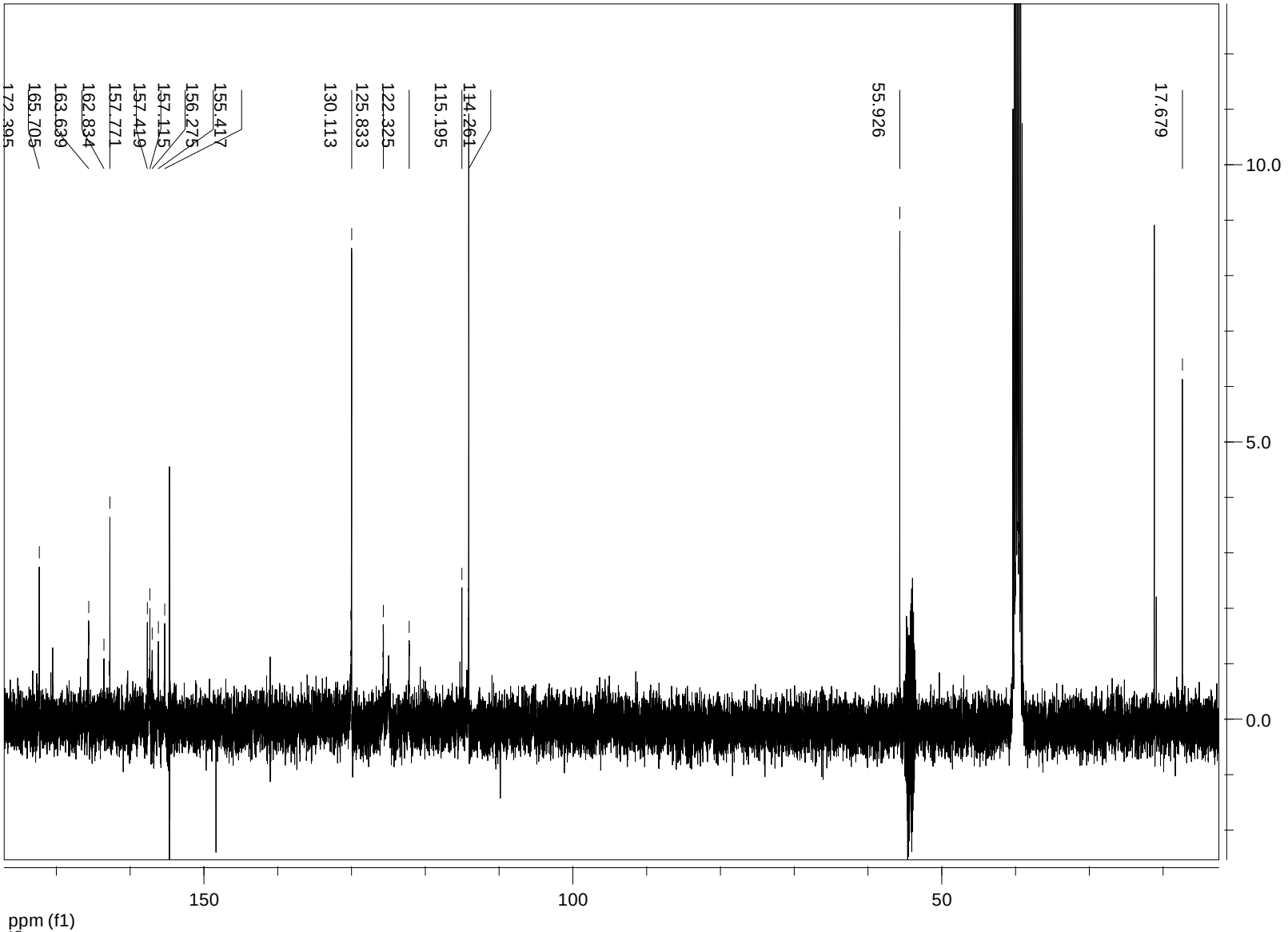
^{1}H NMR spectrum of 3-(2-methylbenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3e**



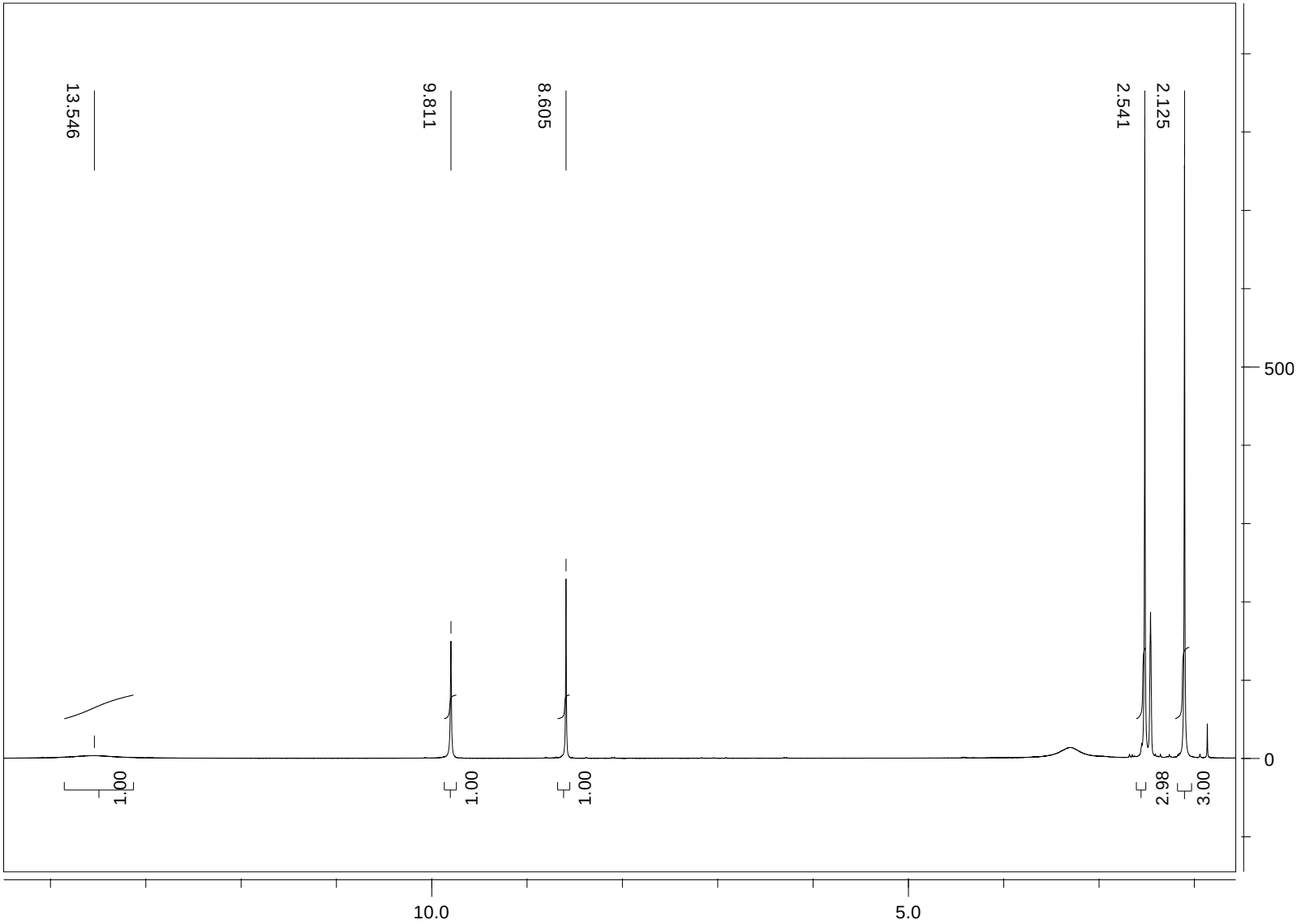
^{13}C NMR spectrum of 3-(2-methylbenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3e**



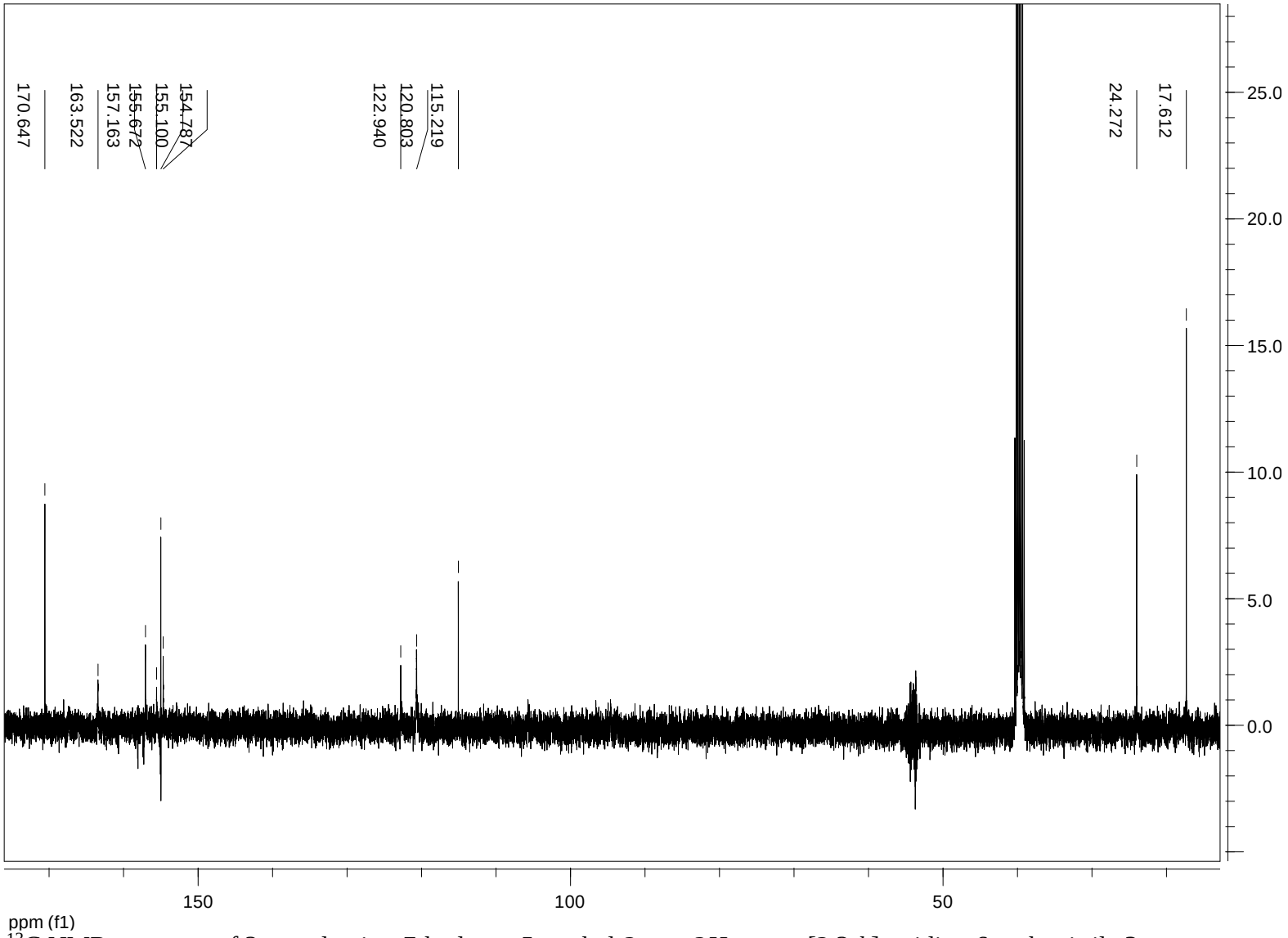
^{1}H NMR spectrum of 3-(4-methoxybenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3f**



^{13}C NMR spectra of 3-(4-methoxybenzoyl)amino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3f**



^{1}H NMR spectrum of 3-acetylamino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3g**



^{13}C NMR spectrum of 3-acetylamino-7-hydroxy-5-methyl-2-oxo-2*H*-pyrano[2,3-*b*]pyridine-6-carbonitrile **3g**