Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Regiocontrolled functionalization of 2,3-dihalogenoimidazo[1,2-*a*]pyridines by Suzuki and Sonogashira cross-coupling reactions

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SUPPORTING INFORMATIONS

General considerations

All reagents were used directly as obtained commercially. Thin-layer chromatography (TLC) were performed using Merk® silica gel $60F_{254}$ plates. Column chromatography were preformed using Merck Geduran® Si 60 (40-63µm) silica. Melting points were determined on a capillary apparatus (Stuart, Staffordshire, United Kingdom) and are uncorrected. Microwave heating was performed using CEM® Explorer SP 12 S class apparatus (max power 300W). NMR experiments were performed at 300 mHz (^{1}H) and 75 mHz (^{13}C) on a Bruker-Avance 300 MHz spectrometer. Assignment of carbons noted C* may be interchanged. Mass spectra were determined on a Hewlett Packard 5988A spectrometer or on a Shimadzu QP 2010 spectrometer by direct inlet at 70 eV. NMR data for compounds **2a**[1], **2b**[2], **3a**[3], **3b**[4], **3d**[5], **3f**[4] and **6a**[6] were previously described in literature.

2,3-diodoimidazo[1,2-*a*]pyridine (1a)

To a stirred solution of 2-iodoimidazo[1,2-*a*]pyridine (1.22g, 5mmol, 1eq) in CH_3CN (20mL) was added NIS (1.24g, 5.5mmol, 1.1eq) in one portion at room temperature. A white solid precipitated quickly. After 3h at room temperature the reaction was quenched with 30mL of water and extracted thrice with 30mL of CH_2Cl_2. The combined organic phases were washed with 50mL of $Na_2S_2O_3$ aqueous saturated solution, dried on Na_2SO_4 and evaporated to dryness. The pale yellow solid obtained (1.7g, 4,6mmol, yield: 92%) is used without further purification. **^{1}H NMR ($CDCl_3$)** δ: 8.03 (d, 1H, J = 9Hz, H-5), 7.54 (d, 1H, J = 9Hz, H-8), 7.20 (ddd, 1H, J = 9.0Hz, 6.9Hz, 1.0Hz H-7), 6.89 (td, 1H, J = 9.0Hz, 0.6Hz, H-6). **^{13}C NMR ($CDCl_3$)** δ: 149.4 (C-8a), 127.0 (C-5), 125.7 (C-7), 117.2 (C-8), 113.9 (C-6), 104.6 (C-2), 73.0 (C-3). **m.p.**: 114-118°C. **HRMS (ESI)**: *m/z* calculated for $C_7H_4I_2N_2$ $[M+H]^+$: 370.85366, found: 370.85389.

2-iodo-3-bromoimidazo[1,2-*a*]pyridine (1b)

To a stirred solution of 2-iodoimidazo[1,2-*a*]pyridine (1.75g, 7.2mmol, 1eq) in CH_3CN (30mL) was added NBS (1.4g, 7.9mmol, 1.1eq) in one portion at room temperature. A white solid precipitated quickly. After 3h at room temperature the reaction was quenched with 30mL of water and extract thrice with 30mL of CH_2Cl_2. The combined organic phases were washed with 50mL of $Na_2S_2O_3$ aqueous saturated solution, dried on Na_2SO_4 and evaporated to dryness. The crude mixture was purified by column chromatography (silica, eluent: CH_2Cl_2). **1b** is obtained as a gray solid (2.1g, 6.5mmol, yield: 90%). **^{1}H NMR ($CDCl_3$)** δ: 8.06 (dt, 1H, J = 6.9Hz, 0.9Hz, H-5), 7.56 (dt, 1H, J = 9.3Hz, 0.9Hz, H-8), 7.21 (ddd, J = 9.0Hz, 6.9Hz, 1.2Hz, H-7), 6.91 (td, 1H, J = 6.9Hz, 0.9Hz, H-6). **^{13}C NMR ($CDCl_3$)** δ: 147.4 (C-8a), 125.3 (C-7), 124.3 (C-5), 117.3 (C-8), 113.7 (C-6), 101.9 (C-2*), 95.9 (C-3*). **m.p.**: 114-118°C. **HRMS (ESI)**: *m/z* calculated for $C_7H_4BrIN_2$ $[M+H]^+$: 322.86753, found: 322.86793.

General procedure for Suzuki coupling at C-2 position or C-3 position.

1b (646mg, 2mmol, 1eq) or **2b-d** (n mmol, 1 eq for C-3 functionalization), $Pd(PPh_3)_4$ (116mg, 0.1mmol, 5%), Na_2CO_3 (424mg, 4mmol, 2eq) and boronic acid (2.2mmol, 1.1eq) were introduced into a microwave tube. The tube was sealed with a rubber septum and then evacuated and refilled with argon thrice. 1,4-Dioxane (8mL) and water (4mL) were then added. The reaction mixture was heated under microwave iradiation at 120°C for 1h. After cooling, the reaction mixture was partitioned between EtOAc (10mL) and water (10mL). The aqueous phase was extracted twice with EtOAc (10mL). Organic phases were combined, dried over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by column chromatography (silica, eluent: mixture of CH_2Cl_2 and EtOAc).

3-bromo-2-(thiophen-3-yl)imidazo[1,2-*a*]pyridine (2c)

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[1] Gao, Y.; Yin, M.; Wu, W.; Huang, H.; Jiang, H. *Adv. Synth. Catal.* **2013**, 355, 2263-2273.
[2] Zhou, X.; Yan, H.; Ma, C.; He, Y.; Li, Y.; Cao, J.; Yan, R.; Huang, G. *J. Org. Chem.* **2016**, 81, 25-31.
[3] Hiebel, M.-A.; Fall, Y.; Scherrmann, M.-C.; Berteina-Raboin, S. *Eur. J. Org. Chem.* **2014**, 4646-4650.
[4] Marhadour, S.; Marchand, P.; Pagniez, F.; Bazin, M.-A.; Picot, C.; Lozach, O.; Ruchaud, S.; Antoine, M.; Meijer, L.; Rachidi, N.; Le Pape, P. *Eur. J. Med. Chem.* **2012**, 58, 543-556.
[5] Enguehard, C.; Renou, J.-L.; Collot, V.; Hervet, M.; Rault, S.; Gueiffier, A. *J. Org. Chem.* **2000**, 65, 6572-6575.
[6] Meng, X.; Yu, C.; Chen, G.; Zhao, P. *Catal. Sci. Technol.* **2015**, 5, 372-379.

Eluent: CH_2Cl_2/EtOAc 98/2→97/3. Pale yellow solid, yield: 80%. **^{1}H NMR ($CDCl_3$)** δ: 8.04 (m, 2H, H-5, thienyl-2), 7.86 (dd, 1H, J = 4.8Hz, 1.2Hz, thienyl-4), 7.56 (dt, 1H, J = 9.0Hz, 0.9Hz, H-8), 7.39 (dd, 1H, J = 4.8Hz, 3.0Hz, thienyl-5), 7.18 (ddd, 1H, J = 9.0Hz, 6.6Hz, 1.2Hz, H-7), 6.84 (td, 1H, J = 6.9Hz, 0.9Hz, H-6). **^{13}C NMR ($CDCl_3$)** δ: 145.2 (C-8-a), 139.1 (C-2), 133.9 (thienyl-3), 127.0 (thienyl-4), 125.8 (thienyl-5), 125.6 (C-7), 124.0 (C-5), 123.8 (thienyl-2), 117.4 (C-8), 113.4 (C-6), 91.5 (C-3). **m.p.**: 130-134°C. **HRMS (ESI)**: *m/z* calculated for $C_{11}H_7BrN_2S$ $[M+H]^+$: 278.95861, found: 278.95892.

3-bromo-2-methylimidazo[1,2-*a*]pyridine (2d)

Eluent: CH_2Cl_2/EtOAc 90/10→80/20. Yellow solid, yield: 42%. **^{1}H NMR ($CDCl_3$)** δ: 7.99 (dt, 1H, J = 6.9Hz, 0.9Hz, H-5), 7.48 (dt, 1H, J = 9.0Hz, 0.9Hz, H-8), 7.15 (ddd, 1H, J = 9.0Hz, 6.9Hz, 1.2Hz, H-7), 6.84 (td, 1H, J = 6.9Hz, 0.9Hz, H-6), 2.43 (s, 3H, CH_3). **^{13}C NMR ($CDCl_3$)** δ: 145.2 (C-8a), 142.0 (C-2), 124.4 (C-7), 123.7 (C-5), 117.0 (C-8), 112.6 (C-6), 93.0 (C-3), 13.7 (CH_3). **m.p.**: 45-49°C. **HRMS (ESI)**: *m/z* calculated for $C_8H_7BrN_2$ $[M+H]^+$: 210.98654, found: 210.98671.

3-(furan-2-yl)-2-phenylimidazo[1,2-*a*]pyridine (3c)

Eluent: CH_2Cl_2/EtOAc 95/5. Brown solid, yield: 67%. **^{1}H NMR ($CDCl_3$)** δ: 8.19 (dt, 1H, J = 6.9Hz, 0.9Hz, H-5), 7.77-7.74 (m, 2H, Ph-2,6), 7.66 (dt, 1H, J = 9.0Hz, 0.9Hz, H-8), 7.63 (t, 1H, J = 1.2Hz, furyl-5), 7.40-7.31 (m, 3H, Ph-3,4,5), 7.22 (ddd, 1H, J = 9.0Hz, 6.9Hz, 1.2Hz, H-7), 6.80 (td, 1H, J = 6.9Hz, 1.2Hz, H-6), 6.56 (m, 2H, furyl-3,4). **^{13}C NMR ($CDCl_3$)** δ: 145.5 (C-8a), 145.3 (furyl-2), 143.6 (C-2), 143.4 (furyl-5), 134.0 (Ph-1), 128.5 (Ph-3,5*), 128.2 (Ph-2,6*), 128.1 (Ph-4), 125.5 (C-7), 124.8 (C-5), 117.6 (C-8), 112.8 (C-6), 111.8 (furyl-3*), 111.6 (furyl-4*). **m.p.**: 111-115°C. **HRMS (ESI)**: *m/z* calculated for $C_{17}H_{12}N_2O$ $[M+H]^+$: 261.10224, found: 261.10229.

3-phenyl-2-(thiophen-3-yl)imidazo[1,2-*a*]pyridine (3e)

Eluent: CH_2Cl_2/EtOAc 100/0→93/7. white solid, yield: 88%. **^{1}H NMR ($CDCl_3$)** δ: 7.91 (dt, 1H J = 6.9Hz, 1.2Hz, H-5), 7.78 (d, 1H, J = 9.3Hz, H-8), 7.65 (dd, 1H, J = 3.0Hz, 1.5Hz, thienyl-2), 7.61-7.48 (m, 5H, Ph-2,3,4,5,6), 7.31-7.21 (m, 3H, H-7, thienyl-4,5), 6.80 (td, 1H, J = 6.9Hz, 1.2Hz, H-6). **^{13}C NMR ($CDCl_3$)** δ: 143.9 (C-8a), 137.5 (C-2), 134.2 (thienyl-3), 131.1 (Ph-3,5*), 129.8 (Ph-2,6*), 129.7 (Ph-4), 129.0 (Ph-1), 127.0 (thienyl-2), 126.0 (C-7), 125.6 (thienyl-4*), 123.62 (C-5*), 123.59 (thienyl-5*), 120.6 (C-3), 116.9 (C-8), 113.2 (C-6). **m.p.**: 148-152°C. **HRMS (ESI)**: *m/z* calculated for $C_{17}H_{12}N_2S$ $[M+H]^+$: 277.07940, found: 277.07945.

2-phenyl-3-(pyridin-4-yl)imidazo[1,2-*a*]pyridine (3f)[4]

1b (200mg, 0.619mmol, 1eq), $Pd(PPh_3)_4$ (36mg, 0.031mmol, 5%), Na_2CO_3 (131mg, 1.24mmol, 2eq) and phenylboronic acid (83mg, 0.681mmol, 1.1eq) were introduced into a microwave tube. The tube was sealed with a rubber septum and then evacuated and refilled with argon thrice. 1,4-Dioxane (2.8mL) and water (1.4mL) were then added. The reaction mixture was heated under microwave irradiation at 120°C for 1h. After cooling, 4-pyridylboronic acid (98mg, 0.681mmol, 1.1eq) was added and the reaction was heated again under microwave irradiation at 120°C for 1h. After cooling, the reaction mixture was partitioned between CH_2Cl_2 (10mL) and water (10mL). The aqueous phase was extracted twice with CH_2Cl_2 (10mL). Organic phases were combined, dried over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by column chromatography (silica, eluent: CH_2Cl_2/EtOAc 100/0→93/7) to afford **3a** as a white solid (106mg), yield: 73%.

General procedure for Sonogashira coupling at C-2 position.

1b (161mg, 0.5mmol, 1eq), $PdCl_2(PPh_3)_2$ (35mg, 0.05mmol, 10%) and CuI (10mg, 0.05mmol, 10%) were introduced into a screw-cap test tube. The tube was sealed with a rubber septum and then evacuated and refilled with argon thrice. DMF (2mL), Et_3N (278µL, 2mmol, 4eq) and alkyne (0.55mmol, 1.1eq) were then added. The reaction mixture was stirred for 30 minutes at room temperature. The reaction mixture was partitioned between CH_2Cl_2 (10mL) and brine (10mL). The aqueous phase was extracted twice with CH_2Cl_2 (10mL). Organic phases were combined, dried over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by column chromatography (silica, eluent: mixture of petroleum ether and diethylether).

3-bromo-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (4a)

Eluent: PE/Et_2O 50/50. Orange solid, yield: 95%. **^{1}H NMR ($CDCl_3$)** δ: 8.08 (dt, 1H, J = 6.9Hz, 0.9Hz, H-5), 7.64-7.61 (m, 3H, 2CH Ph, H-8), 7.38-7.36 (m, 3H, 3CH Ph), 7.31 (ddd, 1H, J = 9.0Hz, 6.6Hz, 1.2Hz, H-7), 6.98 (td, 1H, J = 6.9Hz, 1.2Hz, H-6). **^{13}C NMR ($CDCl_3$)** δ: 145.1 (C-8a), 132.0 (2CH Ph), 129.0 (CH Ph), 128.5 (2CH Ph), 128.4 (C-2), 126.2 (C-7), 124.1 (C-5), 122.5 (Cq Ph), 117.7 (C-8), 114.1 (C-6), 99.4 (C-3), 94.6 (C≡C-Ph), 81.0 (C≡C-Ph). **m.p.**: 117-121°C. **HRMS (ESI)**: *m/z* calculated for $C_{15}H_9BrN_2$ $[M+H]^+$: 297.00219, found: 297.00257.

3-bromo-2-(cyclopropylethynyl)imidazo[1,2-*a*]pyridine (4b)

Eluent: PE/Et_2O 50/50. Yellow solid, yield: 98%. **^{1}H NMR ($CDCl_3$)** δ: 7.96 (dt, 1H, J = 6.9Hz, 0.9Hz, H-5), 7.47 (dt, 1H, J = 9.3Hz, 0.9Hz, H-8), 7.19 (ddd, 1H, J = 9.0Hz, 6.9Hz, 1.2Hz, H-7), 6.87 (td, 1H, J = 6.9Hz, 0.9Hz, H-6), 1.50 (quint, 1H, CH c-Pr), 0.88 (m, 4H, $2CH_2$ c-Pr). **^{13}C NMR ($CDCl_3$)** δ: 144.9 (C-8a), 129.1 (C-2), 125.5 (C-7), 123.8 (C-5), 117.5 (C-8), 113.6 (C-6), 98.9 (C≡C-c-Pr), 98.4 (C-3), 67.6 (C≡C-c-Pr), 9.0 ($2CH_2$ c-Pr), 0.4 (CH c-Pr). **m.p.**: 79-83°C. **HRMS (ESI)**: *m/z* calculated for $C_{12}H_9BrN_2$ $[M+H]^+$: 261.00219, found: 261.00244.

General procedure for Sonogashira coupling at C-3 position.

4a-b (0.5mmol, 1eq), $PdCl_2(PPh_3)_2$ (35mg, 0.05mmol, 10%) and CuI (10mg, 0.05mmol, 10%) were introduced into a screw-cap test tube. The tube was sealed with a rubber septum and then evacuated and refilled with argon thrice. DMF (2mL), Et_3N (278µL, 2mmol, 4eq) and alkyne (0.55mmol, 1.1eq) were then added. The reaction mixture was stirred for 1h30 at 80°C. After cooling, the reaction mixture was partitioned between CH_2Cl_2 (10mL) and brine (10mL). The aqueous phase was extracted twice with CH_2Cl_2 (10mL). Organic phases were combined, dried over $MgSO_4$ and evaporated to dryness. The crude mixture was purified by column chromatography (silica, eluent: mixture of petroleum ether and diethylether).

2-(phenylethynyl)-3-(p-tolylethynyl)imidazo[1,2-*a*]pyridine (5a)

Eluent: PE/Et_2O 50/50. Orange solid, yield: 97%. **^{1}H NMR ($CDCl_3$)** δ: 8.29 (d, 1H, J = 6.6Hz, H-5), 7.65-7.62 (m, 3H, Ph-2,6, H-8), 7.51 (d, 2H, J = 8.1Hz, tolyl-2,6), 7.39-7.35 (m, 3H, Ph-3,4,5), 7.32 (ddd, 1H, J = 9.0Hz, 6.9Hz, 1.2Hz, H-7), 7.21 (d, 2H, J = 7.8Hz, tolyl-3,5), 6.97 (td, 1H, J = 6.6Hz, 0.9Hz, H-6), 2.40 (s, 3H, CH_3 tolyl). **^{13}C NMR ($CDCl_3$)** δ: 144.7 (C-8a), 139.5 (tolyl-4), 132.0 (Ph-2,6), 131.9 (C-2), 131.5 (tolyl-2,6), 129.4 (tolyl-3,5), 128.9 (Ph-4), 128.5 (Ph-3,5), 127.1 (C-7), 125.3 (C-5), 122.7 (Ph-1), 119.3 (tolyl-1), 117.6 (C-8), 113.8 (C-6), 112.2 (C-3), 102.3 (C≡C-tolyl), 94.7 (C≡C-Ph), 82.3 (C≡C-Ph), 75.2 (C≡C-tolyl), 21.7 (CH_3 tolyl). **m.p.**: 113-117°C. **HRMS (ESI)**: *m/z* calculated for $C_{24}H17N_2$ $[M+H]^+$: 333.13917, found: 333.13888.

3-(cyclopropylethynyl)-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (5b)

Eluent: PE/Et_2O 50/50→40/60. Brown solid, yield: 82%. **^{1}H NMR ($CDCl_3$)** δ: 8.16 (dt, 1H, J = 6.9Hz, 0.9Hz, H-5), 7.63-7.59 (m, 2H, Ph-2,6), 7.54 (dt, 1H, J = 9.0Hz, 0.9Hz, H-8), 7.38-7.33 (m, 3H, Ph-3,4,5), 7.24 (ddd, 1H, J = 9.0Hz, 6.6Hz, 1.2Hz, H-7), 6.88 (td, 1H, J = 6.6Hz, 0.9Hz, H-6), 1.70-1.61 (m, 1H, CH c-Pr), 1.04-0.91 (m, 4H, $2CH_2$ c-Pr). **^{13}C NMR ($CDCl_3$)** δ: 144.5 (C-8a), 132.0 (Ph-2,6), 131.9 (C-2), 128.7 (Ph-4), 128.4 (Ph-3,5), 126.3 (C-7), 125.1 (C-5), 123.0 (Ph-1), 117.6 (C-8), 113.3 (C-6), 112.5 (C-3), 106.8 (C≡C-c-Pr), 93.7 (C≡C-Ph), 82.8 (C≡C-Ph), 62.4 (C≡C-c-Pr), 9.6 ($2CH_2$ c-Pr), 0.8 (CH c-Pr). **m.p.**: 105-109°C. **HRMS (ESI)**: *m/z* calculated for $C_{20}H_{14}N_2$ $[M+H]^+$: 283.12298, found: 283.12315.

3-(3-methoxyprop-1-yn-1-yl)-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (5c)

Eluent: PE/Et_2O 40/60. Brown oil, yield: 42%. **^{1}H NMR ($CDCl_3$)** δ: 8.22 (dt, 1H, J = 6.9Hz, 0.9Hz, H-5), 7.62-7.57 (m, 3H, Ph-2,6, H-8), 7.38-7.34 (m, 3H, Ph-3,4,5), 7.30 (ddd, 1H, J = 9.0Hz, 6.9Hz, 1.2Hz, H-7), 6.94 (td, 1H, J = 6.9Hz, 0.9Hz, H-6), 4.53 (s, 2H, $C\underline{H_2}OCH_3$), 3.52 (s, 3H, $CH_2OC\underline{H_3}$). **^{13}C NMR ($CDCl_3$)** δ: 145.1 (C-8a), 133.2 (C-2), 132.0 (Ph-2,6), 128.9 (Ph-4), 128.5 (Ph-3,5), 126.9 (C-7), 125.2 (C-5), 122.7 (Ph-1), 117.8 (C-8), 113.7 (C-6), 111.2 (C-3), 98.2 (C≡C-CH_2OCH_3), 94.1 (C≡C-Ph), 82.3 (C≡C-Ph), 73.5 (C≡C-CH_2OCH_3), 60.8 ($C\underline{H_2}OCH_3$), 57.9 ($CH_2O\underline{C}H_3$). **HRMS (ESI)**: *m/z* calculated for $C_{19}H_{14}N_2O$ $[M+H]^+$: 287.11789, found: 287.11822.

2-(cyclopropylethynyl)-3-(phenylethynyl)imidazo[1,2-*a*]pyridine (5d)

Eluent: PE/Et_2O 50/50. Brown oil, yield: 54%. **^{1}H NMR ($CDCl_3$)** δ: 8.23 (dt, 1H, J = 6.9Hz, 0.9Hz, H-5), 7.60-7.54 (m, 3H, Ph-2,6, H-8), 7.41-7.37 (m, 3H, Ph-3,4,5), 7.27 (ddd, 1H, J = 8.7Hz, 6.6Hz, 1.2Hz, H-7), 6.93 (td, 1H, J = 6.9Hz, 1.2Hz, H-6), 1.60-1.51 (m, 1H, CH c-Pr), 0.93-0.90 (m, 4H, $2CH_2$ c-Pr). **^{13}C NMR ($CDCl_3$)** δ: 144.6 (C-8a), 132.9 (C-2), 131.5 (Ph-2,6), 128.9 (Ph-4), 128.6 (Ph-3,5), 126.8 (C-7), 125.1 (C-5), 122.5 (Ph-1), 117.5 (C-8), 113.6 (C-6), 113.3 (C-3), 101.5 (C≡C-Ph), 99.5 (C≡C-c-Pr), 76.1 (C≡C-Ph), 68.5 (C≡C-c-Pr), 9.1 ($2CH_2$ c-Pr), 0.6 (CH c-Pr). **HRMS (ESI)**: *m/z* calculated for $C_{20}H_{14}N_2$ $[M+H]^+$: 283.12298, found: 283.12319.

3-((4-methoxyphenyl)ethynyl)-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (5e)

1b (200mg, 0.619mmol, 1eq), $PdCl_2(PPh_3)_2$ (43mg, 0.062mmol, 10%) and CuI (12mg, 0.062mmol, 10%) were introduced into a screw-cap test tube. The tube was sealed with a rubber septum and then evacuated and refilled with argon thrice. DMF (2.5mL), Et_3N (344µL, 2.48mmol, 4eq) and phenylacetylene (75µL, 0.68mmol, 1.1eq) were then added. The reaction mixture was stirred for 30 minutes at room temperature. 4-methoxyphenylacetylene (120µL, 0.929mmol, 1.5eq) was added, and the reaction heated at 80°C for 1h30. After cooling, the reaction mixture was partitioned between CH_2Cl_2 (12mL) and brine (12mL). The aqueous phase was extracted twice with CH_2Cl_2 (12mL). Organic phases were combined, dried over $MgSO_4$ and evaporate to dryness. The crude mixture was purified by column chromatography (silica, eluent: PE/Et_2O 40/60→20/80) to afford **5e** as a dark yellow solid (140mg), yield: 65%. **^{1}H NMR ($CDCl_3$)** δ: 8.25 (dt, 1H, J = 6.6Hz, 0.9Hz, H-5), 7.65-7.59 (m, 3H, Ph-2,6, H-8), 7.54 (d, 2H, J = 8.7Hz, 4-MeOPh-2,6), 7.37-7.34 (m, 3H, Ph-3,4,5), 7.29 (ddd, 1H, J = 9.0Hz, 6.9Hz, 1.5Hz, H-7), 6.96-6.89 (m, 3H, 4-MeOPh-3,5, H-6), 3.83 (s, 3H, OCH_3). **^{13}C NMR ($CDCl_3$)** δ: 160.3 (4-MeOPh-4), 144.7 (C-8a), 133.4 (C-2*), 133.2 (4-MeOPh-2,6), 132.0 (Ph-2,6), 131.7 (4-MeOPh-1*), 128.8 (Ph-4), 128.4 (Ph-3,5), 126.9 (C-7), 125.2 (C-5), 122.7 (Ph-1), 117.6 (C-8), 114.3 (4-MeOPh-3,5), 113.7 (C-6), 112.3 (C-3), 102.1 (C≡C-4-MeOPh), 94.5 (C≡C-Ph), 82.4 (C≡C-Ph*), 74.5 (C≡C-4-MeOPh*), 55.4 (OCH_3). **m.p.**: 54-58°C. **HRMS (ESI)**: *m/z* calculated for $C_{24}H_{16}N_2O$ $[M+H]^+$: 349.13354, found: 349.13389.

2-methyl-3-(phenylethynyl)imidazo[1,2-*a*]pyridine (6b)

Eluent: PE/Et_2O 50/50→20/80. Orange oil, yield: 67%. **^{1}H NMR ($CDCl_3$)** δ: 8.24 (dt, 1H, J = 6.9Hz, 0.9Hz, H-5), 7.57-7.53 (m, 3H, Ph-2,6, H-8), 7.40-7.33 (m, 3H, Ph-3,4,5), 7.21 (ddd, 1H, J = 9.0Hz, 6.9Hz, 1.2Hz, H-7), 6.87 (td, 1H, J = 6.9Hz, 1.2Hz, H-6), 2.58 (s, 3H, CH_3). **^{13}C NMR ($CDCl_3$)** δ: 148.5 (C-2), 144.9 (C-8a), 131.3 (Ph-2,6), 128.6 (Ph-3,4,5), 125.7 (C-7), 125.1 (C-5), 122.9 (Ph-1), 116.9 (C-8), 112.8 (C-6), 106.4 (C-3), 100.7 (C≡C-Ph), 76.9 (C≡C-Ph), 14.4 (CH_3). **HRMS (ESI)**: *m/z* calculated for $C_{16}H_{12}N_2$ $[M+H]^+$: 233.10732, found: 233.10744.

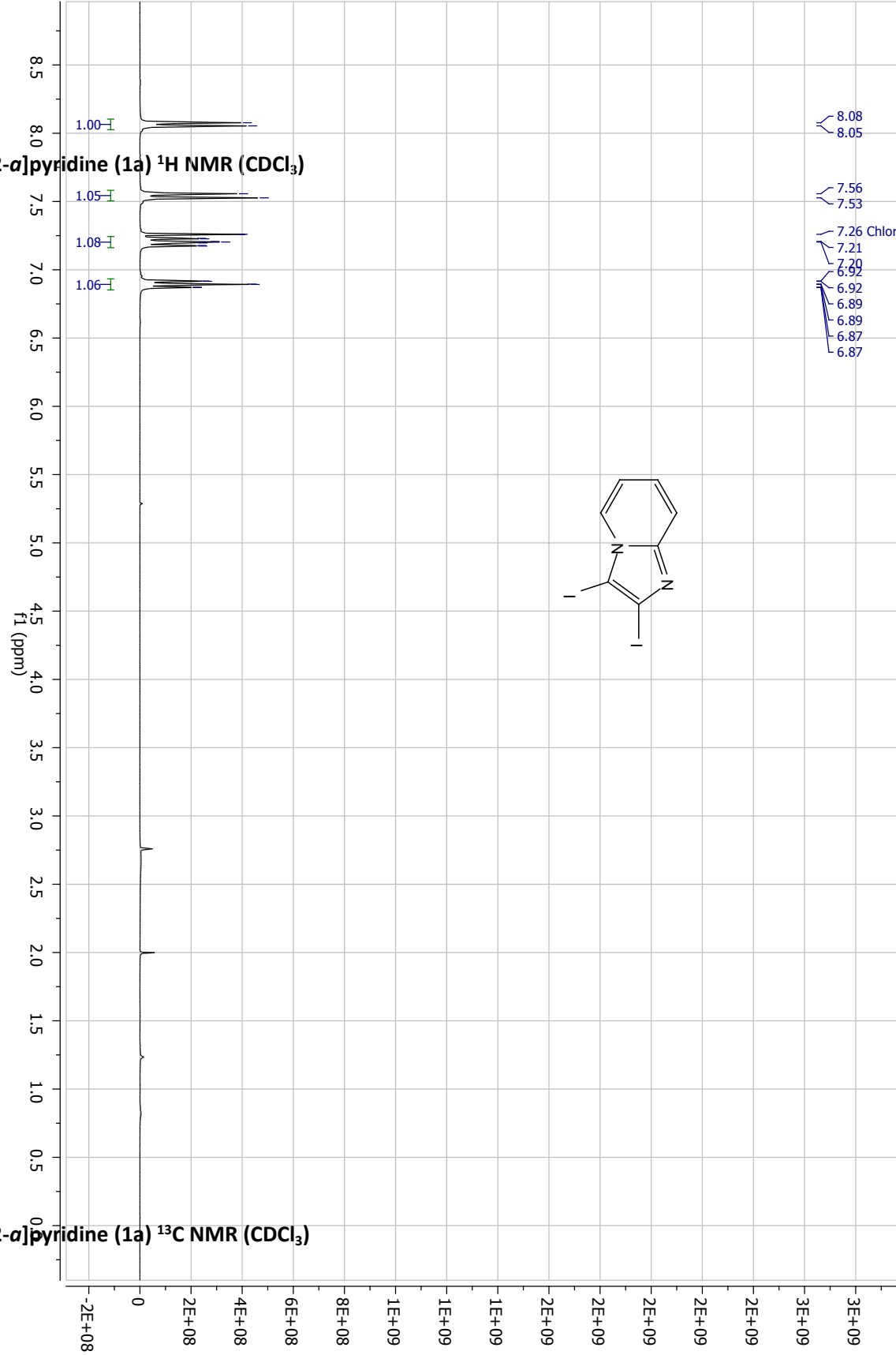
3-methyl-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (6c)

Eluent: CH_2Cl_2/MeOH 99/1. Brown solid, yield: 70%. **^{1}H NMR ($CDCl_3$)** δ: 7.82 (dt, 1H, J = 6.9Hz, 0.9Hz, H-5), 7.60-7.53 (m, 3H, Ph-2,6, H-8), 7.37-7.33 (m, 3H, Ph-3,4,5), 7.18 (ddd, 1H, J = 9.3Hz, 6.9Hz, 1.2Hz, H-7), 6.85 (td, 1H, J = 6.6Hz, 0.9Hz, H-6), 2.59 (s, 3H, CH_3). **^{13}C NMR ($CDCl_3$)** δ: 144.5 (C-8a), 131.7 (Ph-2,6), 128.4 (Ph-3,4,5), 126.5 (C-2), 124.4 (C-7), 123.8 (C-3*), 123.2 (Ph-1*), 122.9 (C-5), 117.7 (C-8), 112.8 (C-6), 92.7 (C≡C-Ph), 83.1 (C≡C-Ph), 9.2 (CH_3). **m.p.**: 119-123°C. **HRMS (ESI)**: *m/z* calculated for $C_{16}H_{12}N_2$ $[M+H]^+$: 233.10732, found: 233.10750.

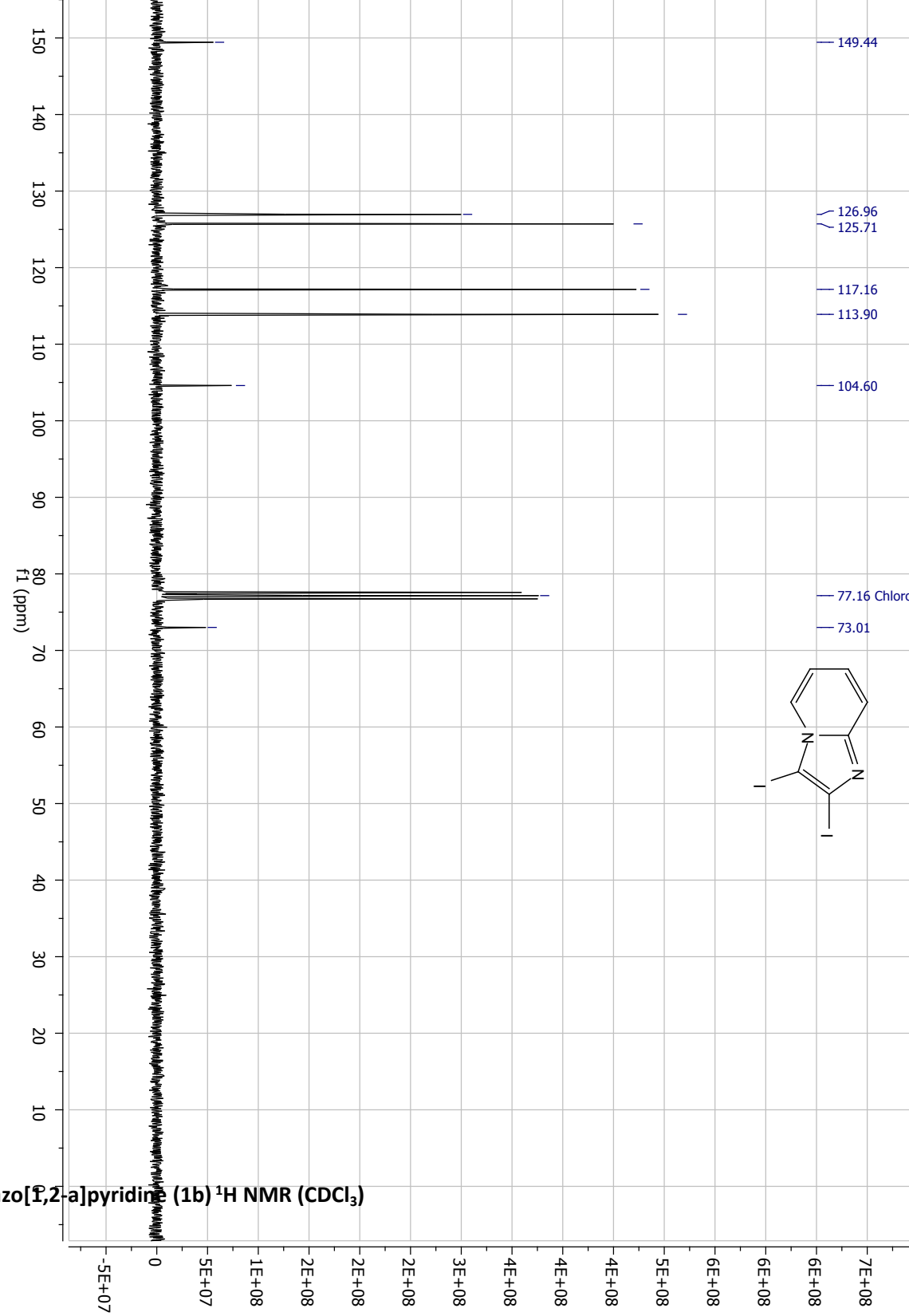
2-(phenylethynyl)-3-(pyridin-4-yl)imidazo[1,2-*a*]pyridine (6d)

Eluent: CH_2Cl_2/MeOH 99/1. Off-white solid, yield: 89%. **^{1}H NMR ($CDCl_3$)** δ: 8.81 (bd, 1H, J = 4.5Hz, Pyridyl-2,6), 8.37 (d, 1H, J = 7.2Hz, H-5), 7.76 (d, 1H, J = 5.7Hz, Pyridyl-3,5), 7.67 (d, 1H, J = 9.0Hz, H-8), 7.54-7.48 (m, 2H, Ph-2,6), 7.37-7.30 (m, 4H, Ph-3,4,5, H-7), 6.93 (td, 1H, J = 6.9Hz, 0.9Hz, H-6). **^{13}C NMR ($CDCl_3$)** δ: 150.1 (Pyridyl-2,6), 146.2 (C-8a), 136.9 (Pyridyl-4), 131.9 (Ph-2,6), 129.0 (Ph-4), 128.9 (C-2), 128.6 (Ph-3,5), 126.8 (C-7), 124.6 (Ph-1), 123.4 (C-5), 122.4 (Pyridyl-3,5), 118.5 (C-8), 114.2 (C-6), 93.4 (C≡C-Ph), 82.7 (C≡C-Ph), (C-3 is missing). **m.p.**: 87-91°C. **HRMS (ESI)**: *m/z* calculated for $C_{20}H_{13}N_3$ $[M+H]^+$: 296.11822, found: 296.11851.

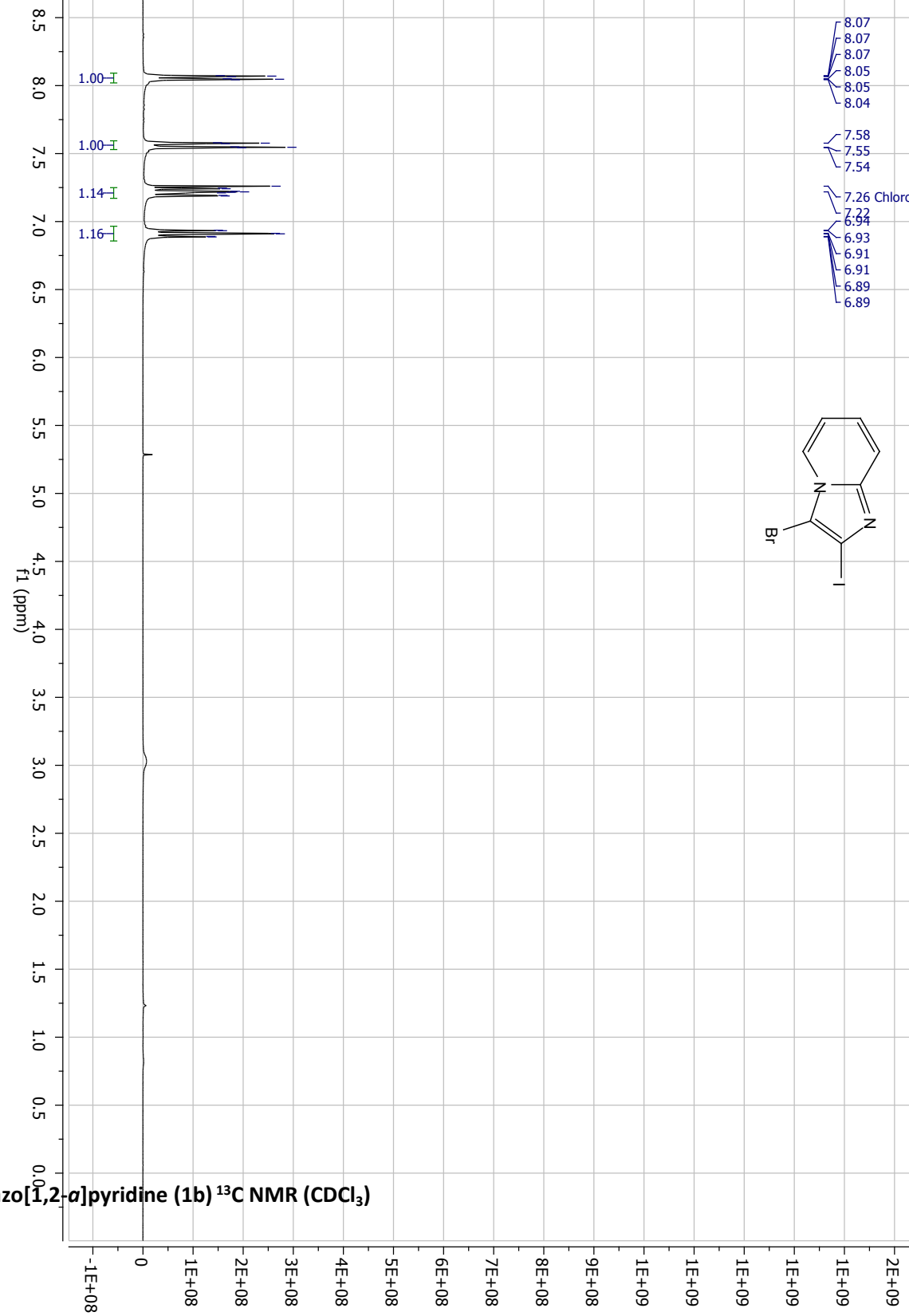
2,3-diiodoimidazo[1,2-*a*]pyridine (1a) ^{1}H NMR ($CDCl_3$)



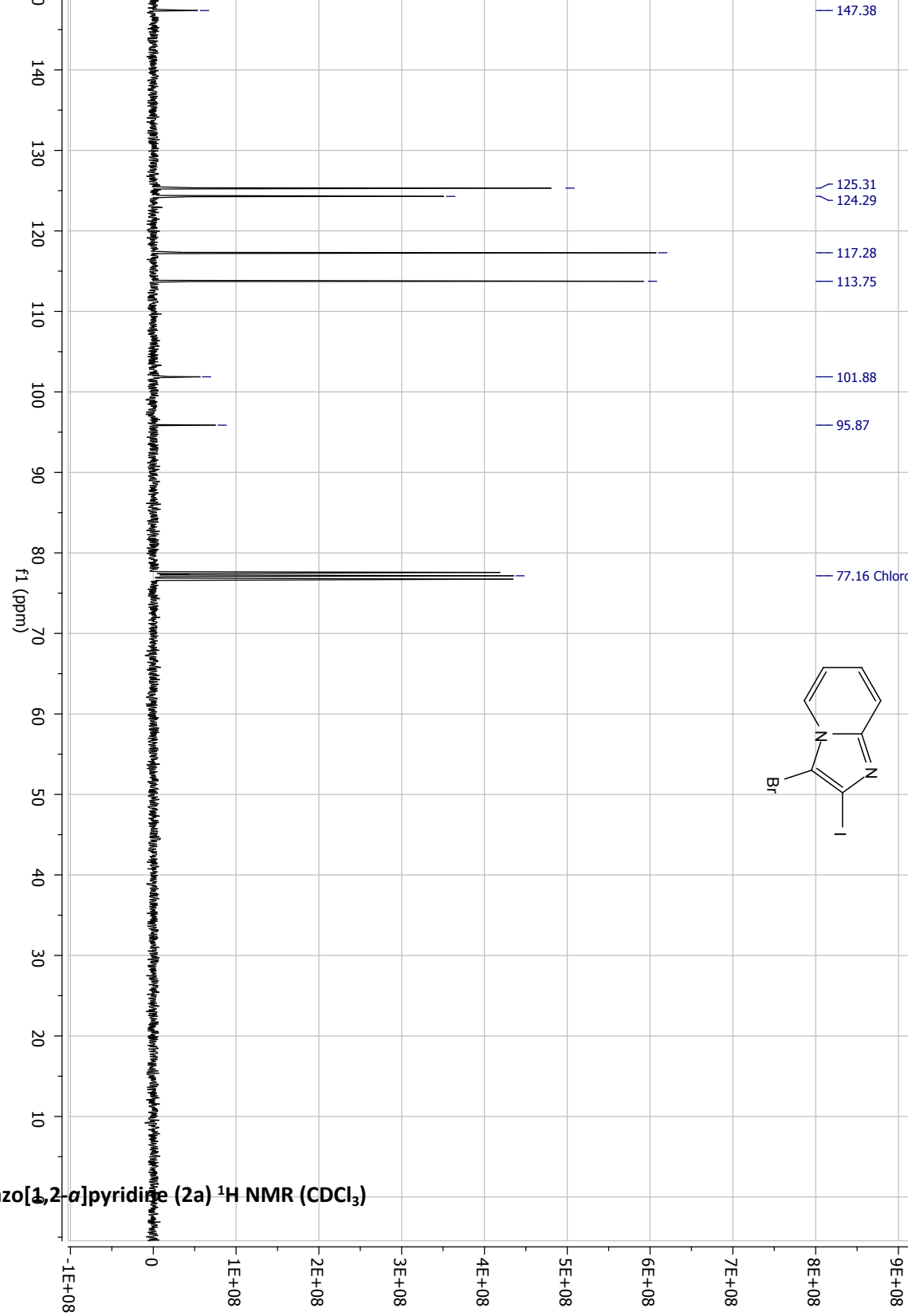
2,3-diiodoimidazo[1,2-*a*]pyridine (1a) ^{13}C NMR ($CDCl_3$)



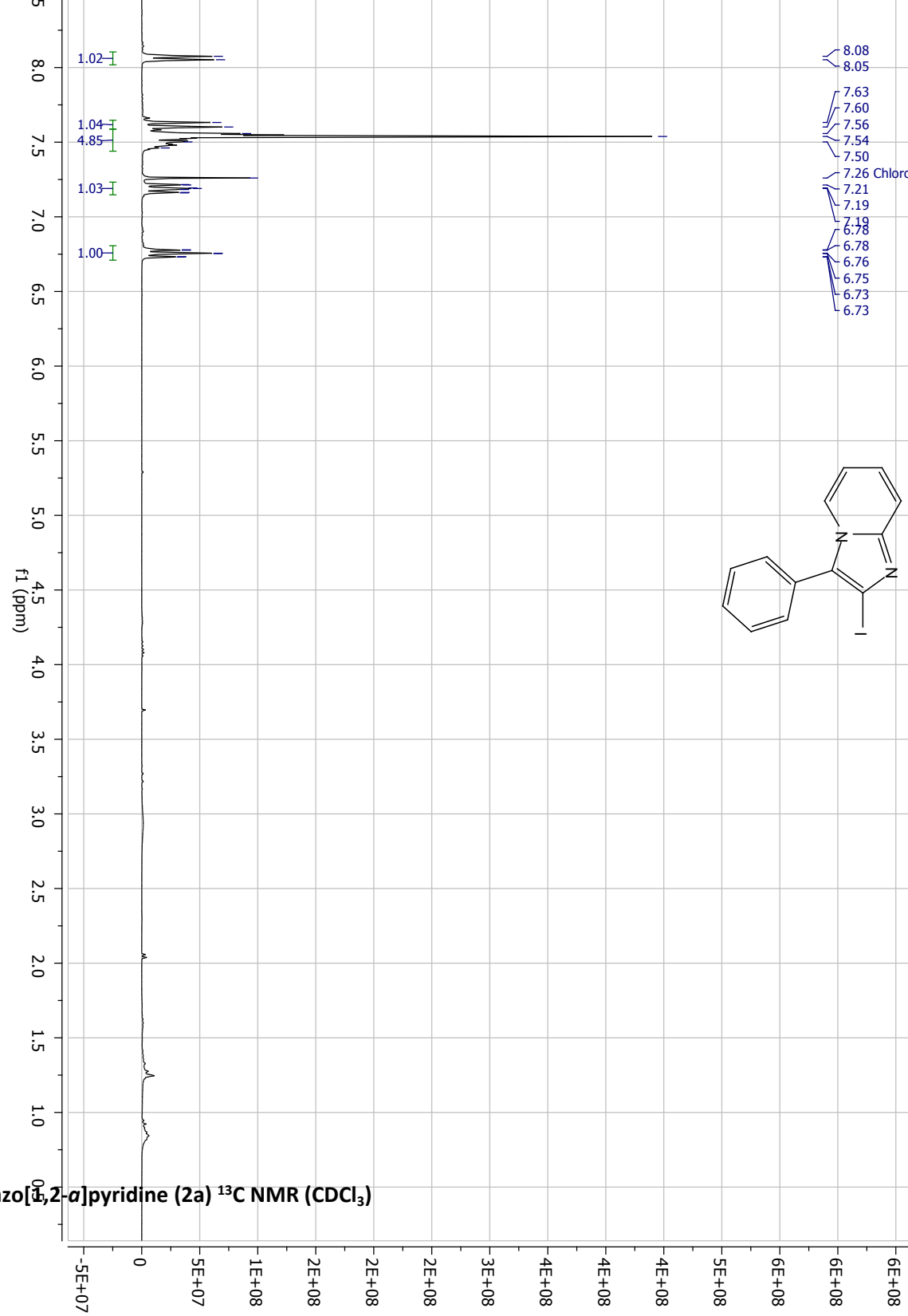
3-bromo-2-iodoimidazo[1,2-a]pyridine (1b) ^{1}H NMR ($CDCl_3$)



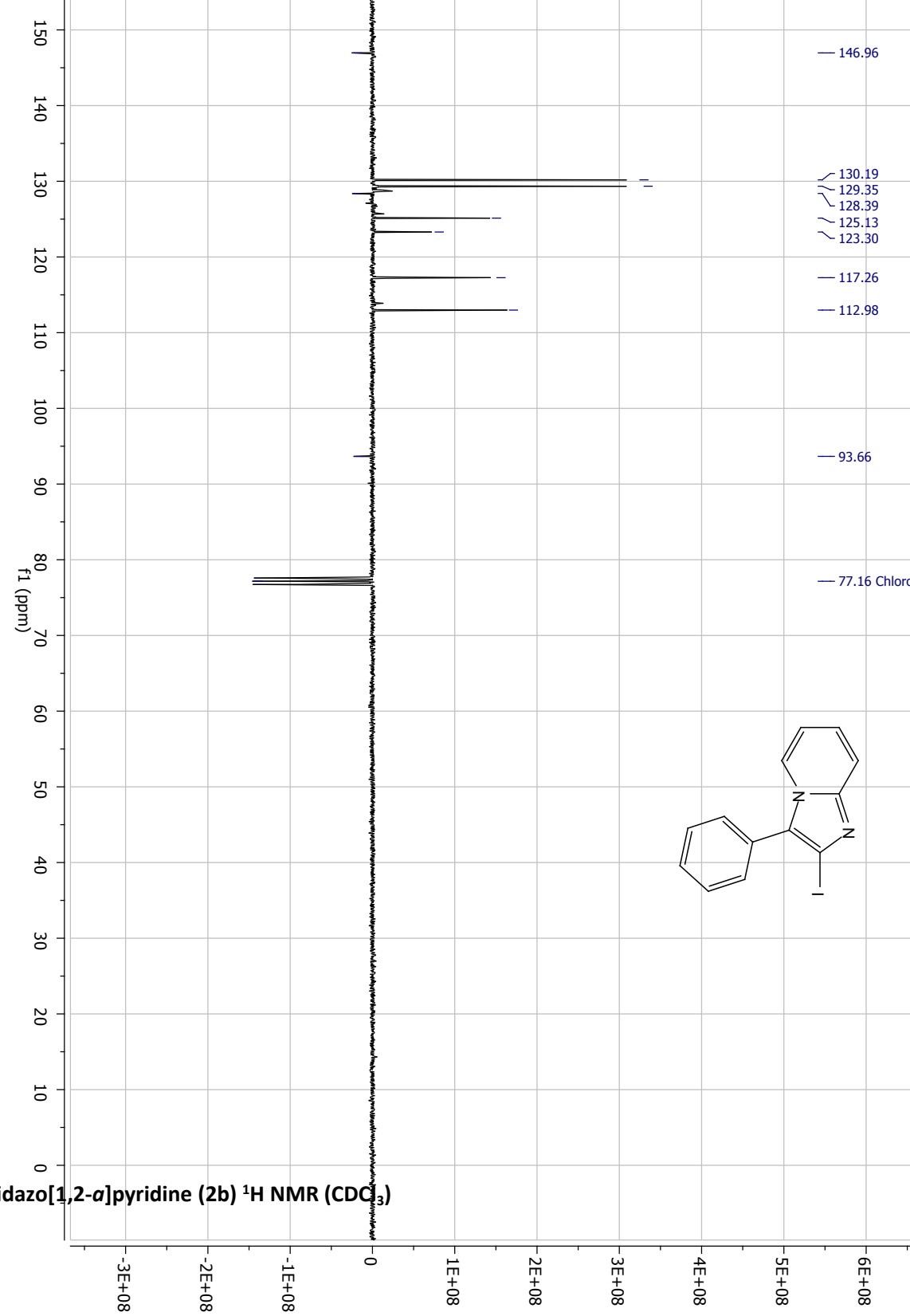
3-bromo-2-iodoimidazo[1,2-*a*]pyridine (1b) ^{13}C NMR ($CDCl_3$)



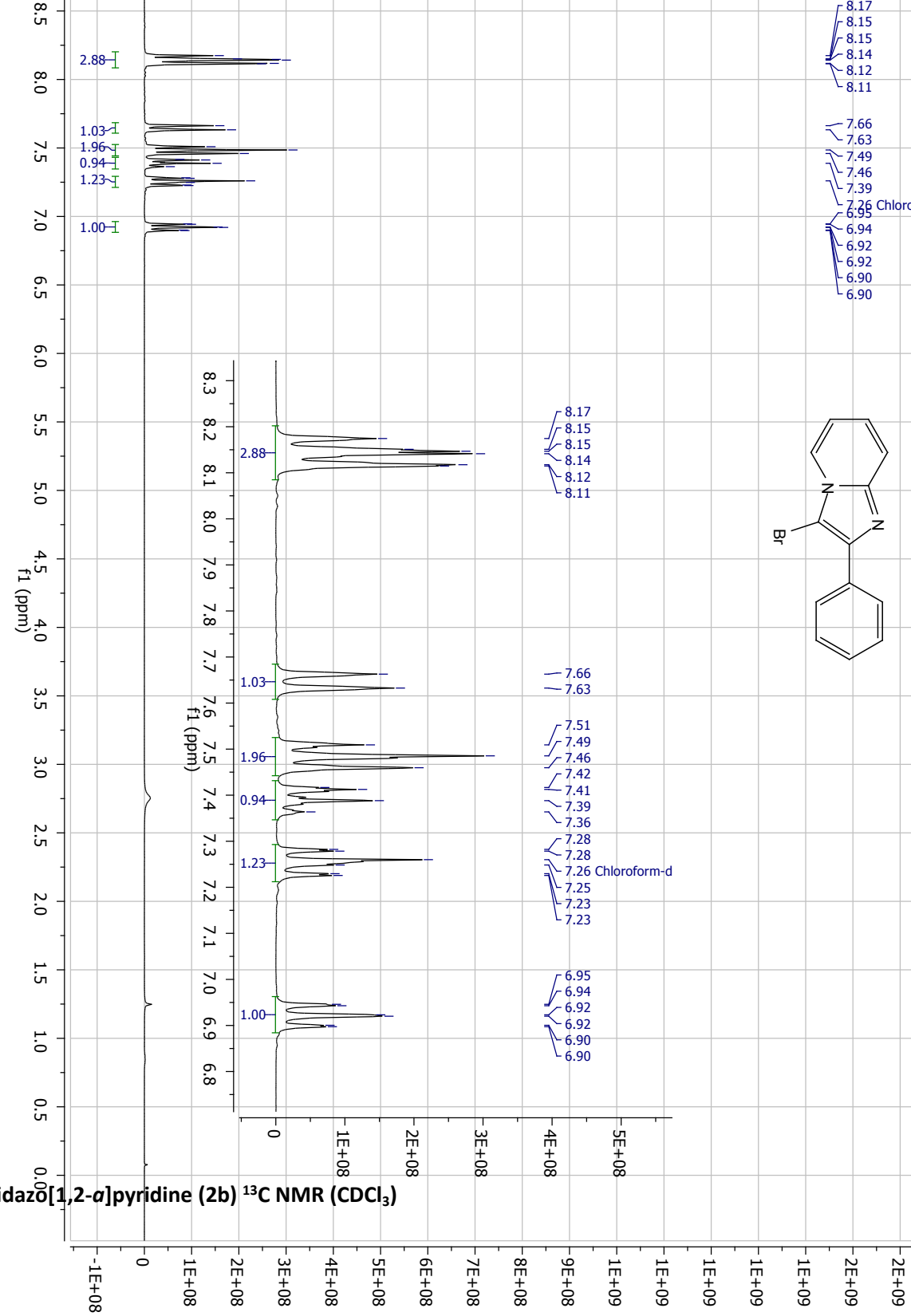
2-iodo-3-phenylimidazo[1,2-*a*]pyridine (2a) ^{1}H NMR ($CDCl_3$)



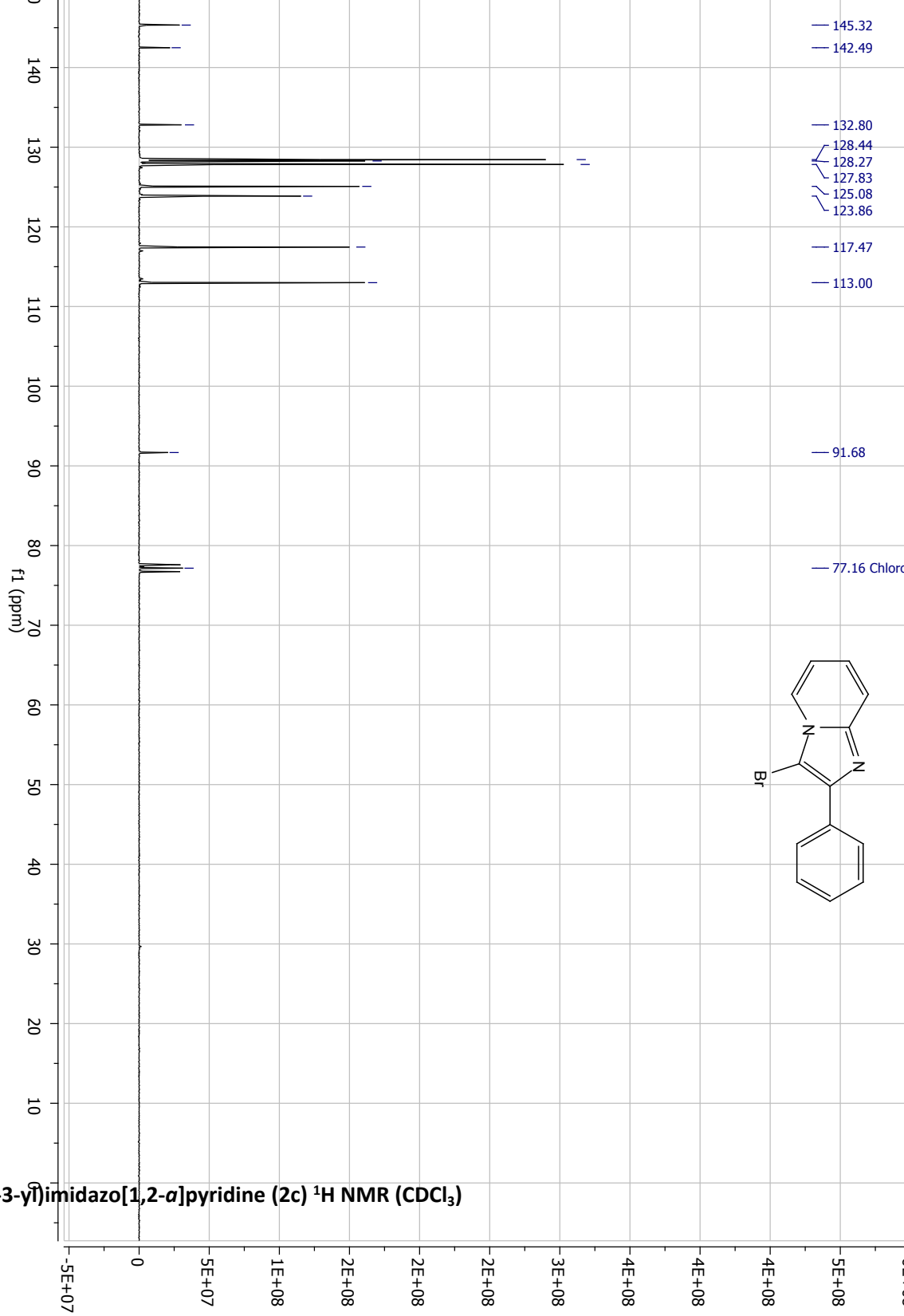
2-iodo-3-phenylimidazo[1,2-*a*]pyridine (2a) ^{13}C NMR ($CDCl_3$)



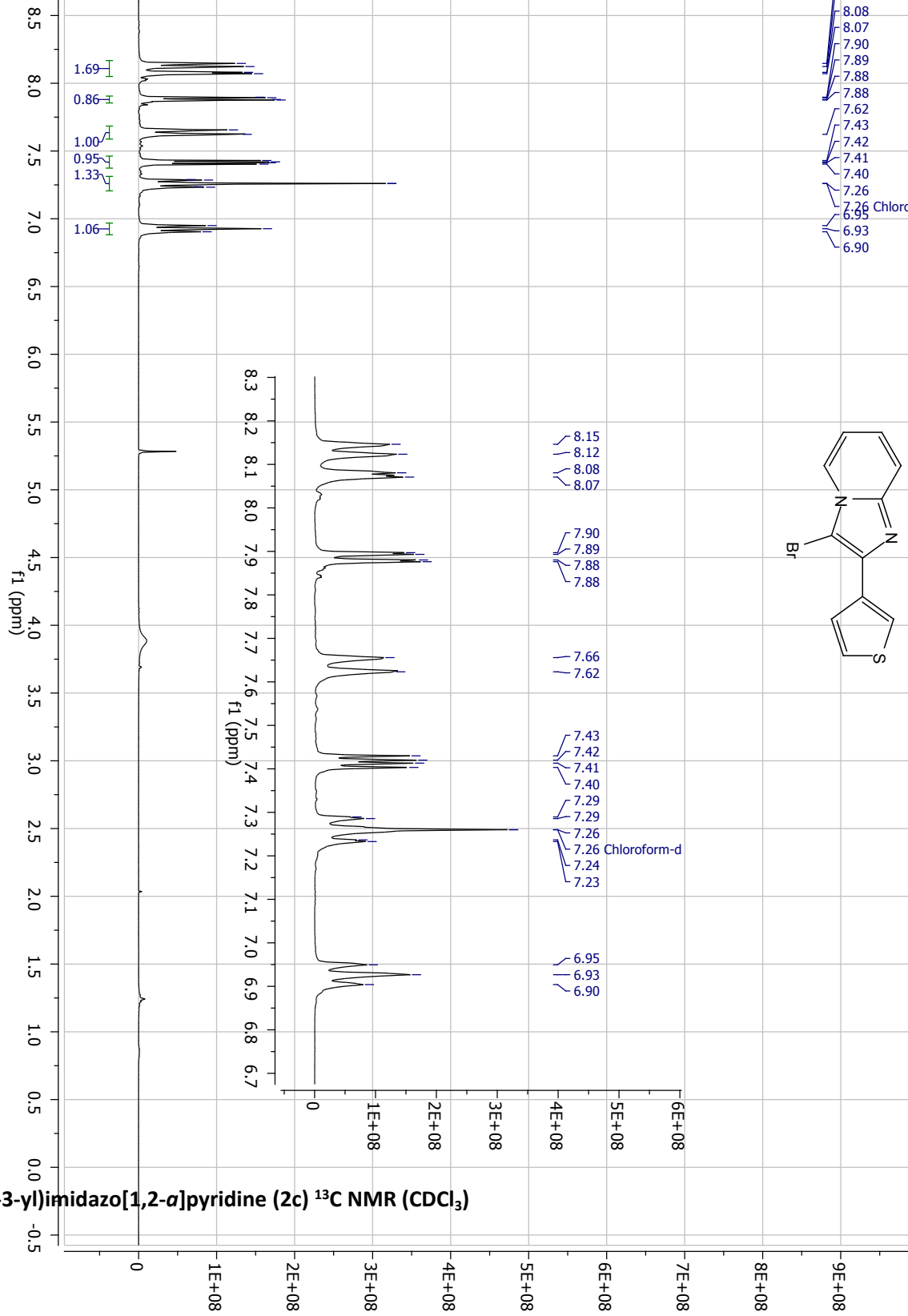
3-bromo-2-phenylimidazo[1,2-*a*]pyridine (2b) ^{1}H NMR ($CDCl_3$)



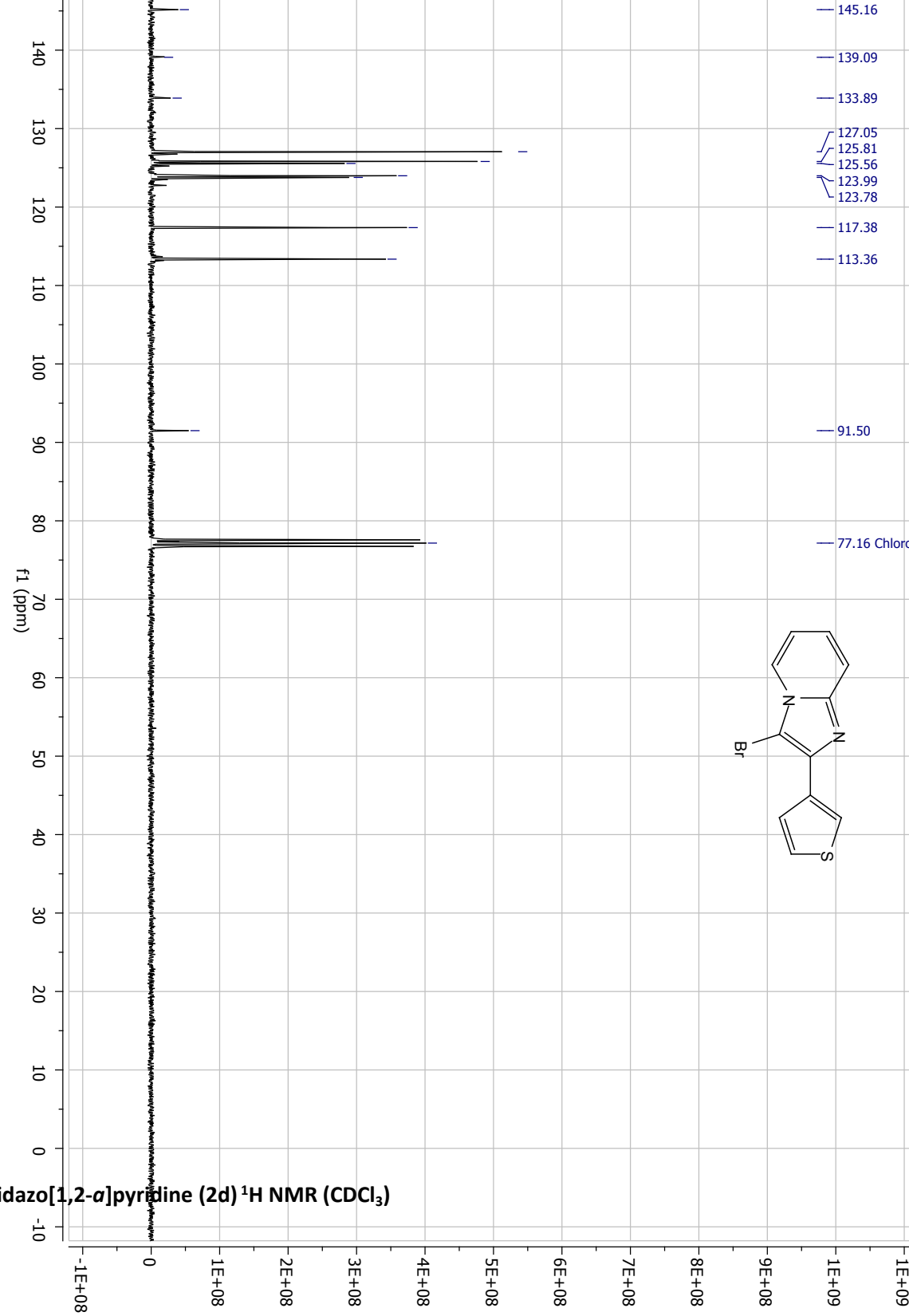
3-bromo-2-phenylimidazo[1,2-*a*]pyridine (2b) ^{13}C NMR ($CDCl_3$)



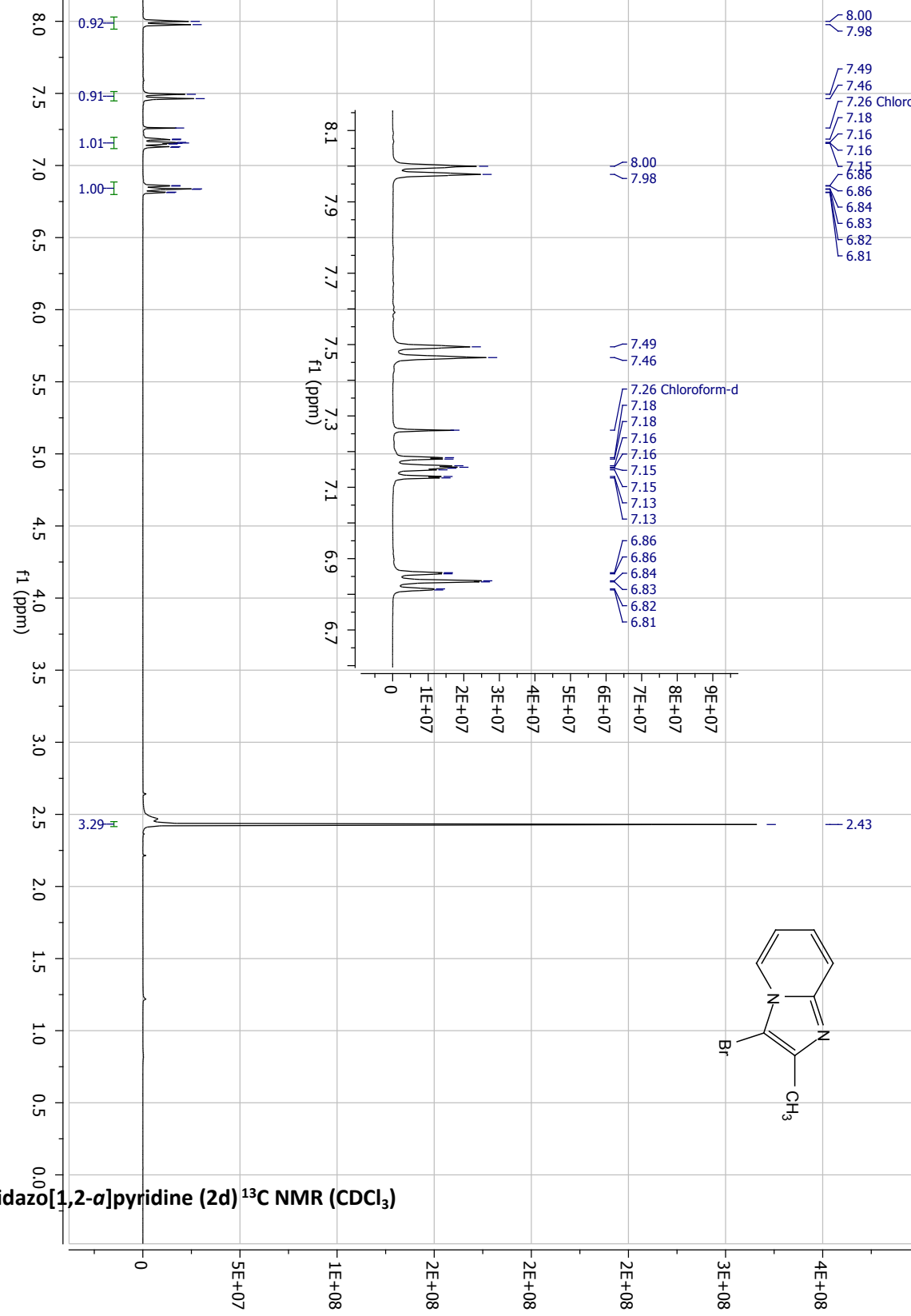
3-bromo-2-(thiophen-3-yl)imidazo[1,2-*a*]pyridine (2c) ^{1}H NMR ($CDCl_3$)



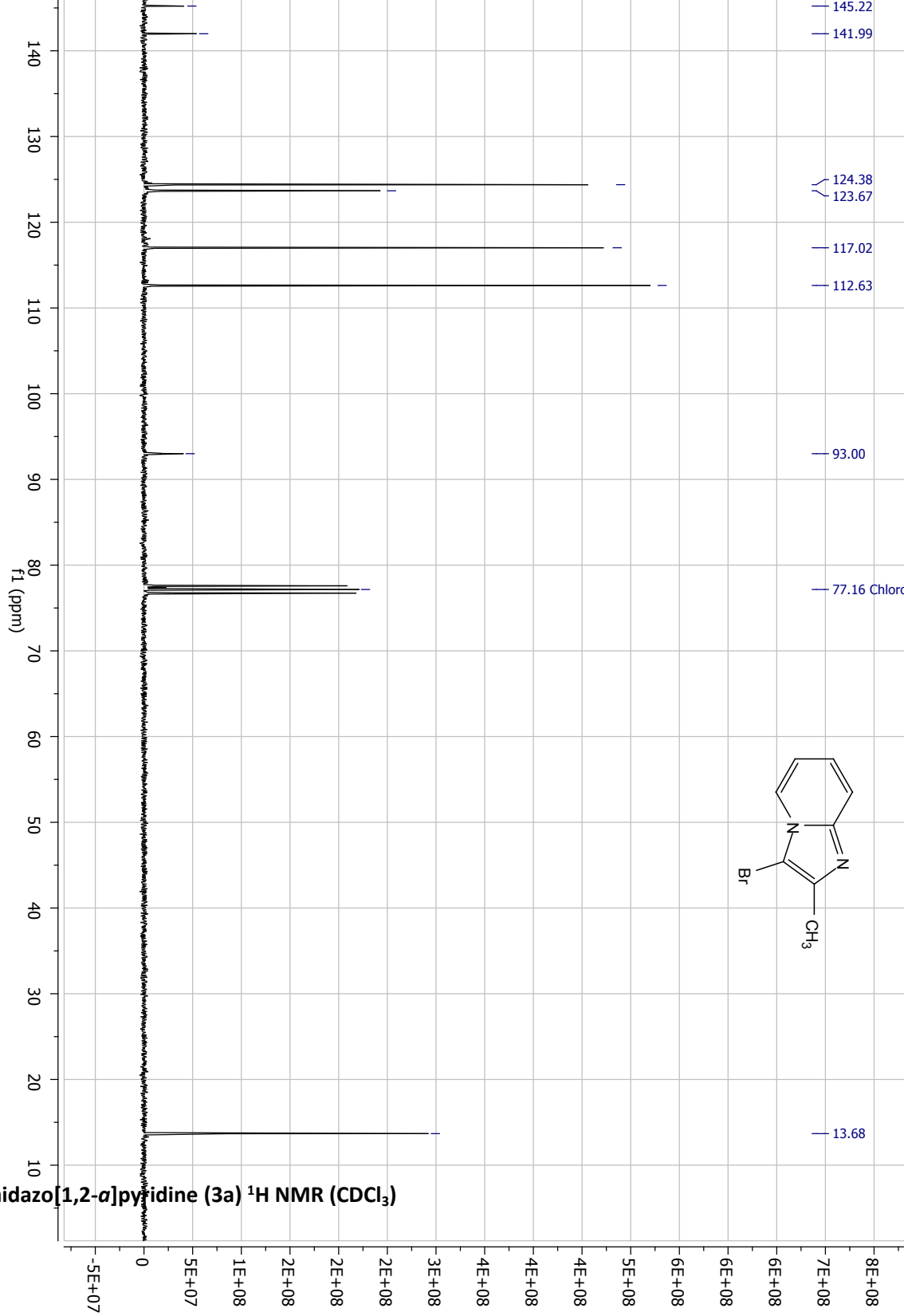
3-bromo-2-(thiophen-3-yl)imidazo[1,2-*a*]pyridine (2c) ^{13}C NMR ($CDCl_3$)



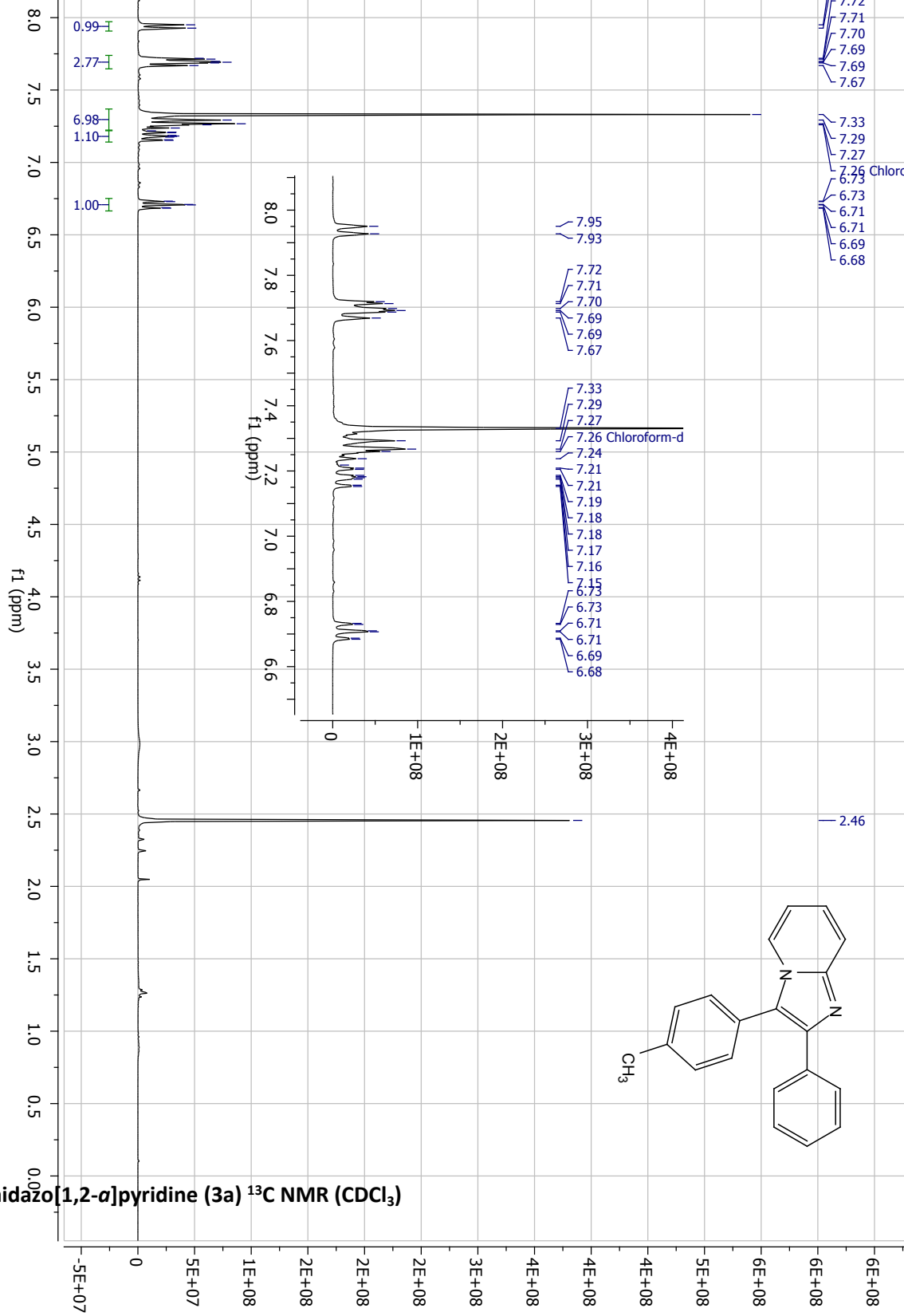
3-bromo-2-methylimidazo[1,2-*a*]pyridine (2d) ^{1}H NMR ($CDCl_3$)



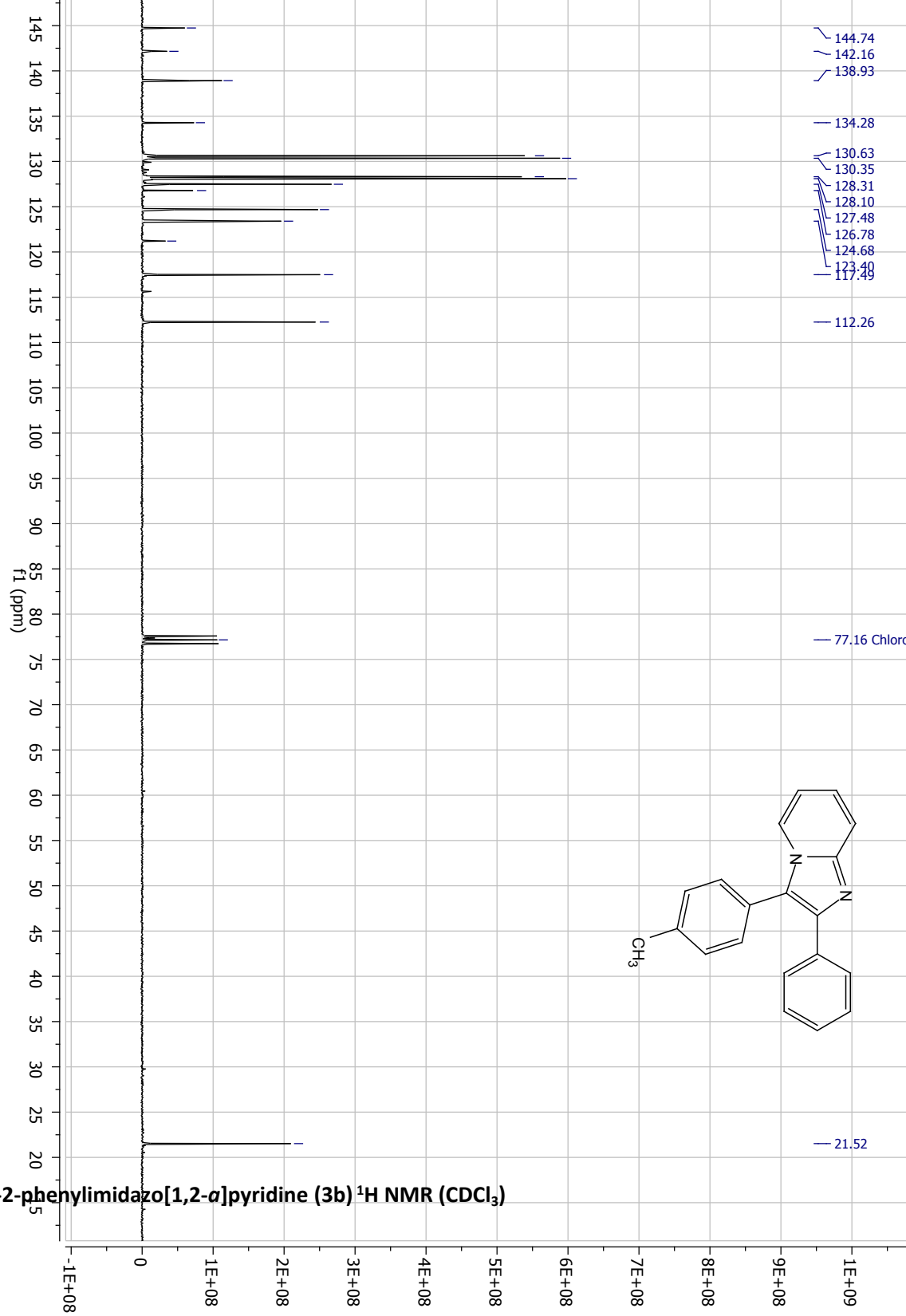
3-bromo-2-methylimidazo[1,2-*a*]pyridine (2d) ^{13}C NMR ($CDCl_3$)



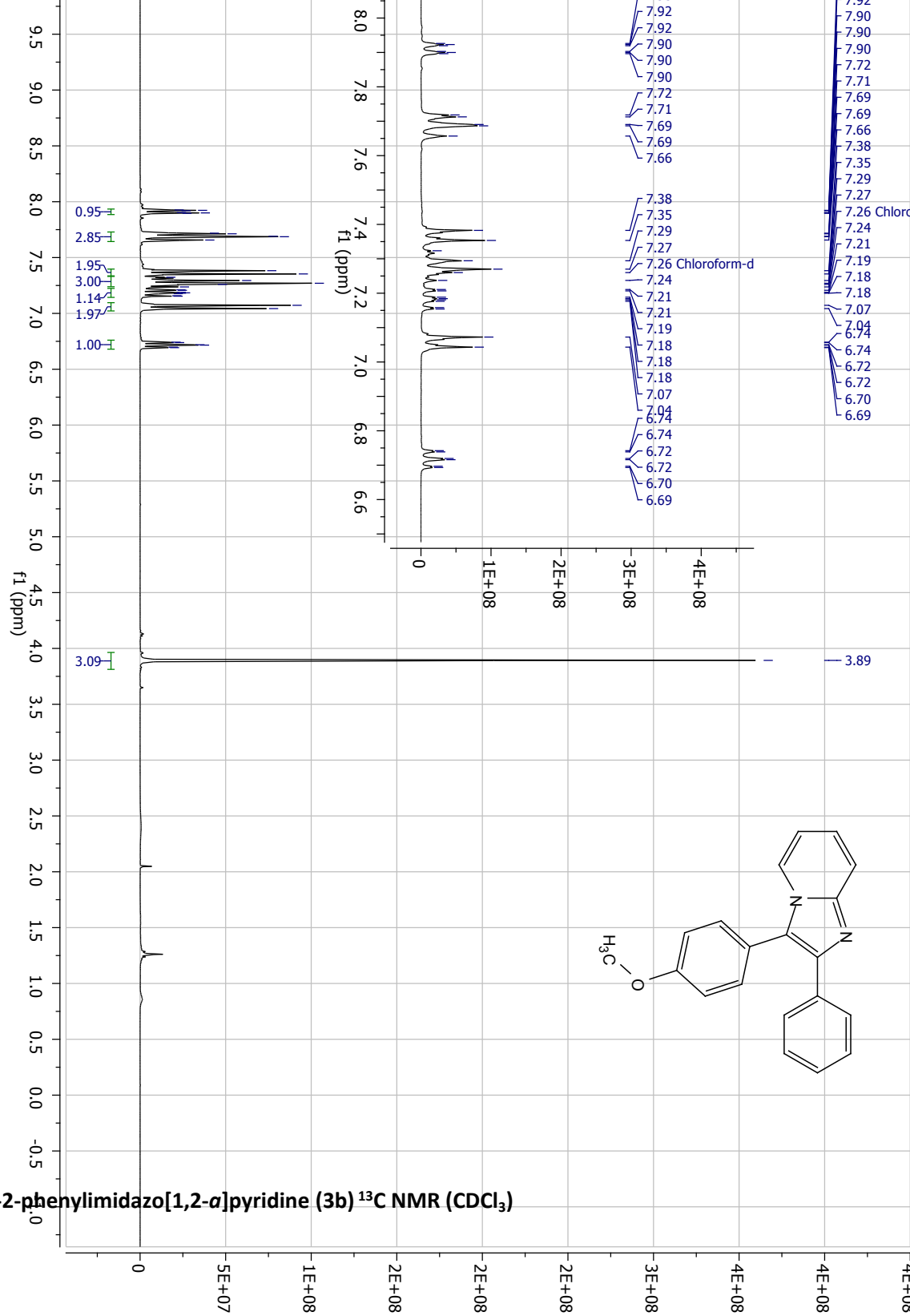
2-phenyl-3-(*p*-tolyl)imidazo[1,2-*a*]pyridine (3a) ^{1}H NMR ($CDCl_3$)



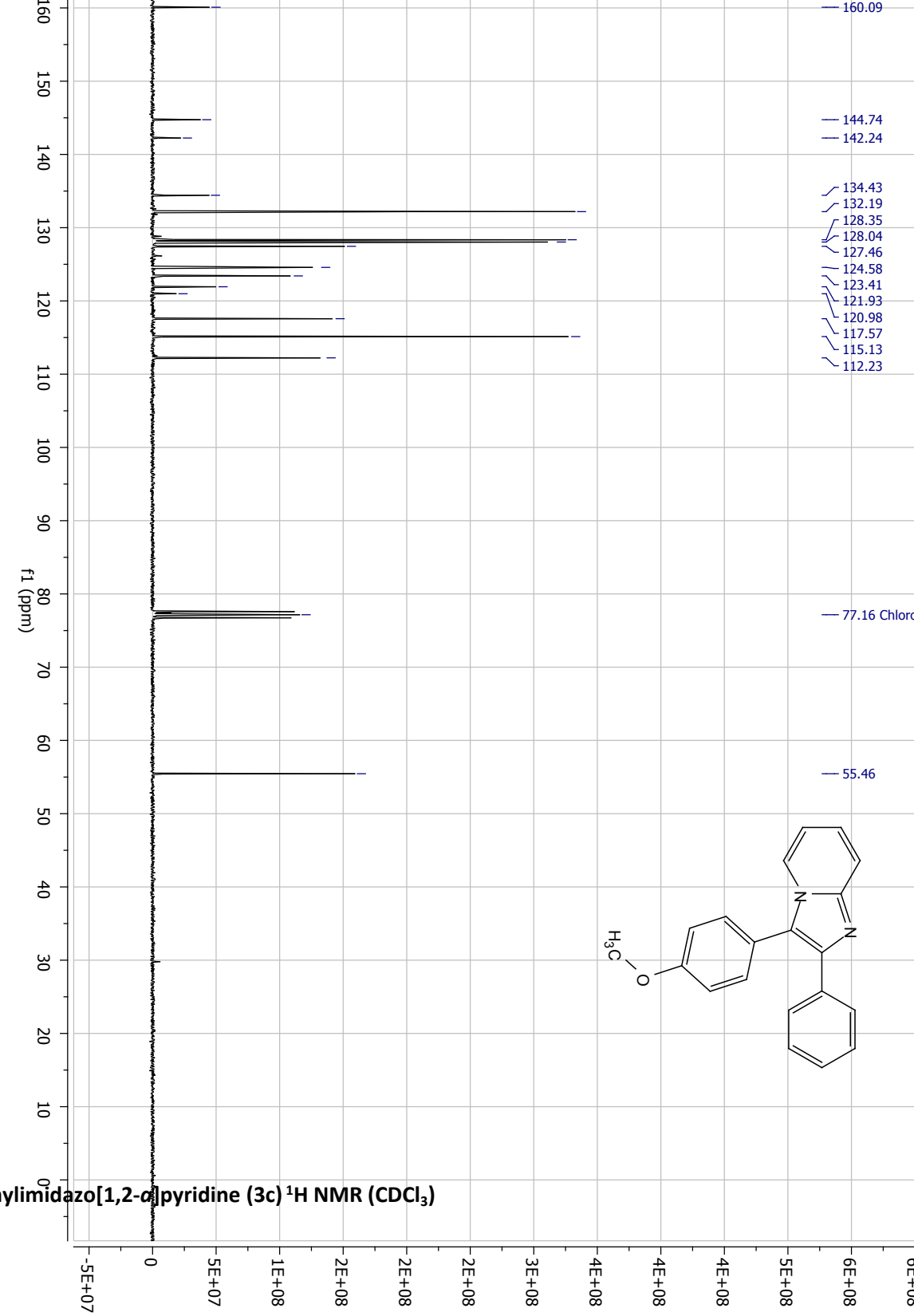
2-phenyl-3-(*p*-tolyl)imidazo[1,2-*a*]pyridine (3a) ^{13}C NMR ($CDCl_3$)



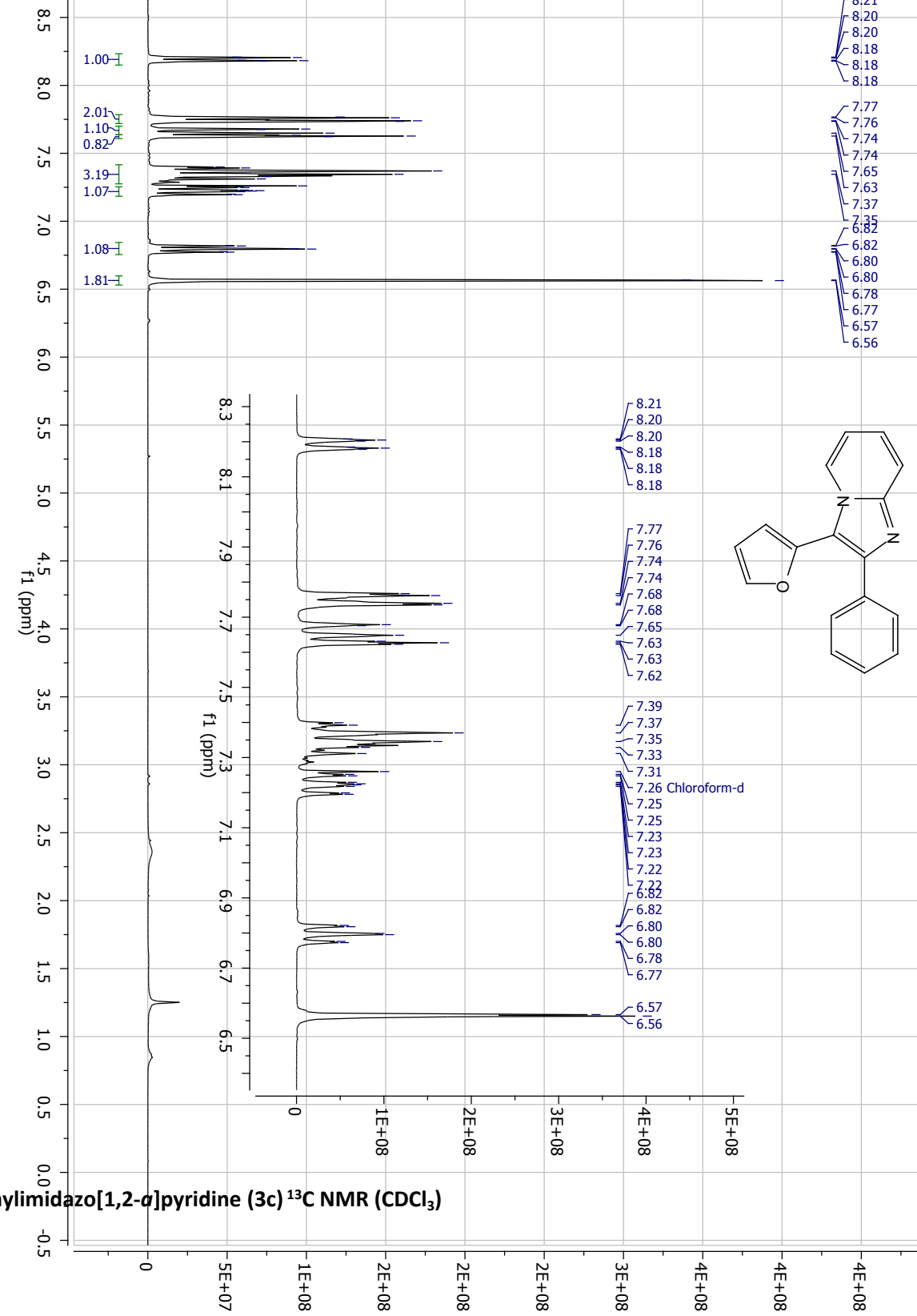
3-(4-methoxyphenyl)-2-phenylimidazo[1,2-*a*]pyridine (3b) ^{1}H NMR ($CDCl_3$)



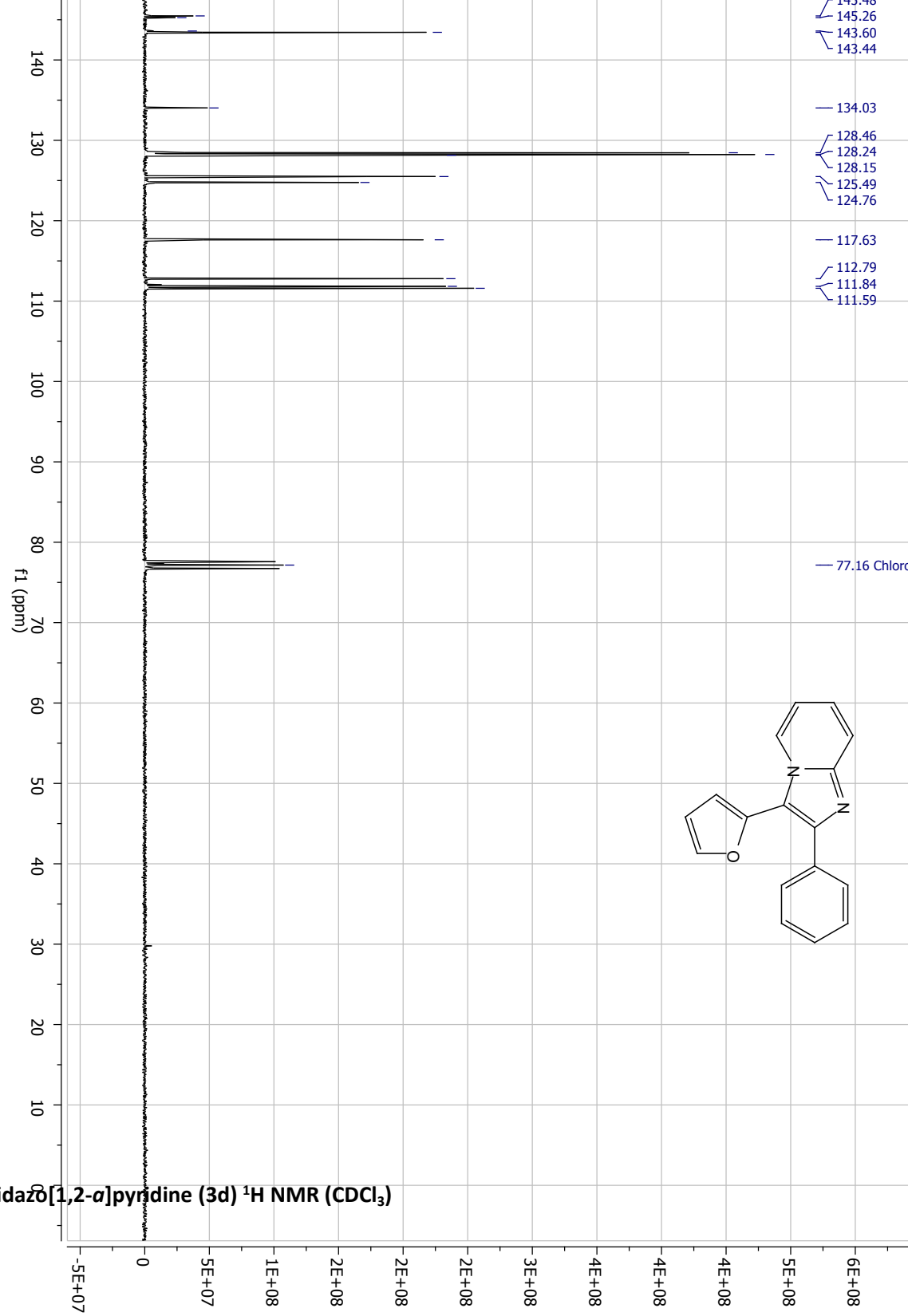
3-(4-methoxyphenyl)-2-phenylimidazo[1,2-*a*]pyridine (3b) ^{13}C NMR ($CDCl_3$)



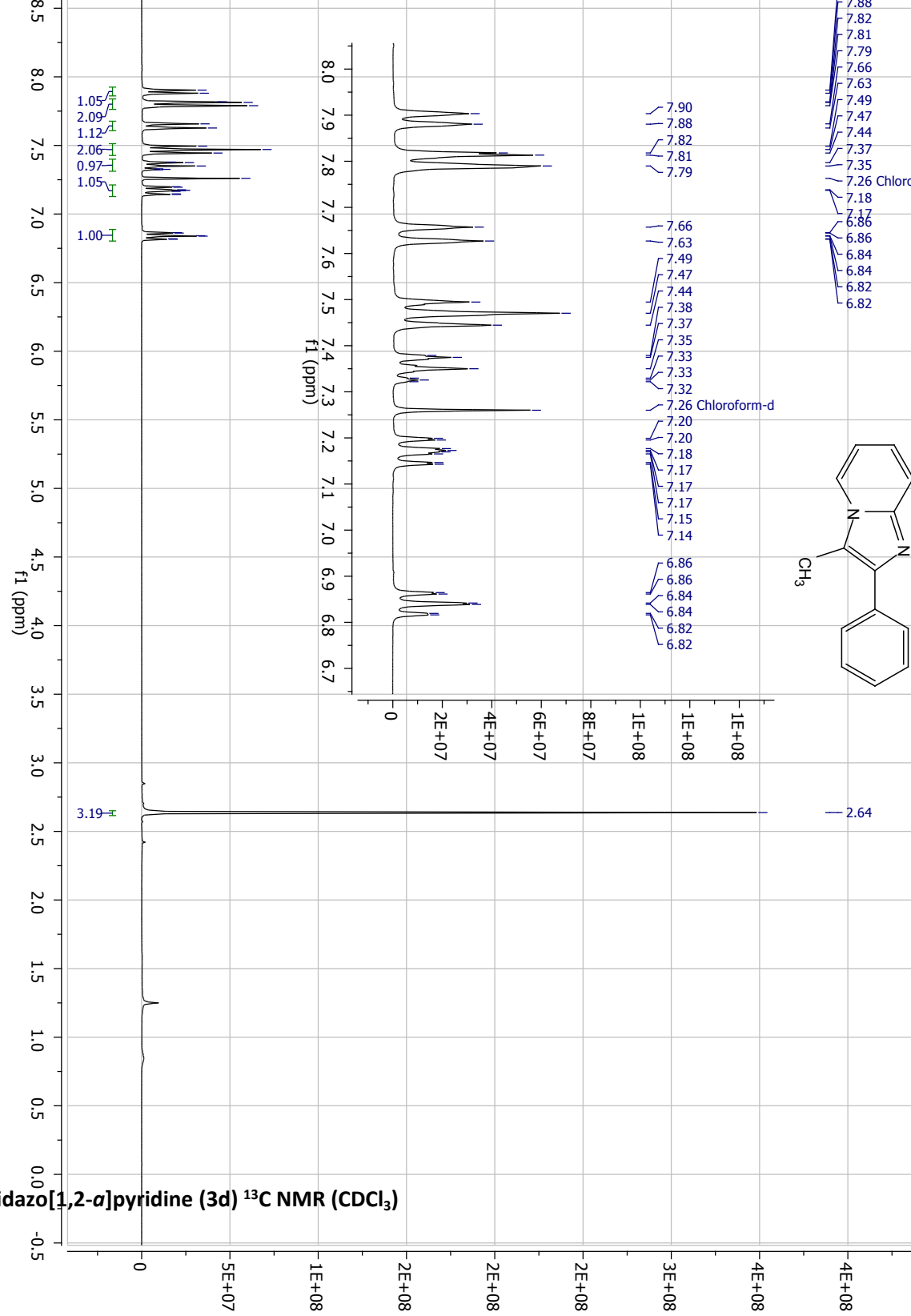
3-(furan-2-yl)-2-phenylimidazo[1,2-*a*]pyridine (3c) ^{1}H NMR ($CDCl_3$)



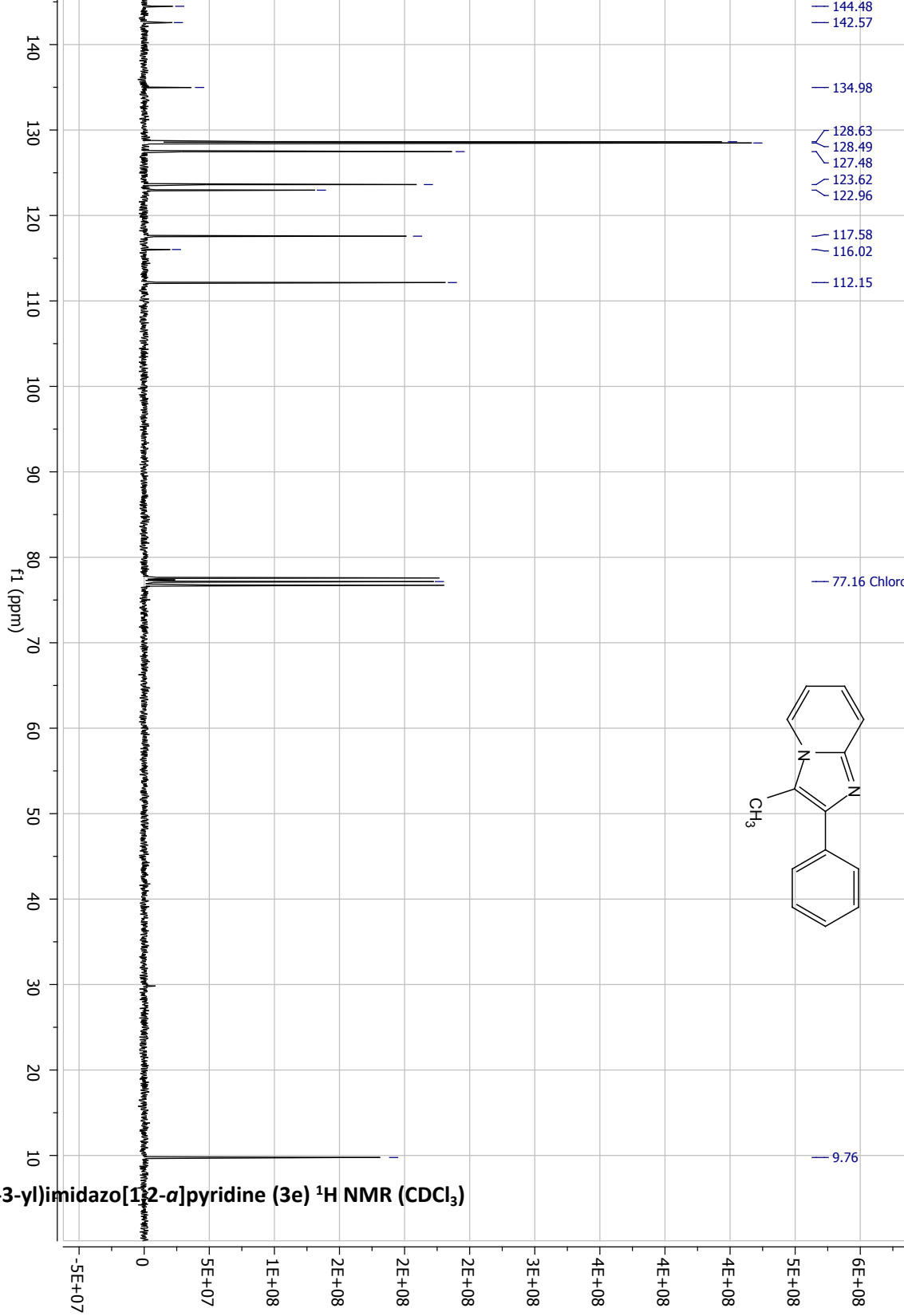
3-(furan-2-yl)-2-phenylimidazo[1,2-*a*]pyridine (3c) ^{13}C NMR ($CDCl_3$)



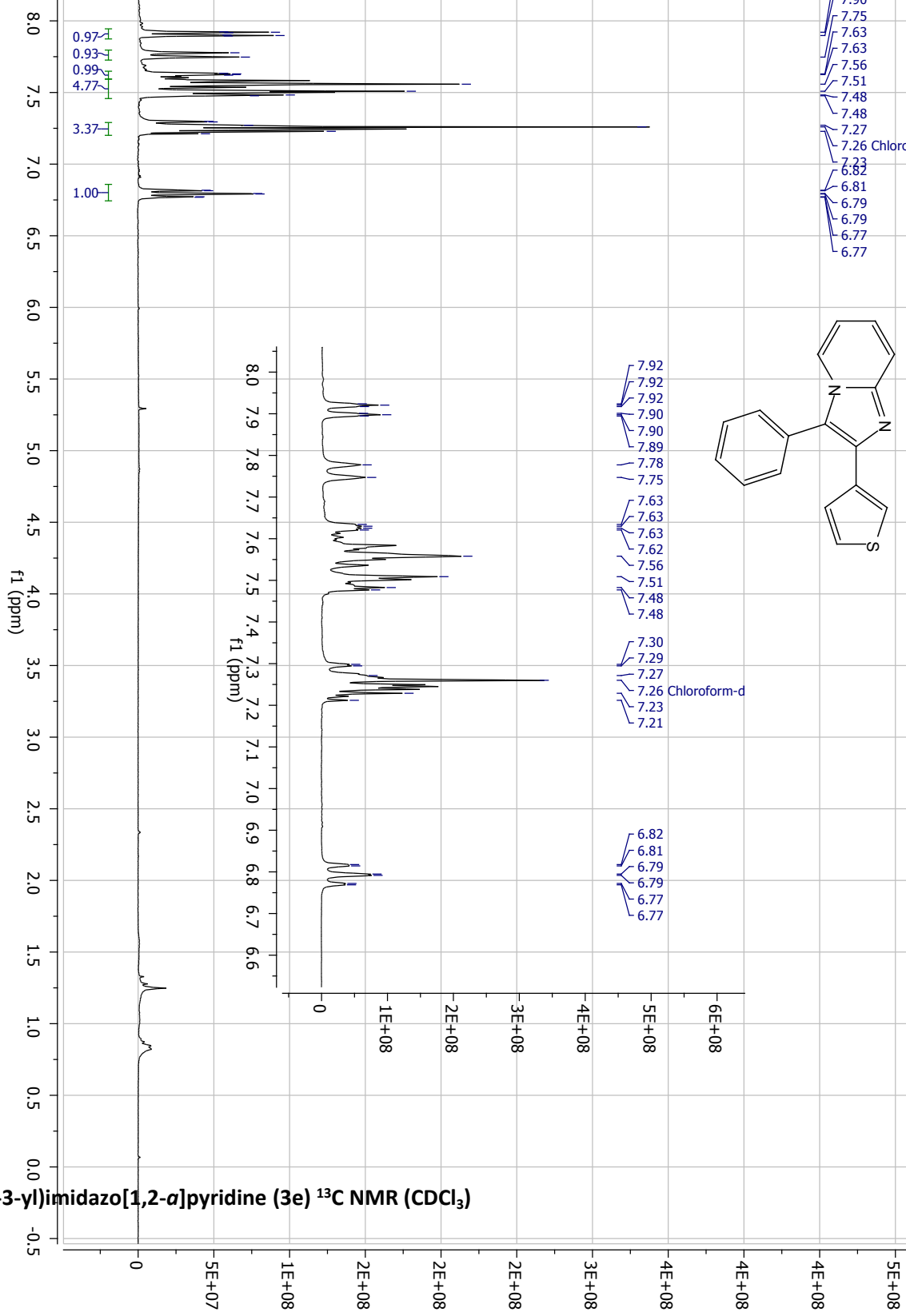
3-methyl-2-phenylimidazo[1,2-*a*]pyridine (3d) ^{1}H NMR ($CDCl_3$)



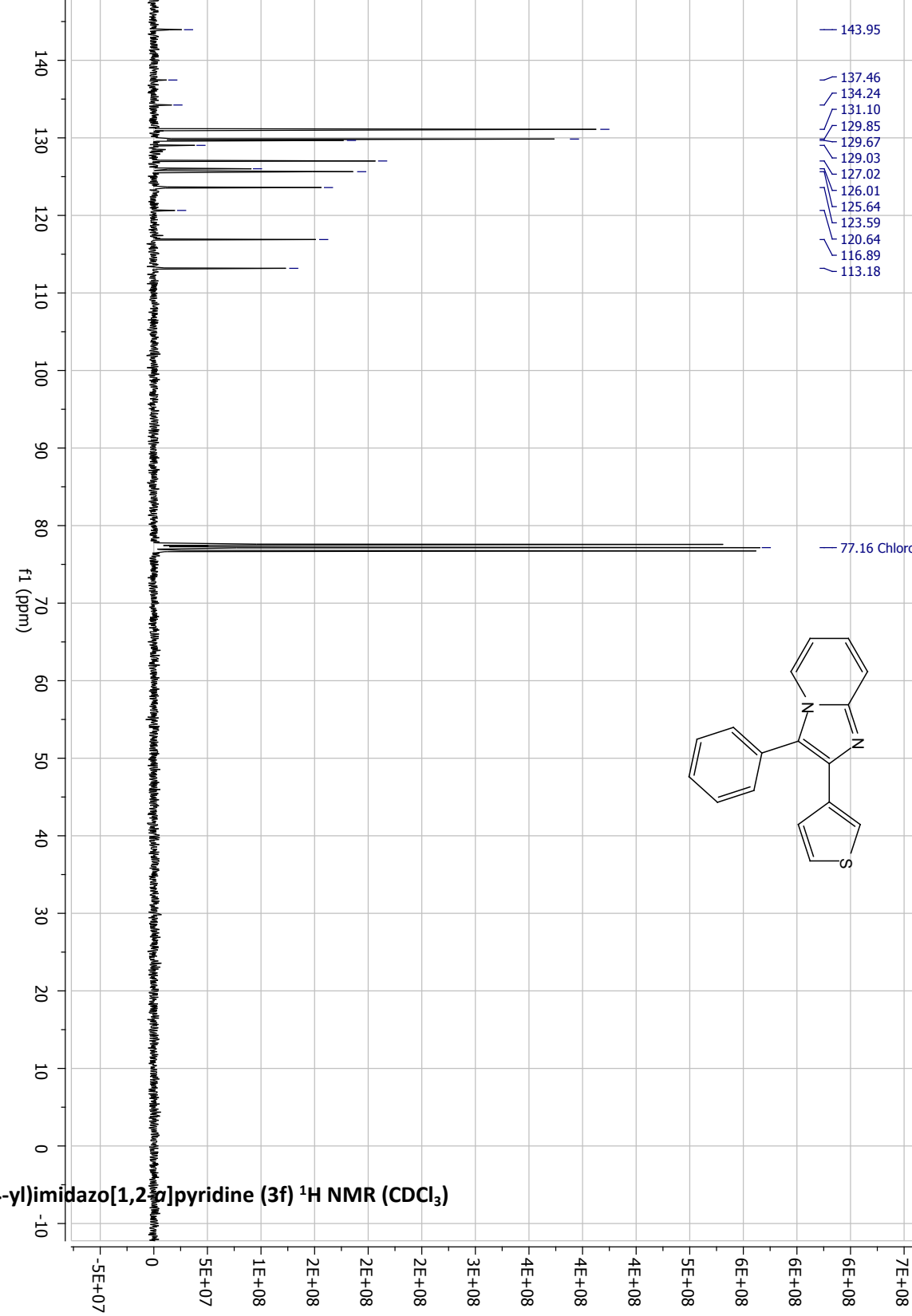
3-methyl-2-phenylimidazo[1,2-*a*]pyridine (3d) ^{13}C NMR ($CDCl_3$)



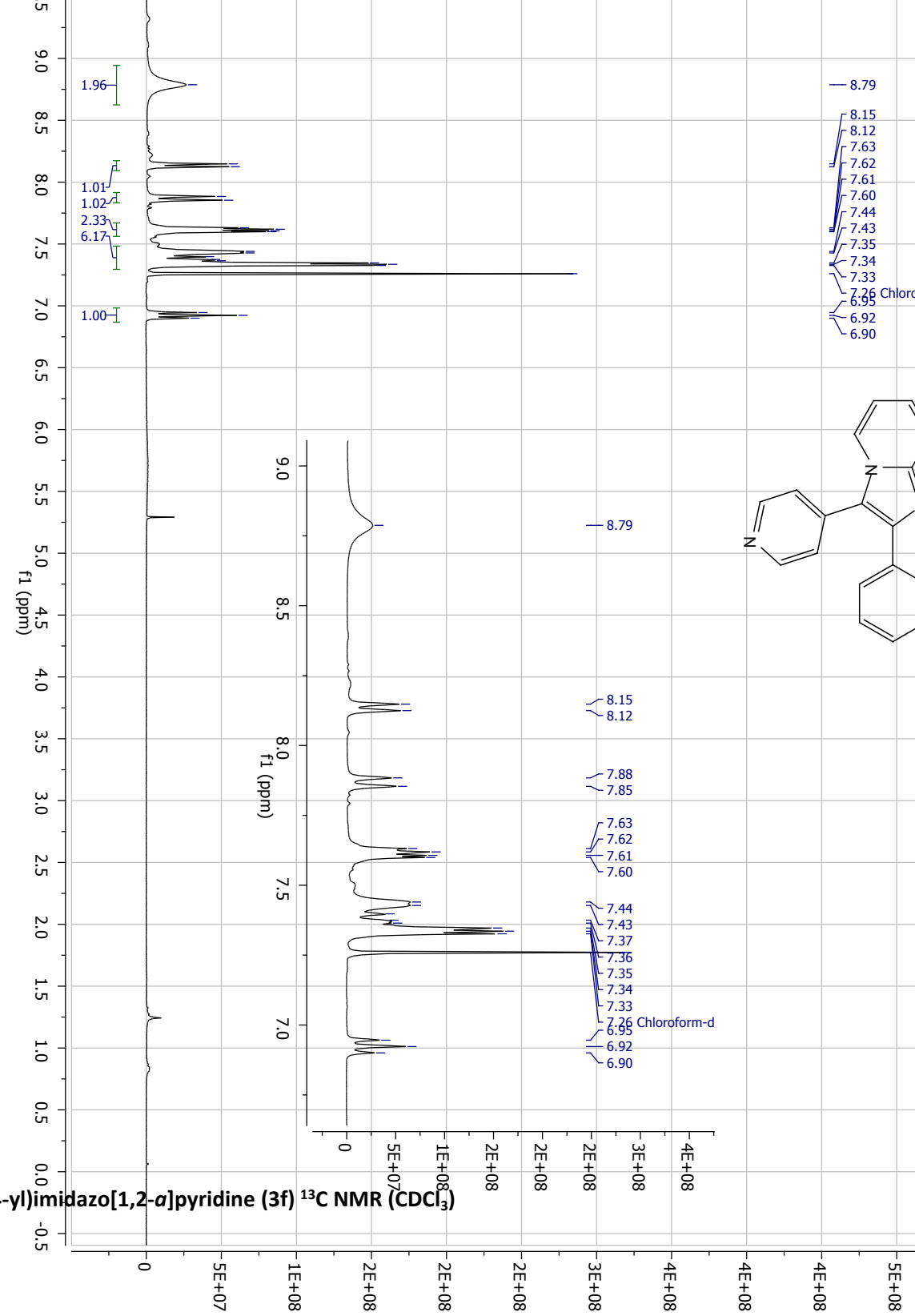
3-phenyl-2-(thiophen-3-yl)imidazo[1,2-*a*]pyridine (3e) ^{1}H NMR ($CDCl_3$)



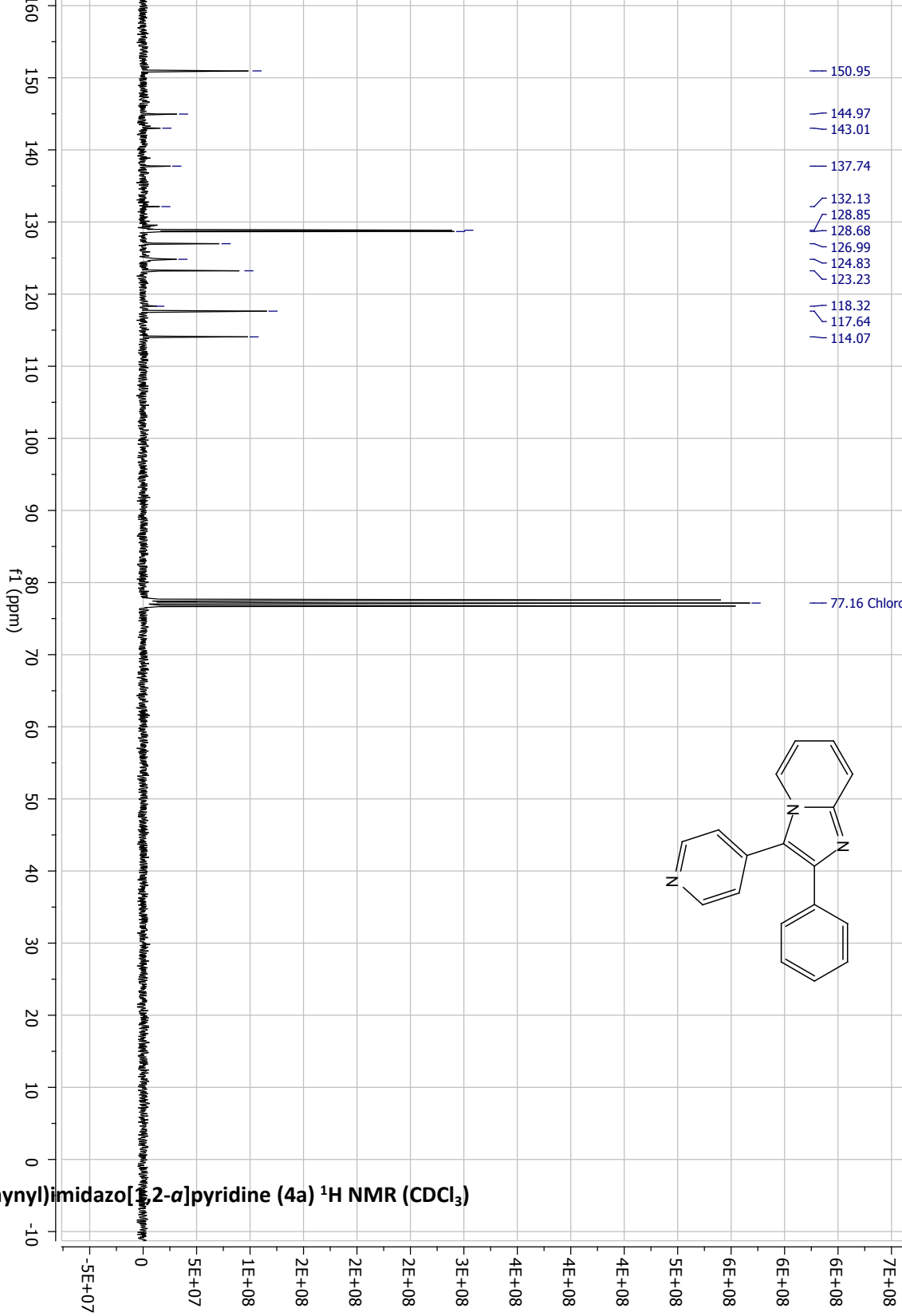
3-phenyl-2-(thiophen-3-yl)imidazo[1,2-*a*]pyridine (3e) ^{13}C NMR ($CDCl_3$)



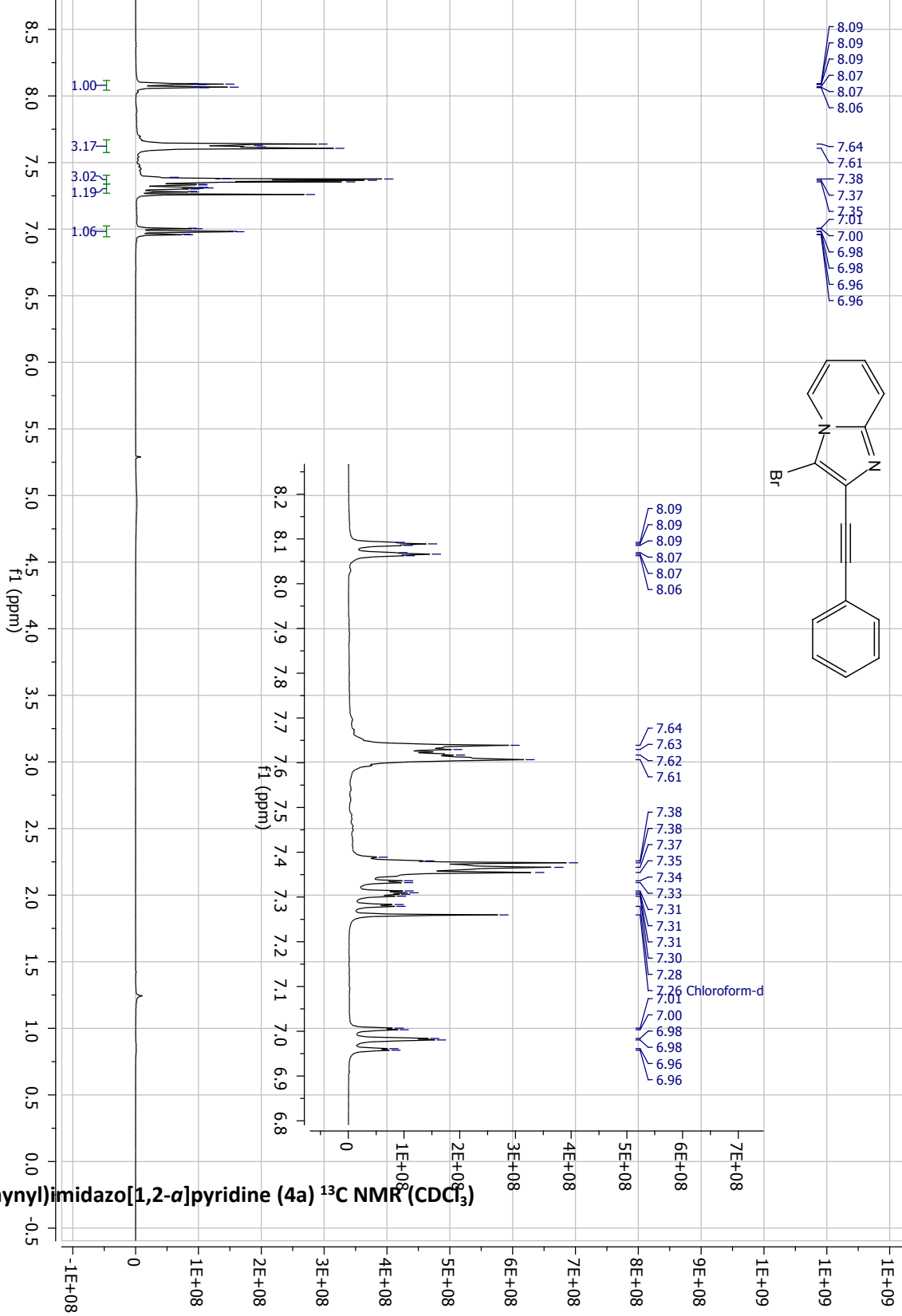
2-phenyl-3-(pyridin-4-yl)imidazo[1,2-*a*]pyridine (3f) ^{1}H NMR ($CDCl_3$)



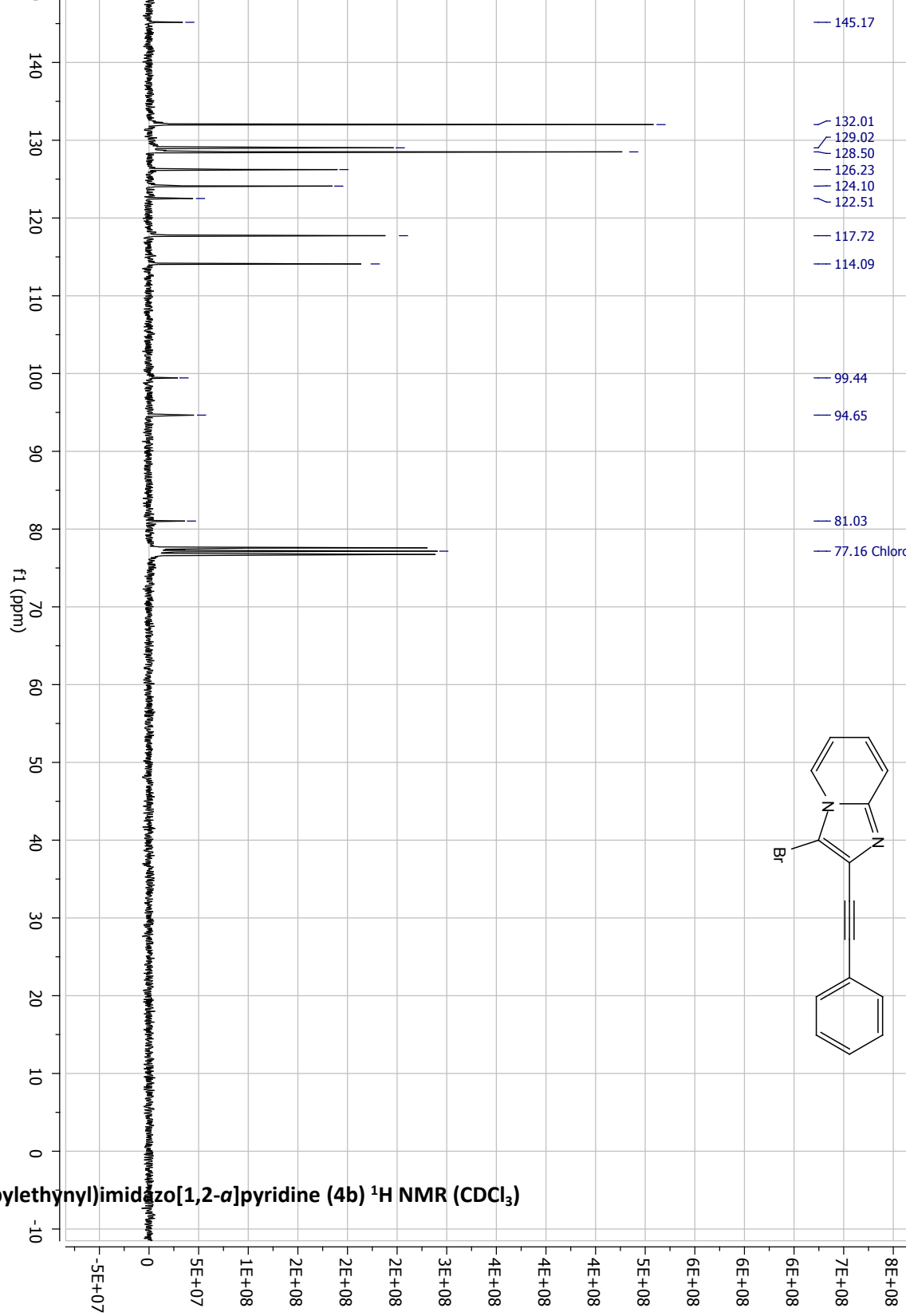
2-phenyl-3-(pyridin-4-yl)imidazo[1,2-*a*]pyridine (3f) ^{13}C NMR ($CDCl_3$)



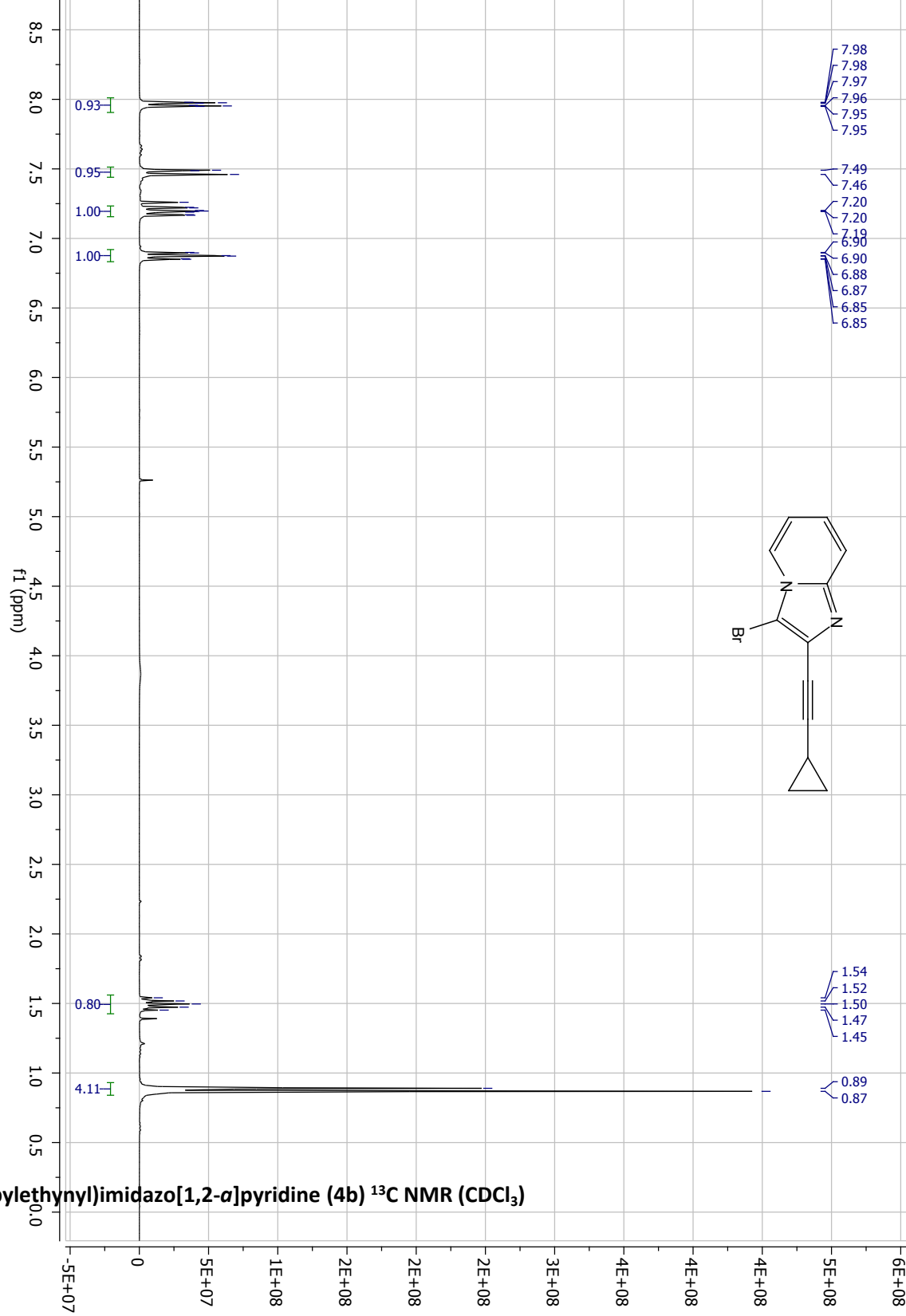
3-bromo-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (4a) ^{1}H NMR ($CDCl_3$)



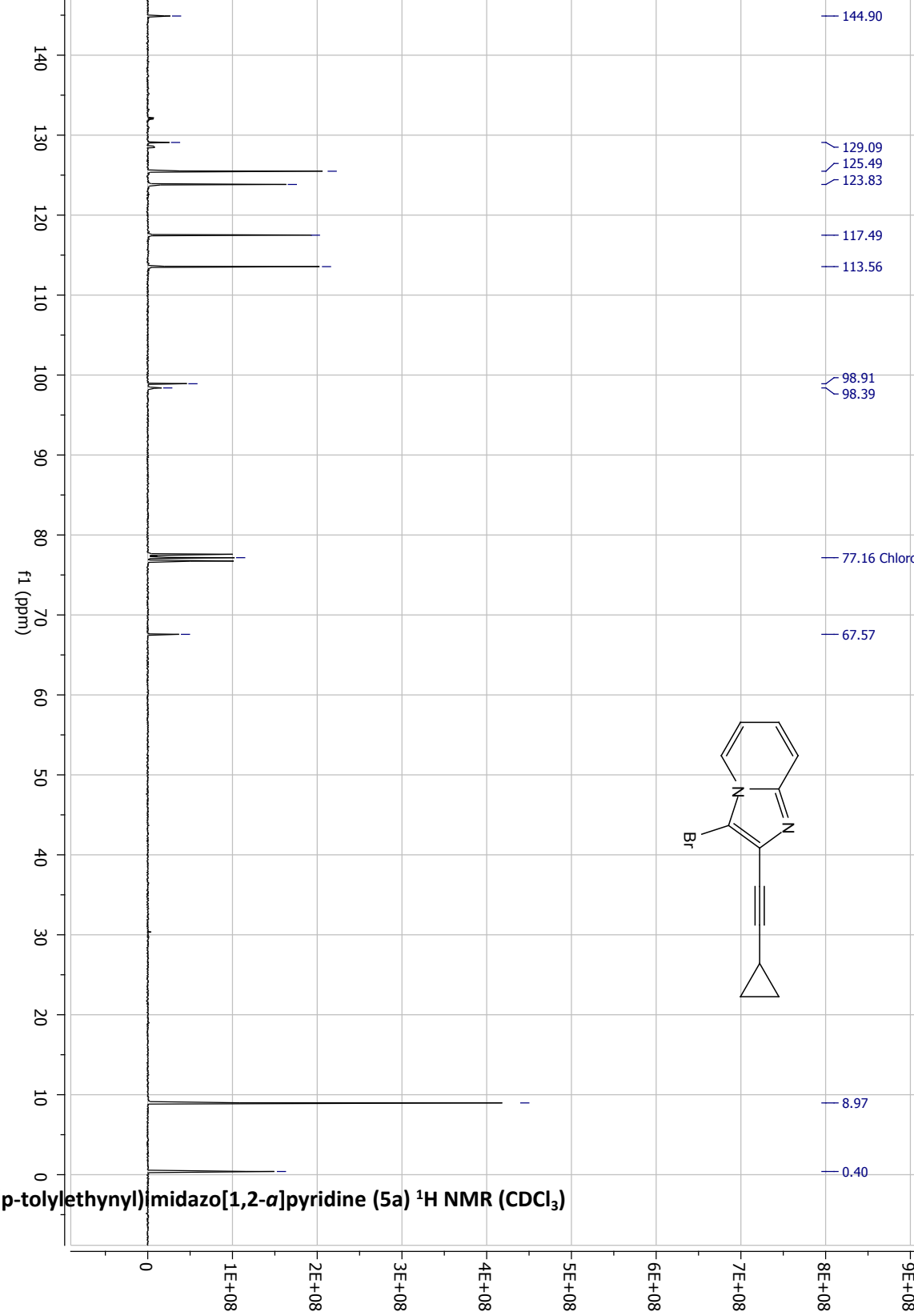
3-bromo-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (4a) ^{13}C NMR (CDCl$_3$)



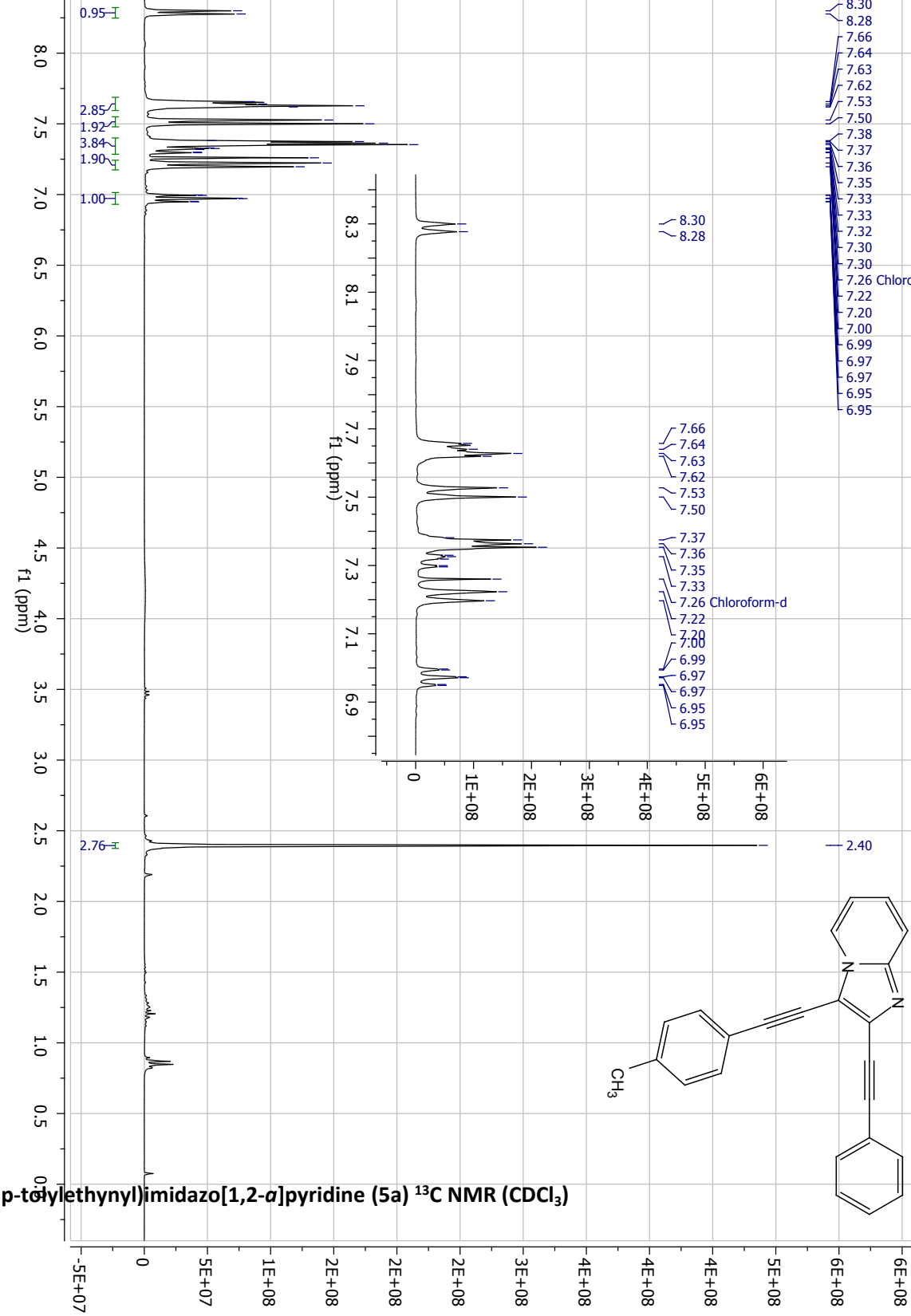
3-bromo-2-(cyclopropylethynyl)imidazo[1,2-*a*]pyridine (4b) ^{1}H NMR ($CDCl_3$)



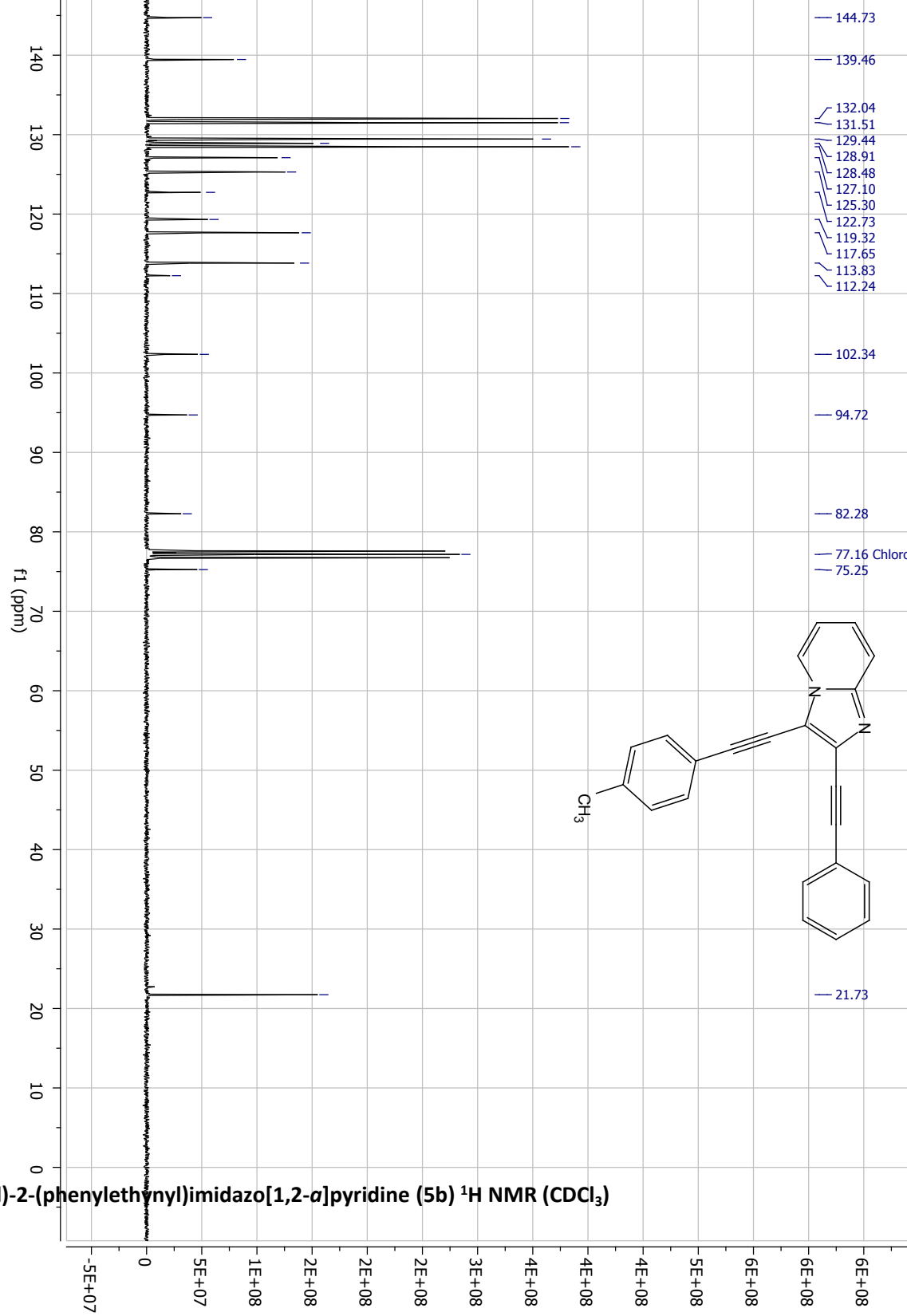
3-bromo-2-(cyclopropylethynyl)imidazo[1,2-*a*]pyridine (4b) ^{13}C NMR ($CDCl_3$)



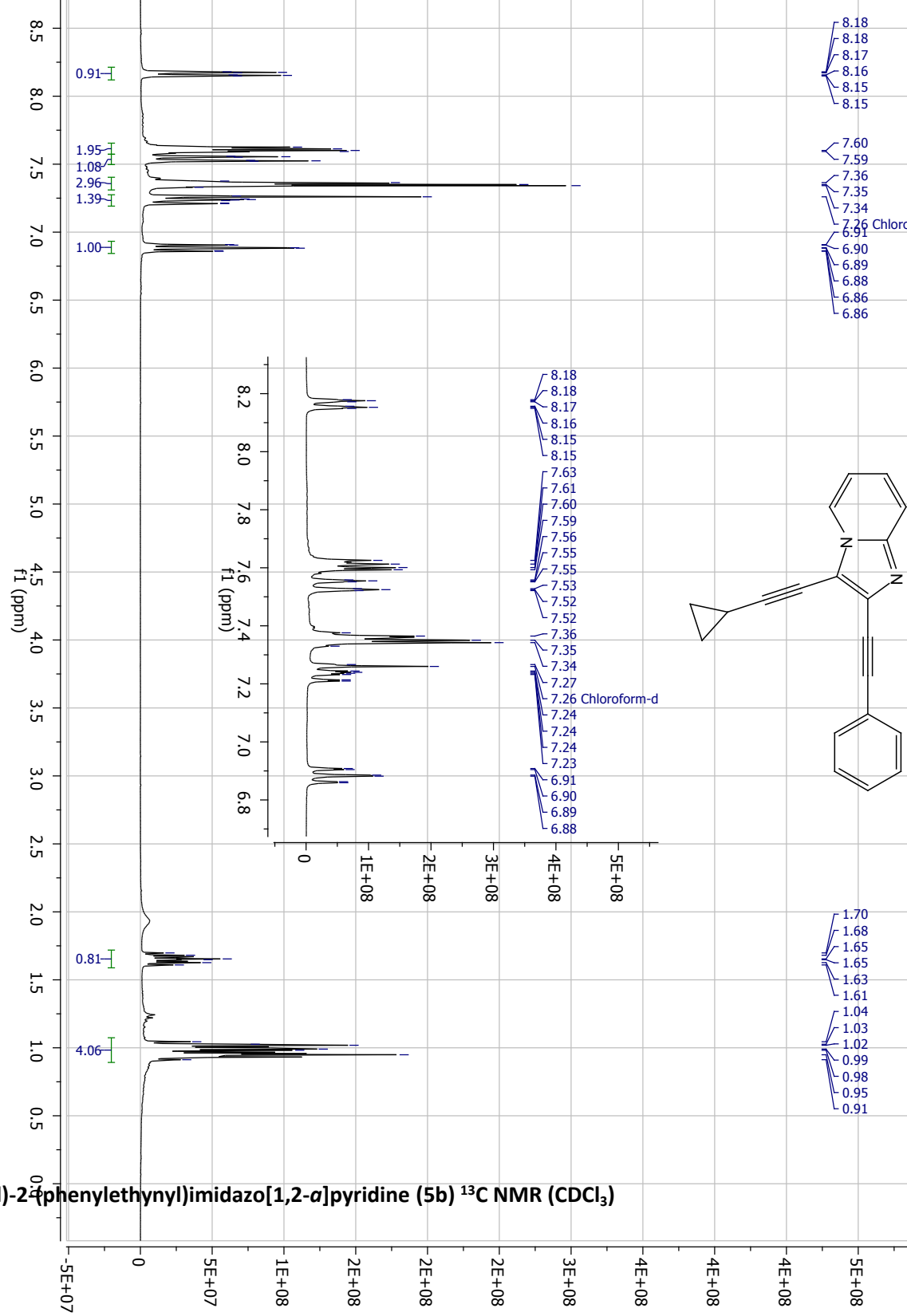
2-(phenylethynyl)-3-(p-tolylethynyl)imidazo[1,2-*a*]pyridine (5a) ^{1}H NMR ($CDCl_3$)



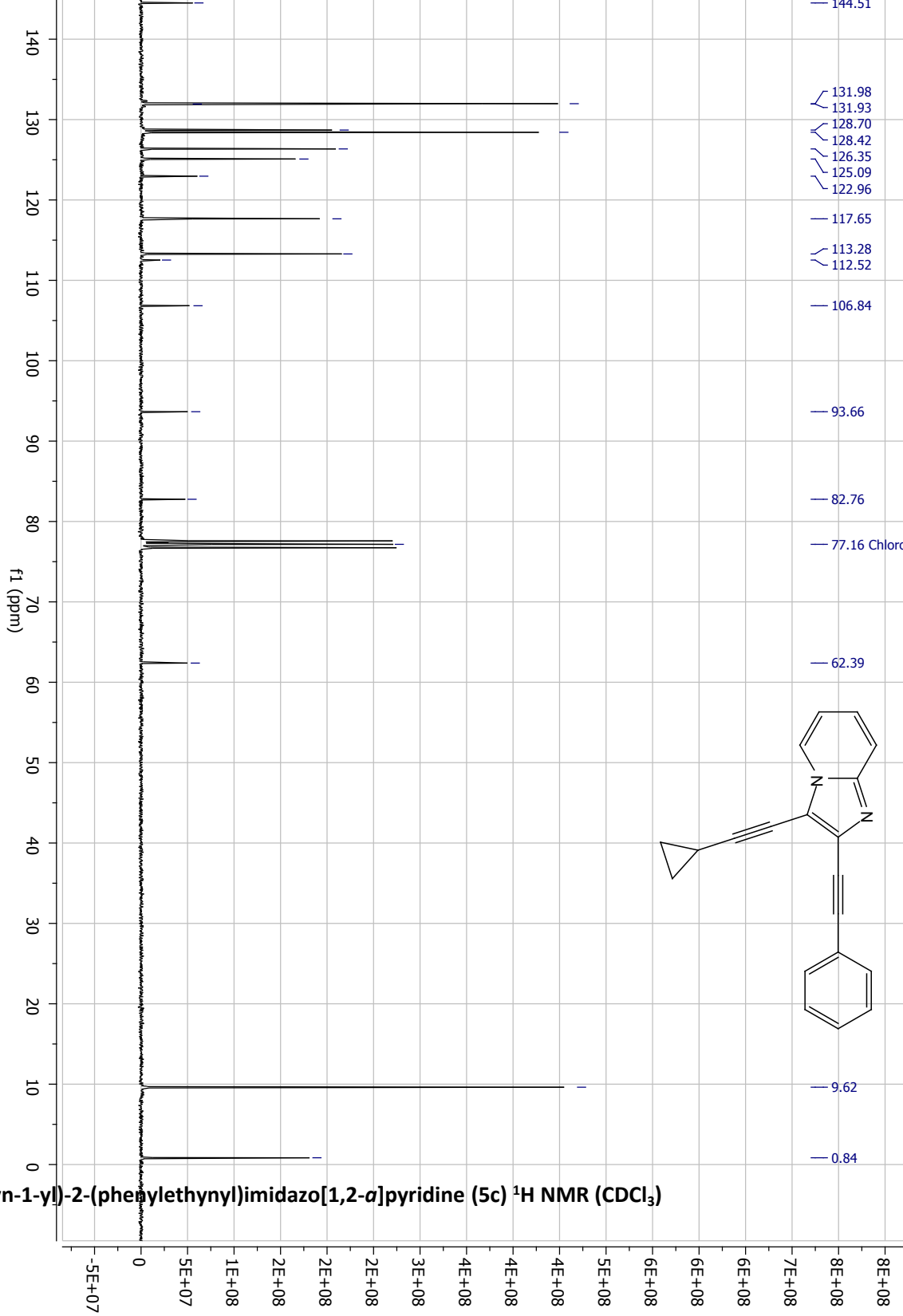
2-(phenylethynyl)-3-(p-tolylethynyl)imidazo[1,2-*a*]pyridine (5a) ^{13}C NMR ($CDCl_3$)



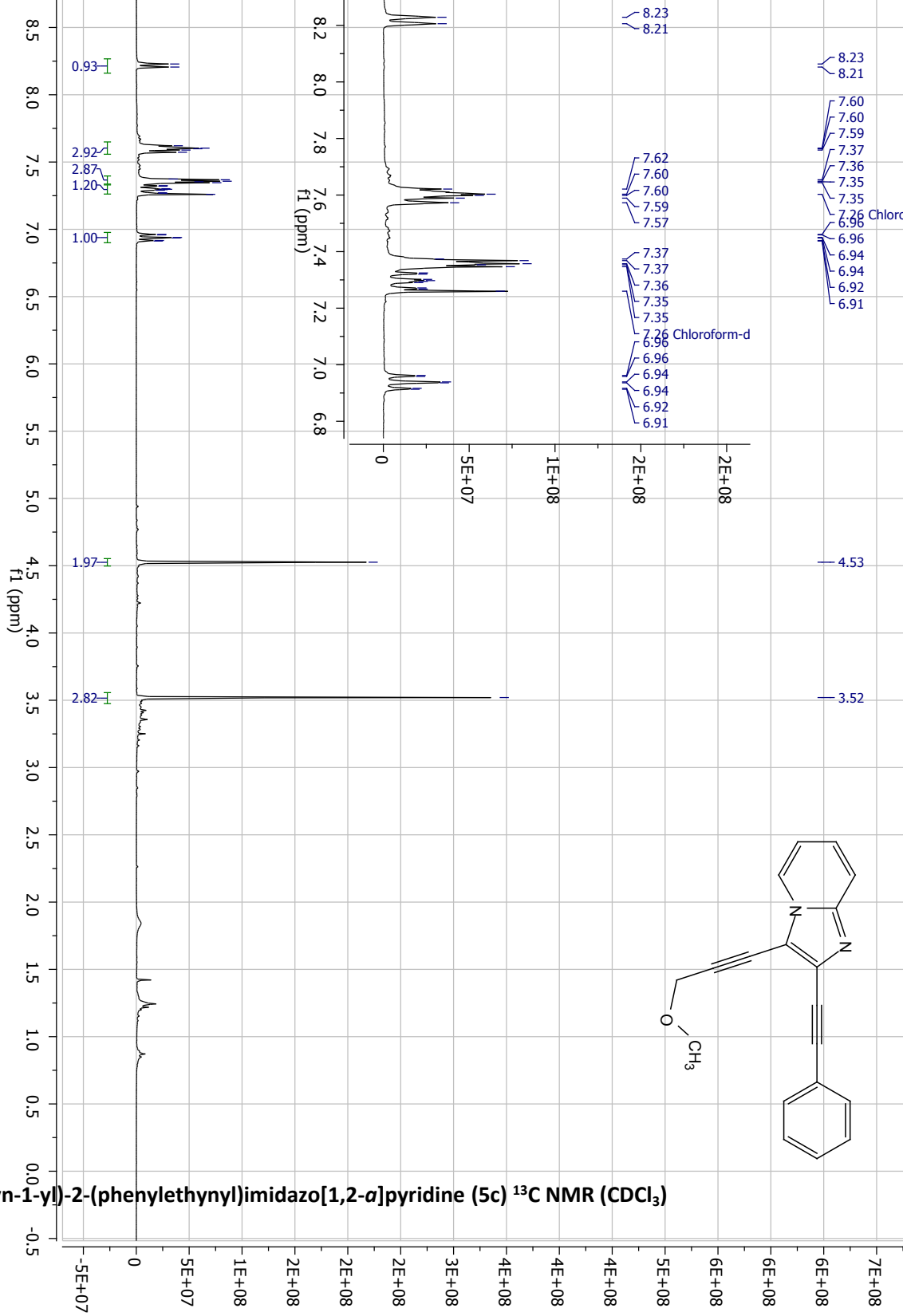
3-(cyclopropylethynyl)-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (5b) ^{1}H NMR ($CDCl_3$)



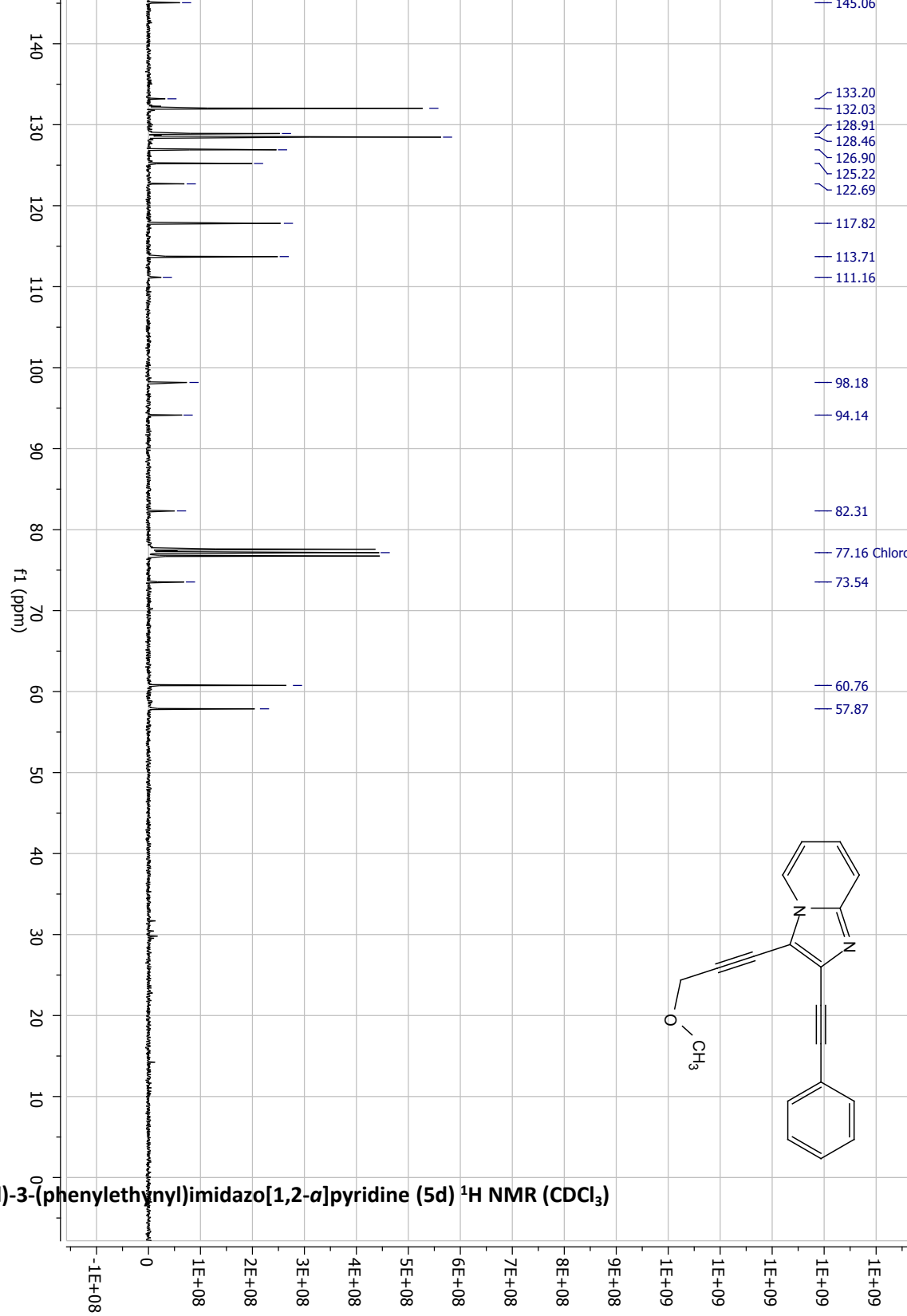
3-(cyclopropylethynyl)-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (5b) ^{13}C NMR ($CDCl_3$)



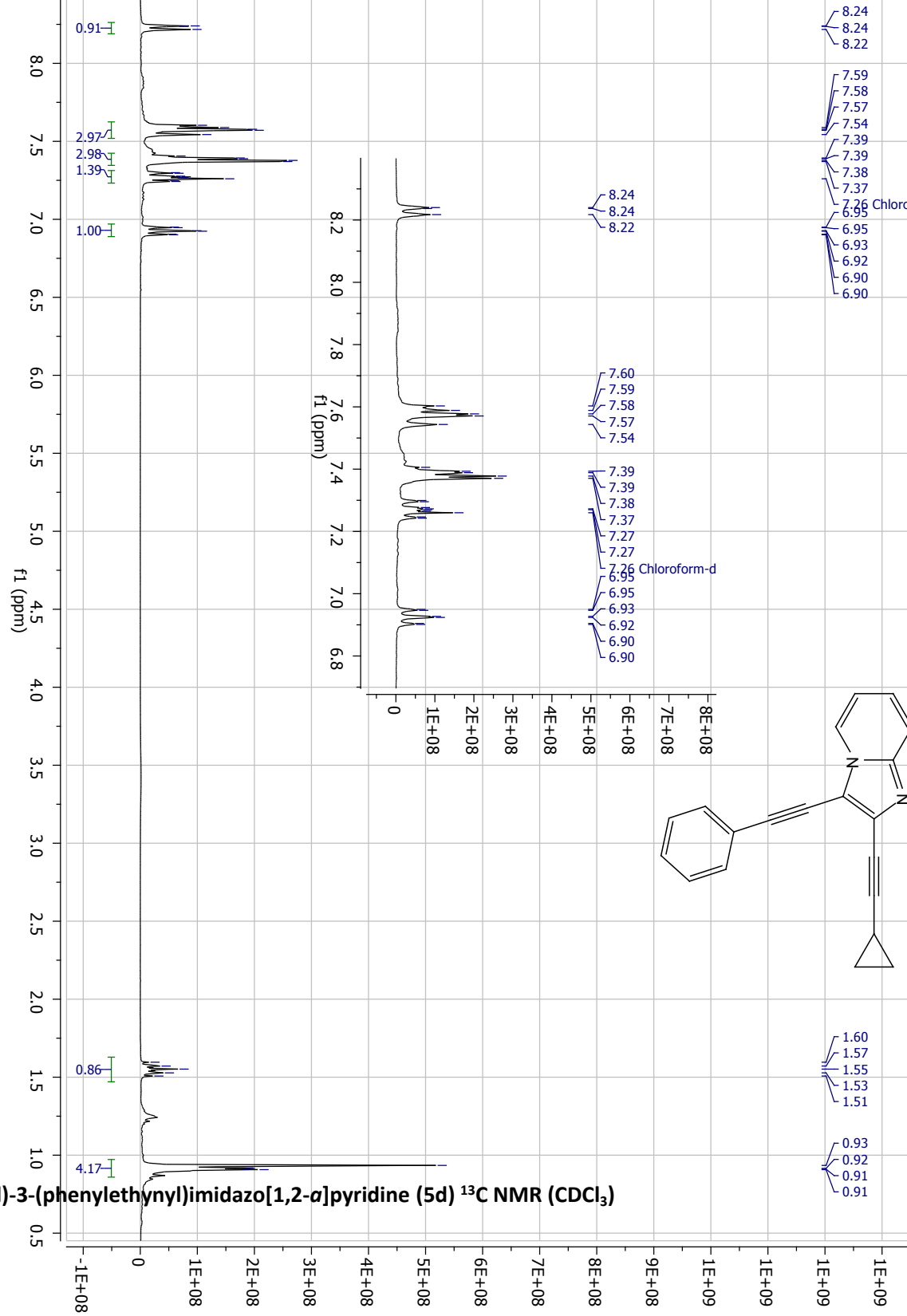
3-(3-methoxyprop-1-yn-1-yl)-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (5c) ^{1}H NMR ($CDCl_3$)



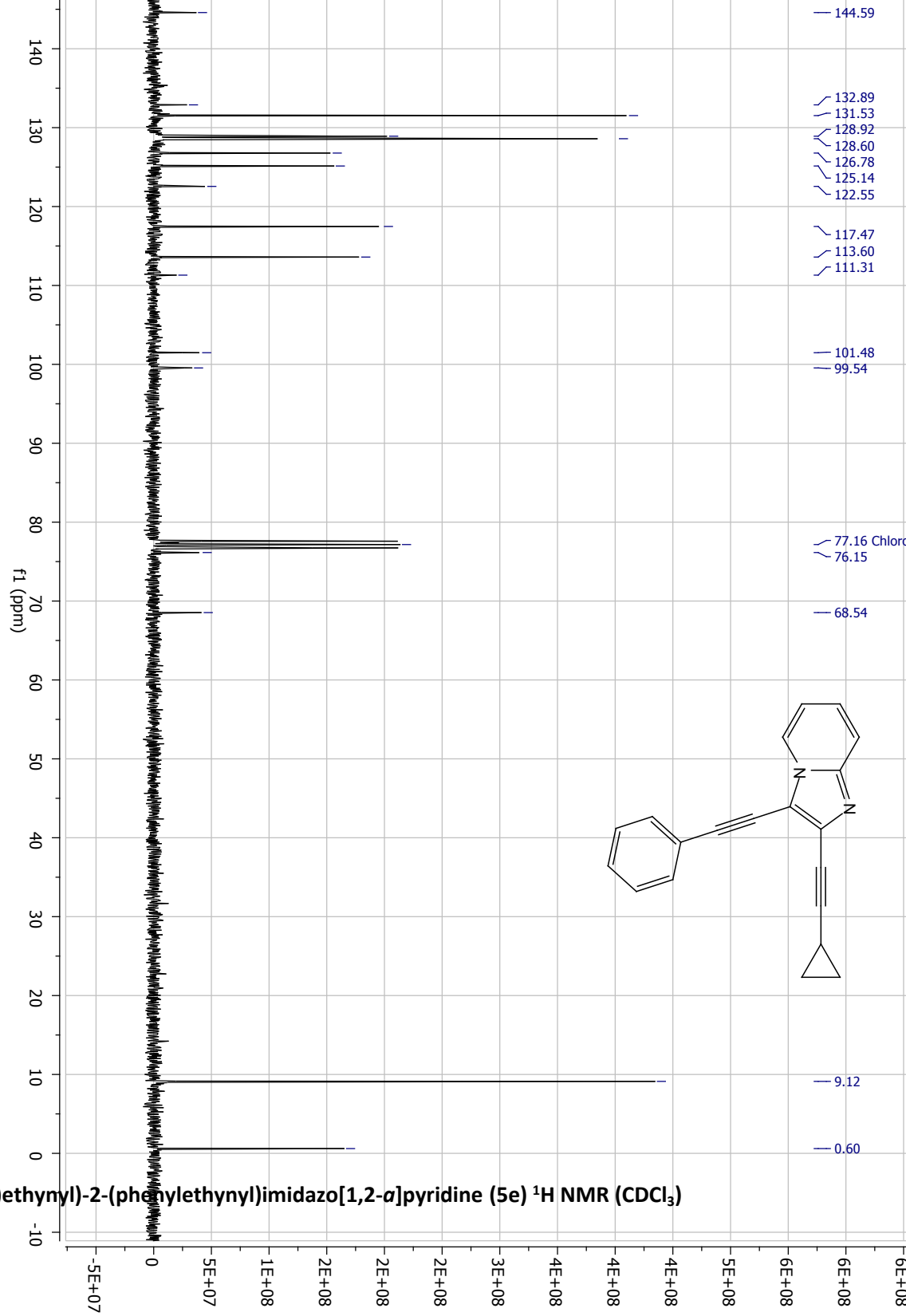
3-(3-methoxyprop-1-yn-1-yl)-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (5c) ^{13}C NMR ($CDCl_3$)



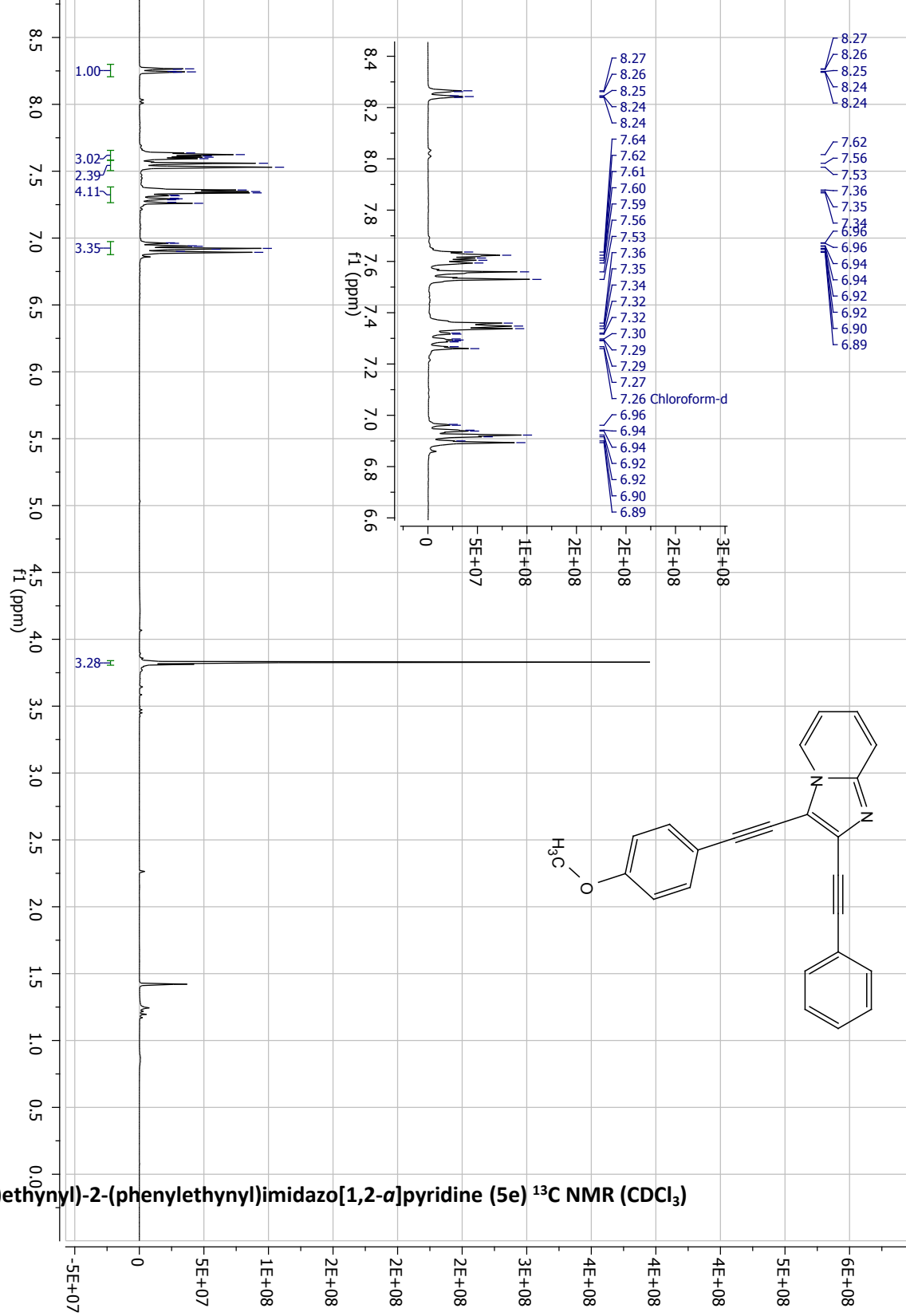
2-(cyclopropylethynyl)-3-(phenylethynyl)imidazo[1,2-*a*]pyridine (5d) ^{1}H NMR ($CDCl_3$)



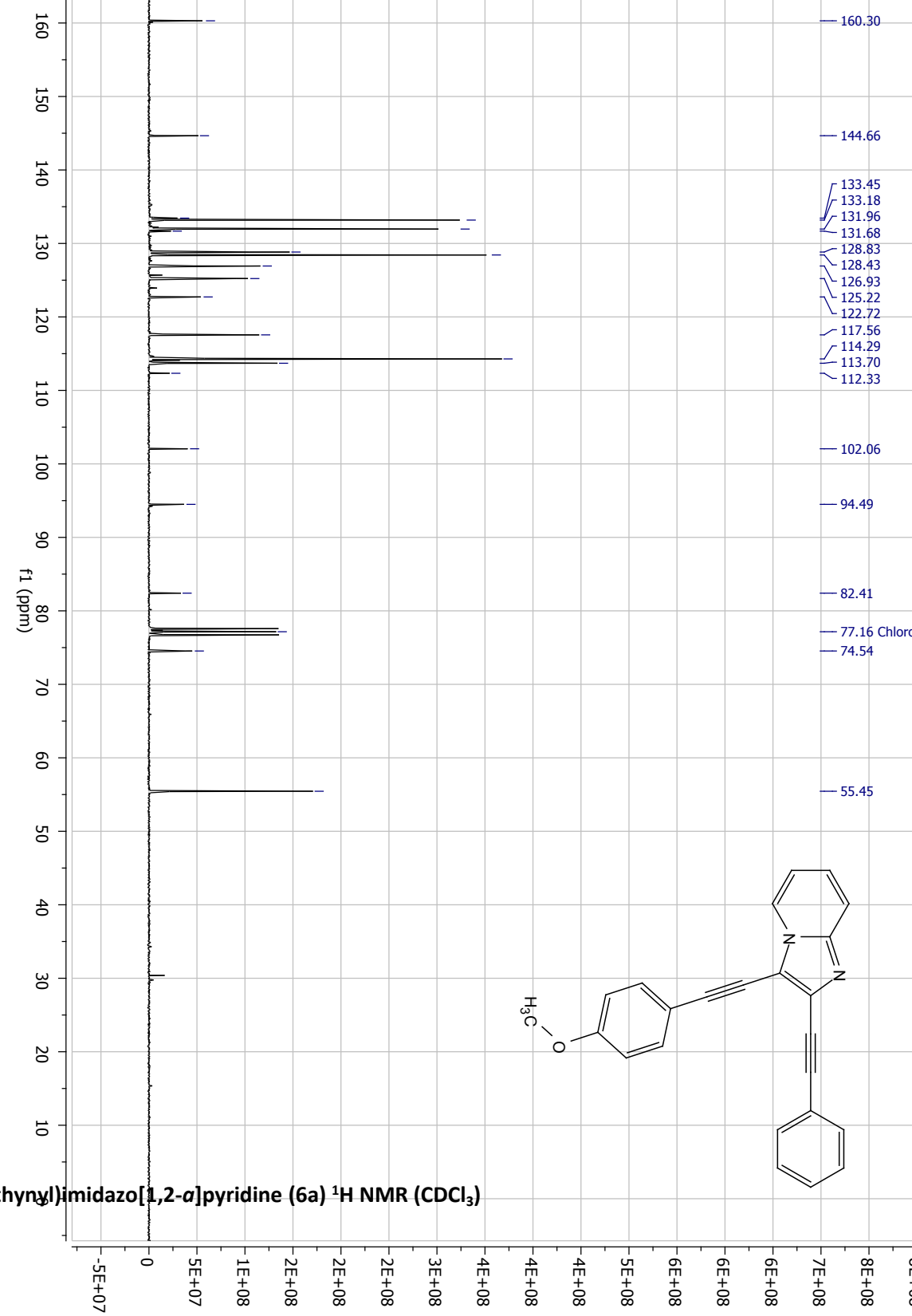
2-(cyclopropylethynyl)-3-(phenylethynyl)imidazo[1,2-*a*]pyridine (5d) ^{13}C NMR ($CDCl_3$)



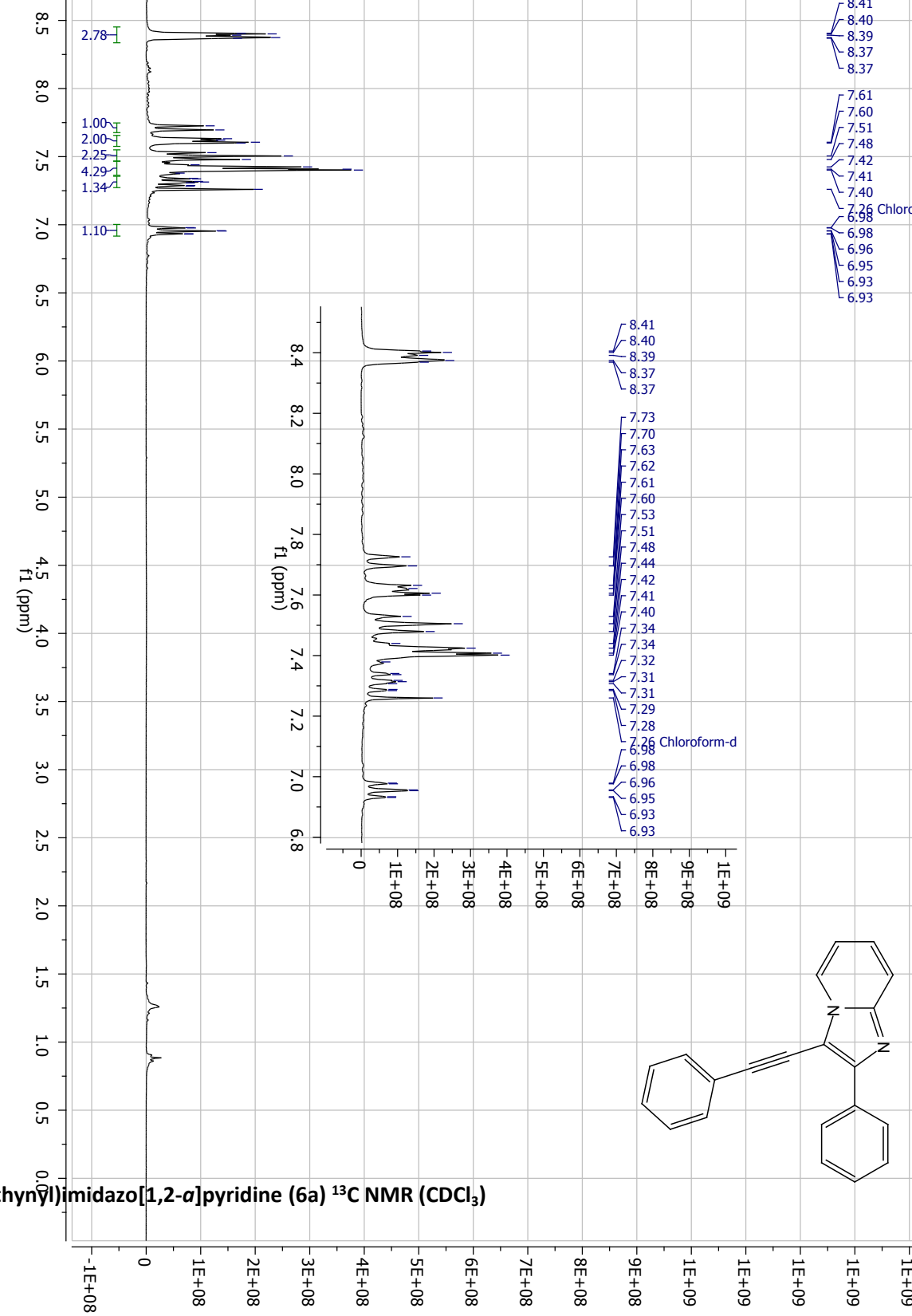
3-((4-methoxyphenyl)ethynyl)-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (5e) ^{1}H NMR ($CDCl_3$)



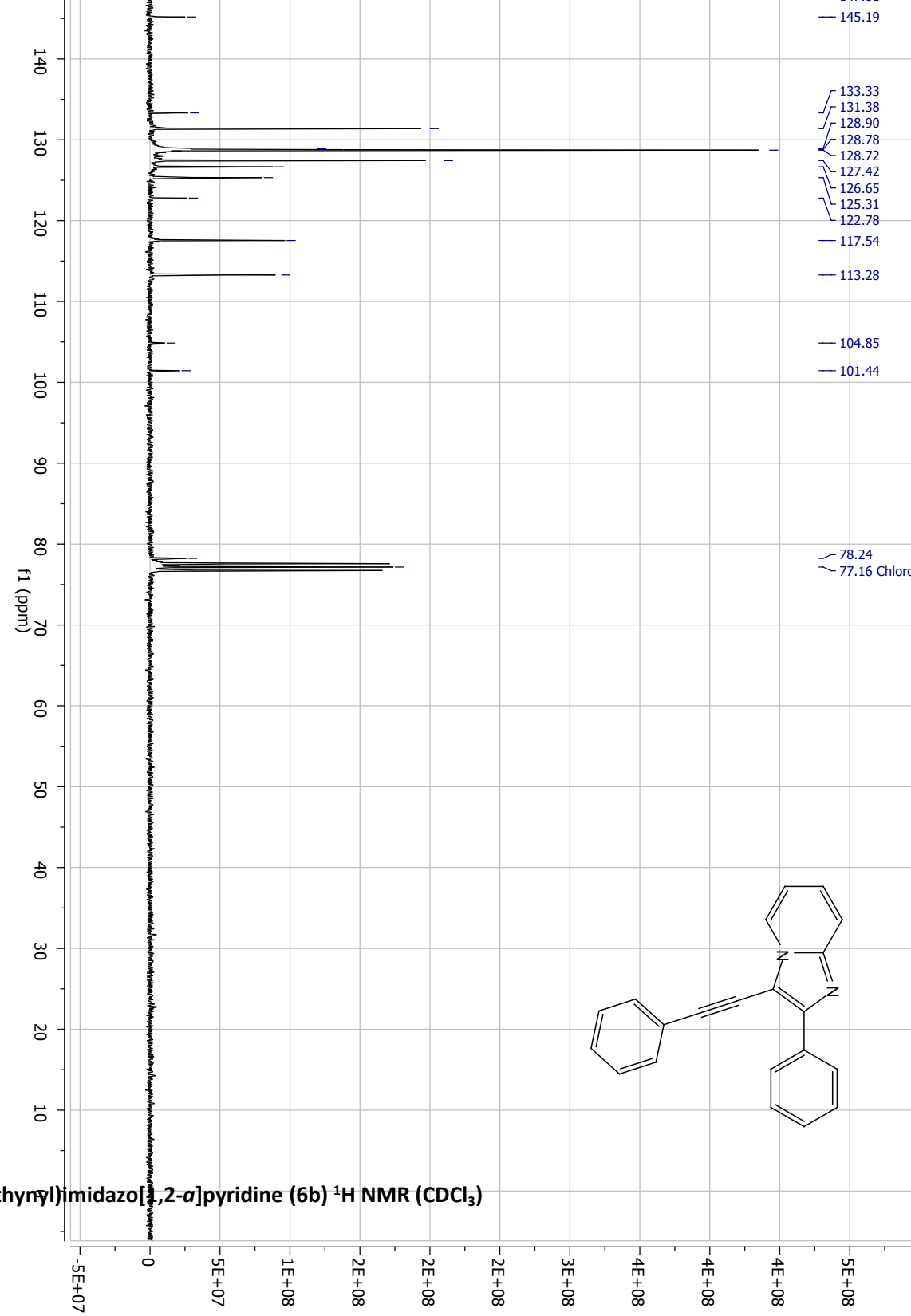
3-((4-methoxyphenyl)ethynyl)-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (5e) ^{13}C NMR ($CDCl_3$)



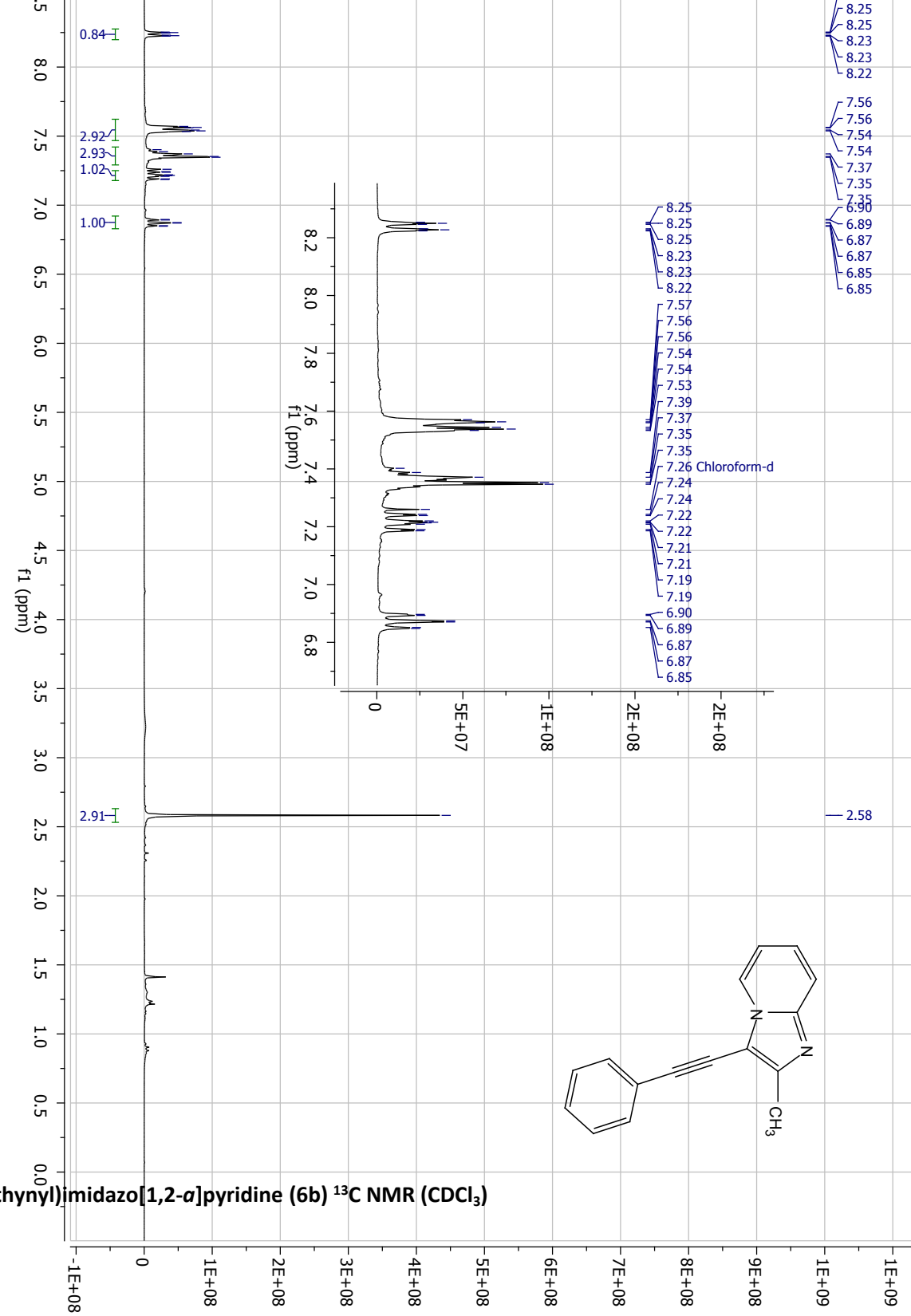
2-phenyl-3-(phenylethynyl)imidazo[1,2-*a*]pyridine (6a) ^{1}H NMR ($CDCl_3$)



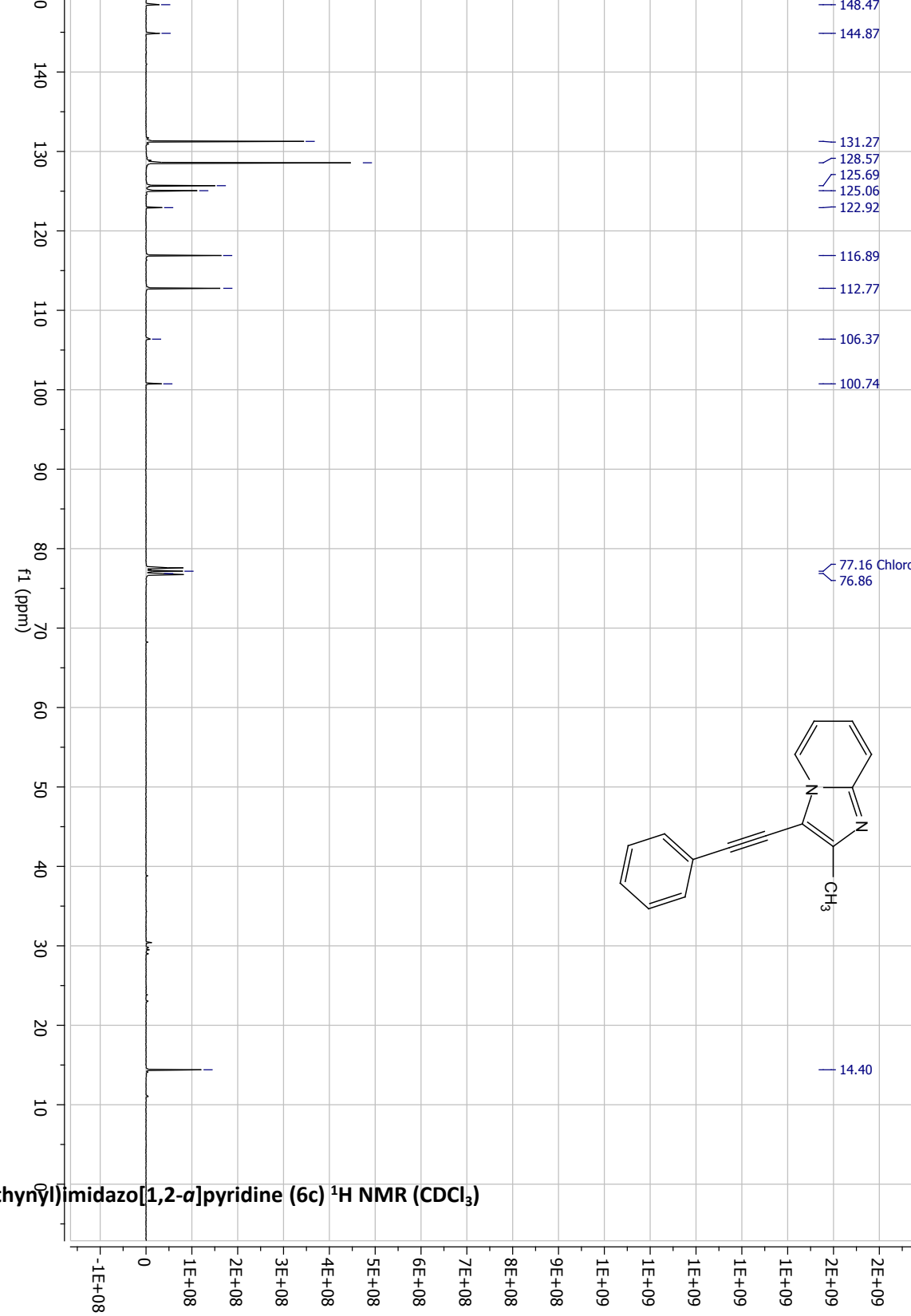
2-phenyl-3-(phenylethynyl)imidazo[1,2-*a*]pyridine (6a) ^{13}C NMR ($CDCl_3$)



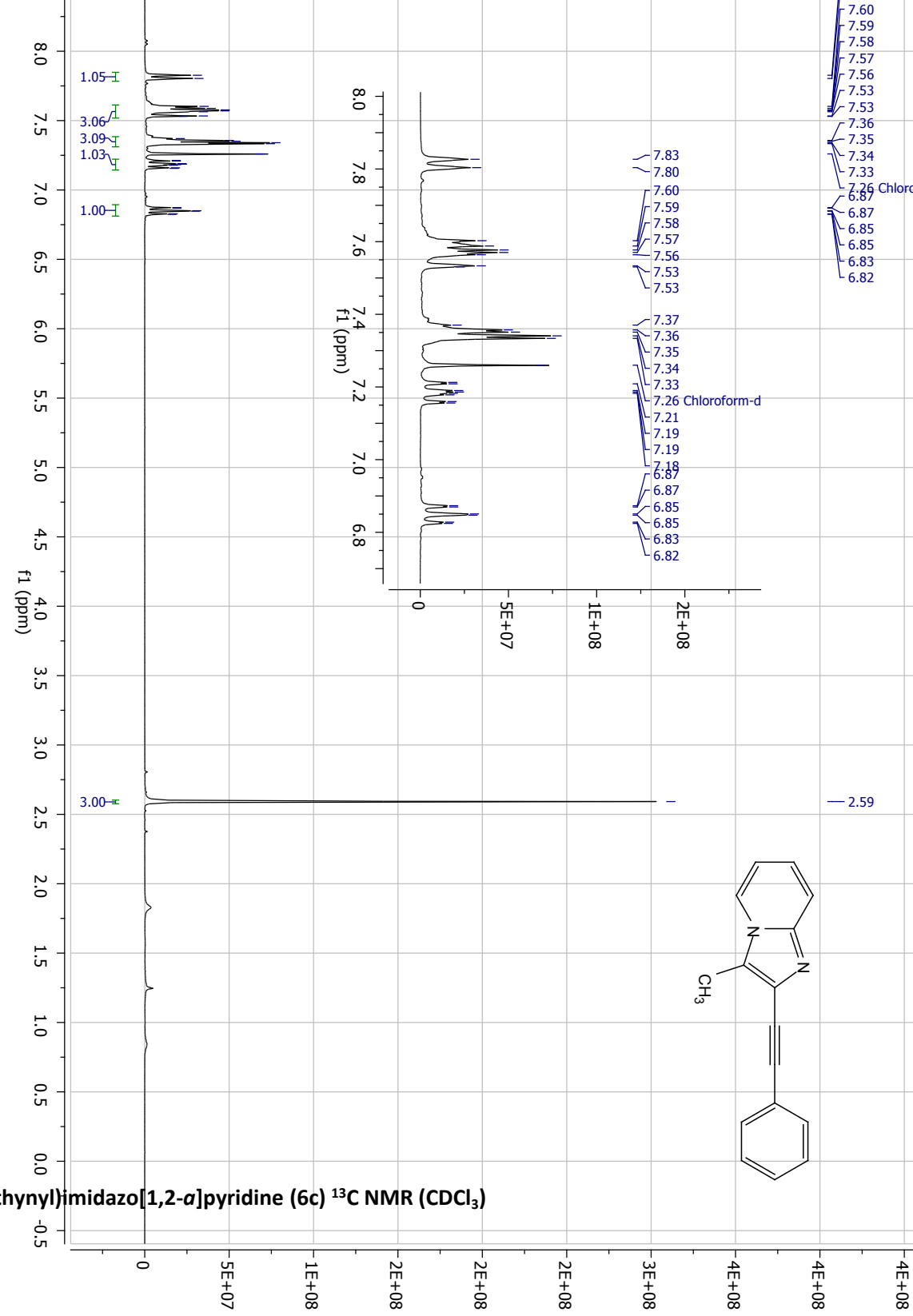
2-methyl-3-(phenylethynyl)imidazo[1,2-*a*]pyridine (6b) ^{1}H NMR ($CDCl_3$)



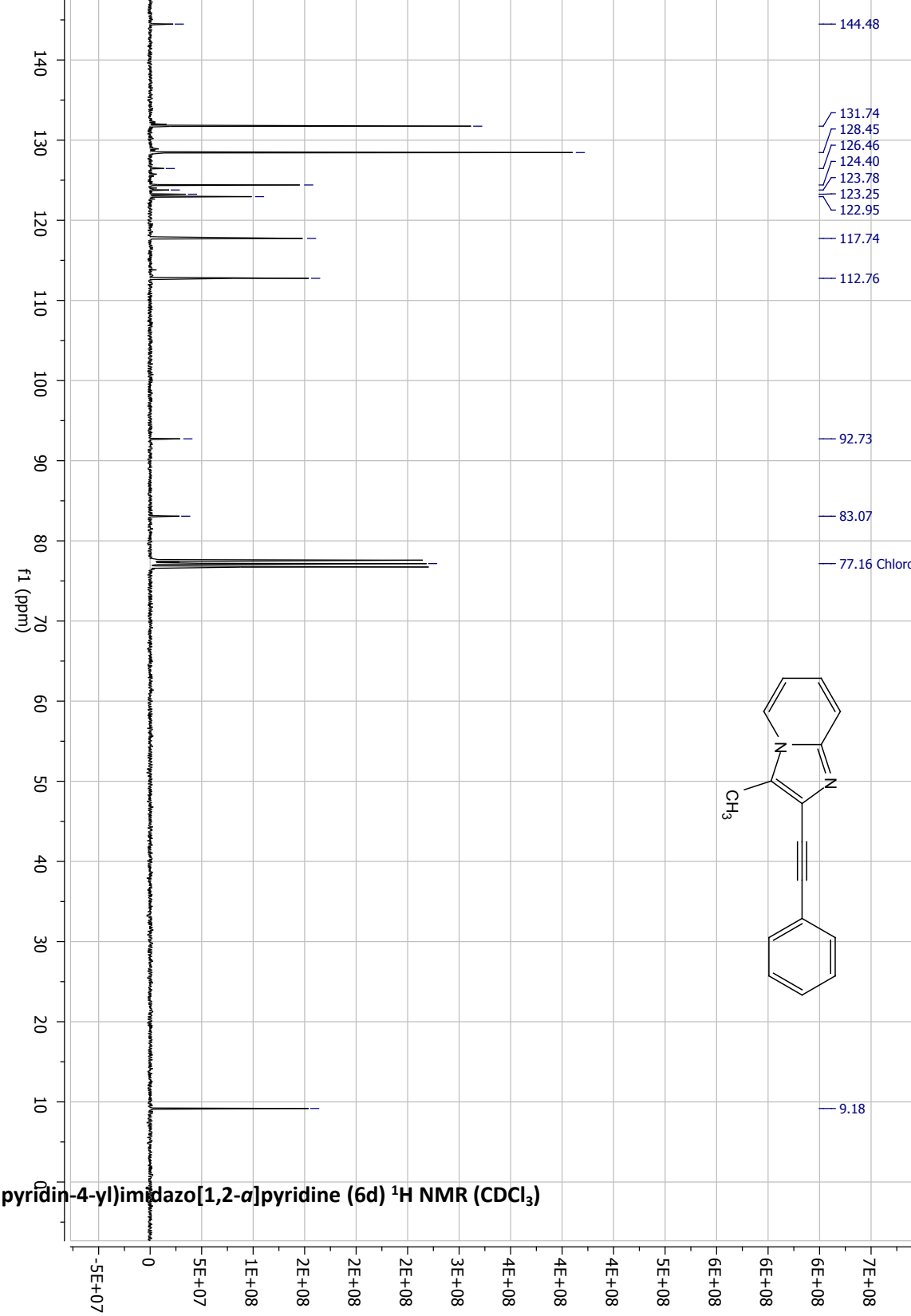
2-methyl-3-(phenylethynyl)imidazo[1,2-*a*]pyridine (6b) ^{13}C NMR ($CDCl_3$)



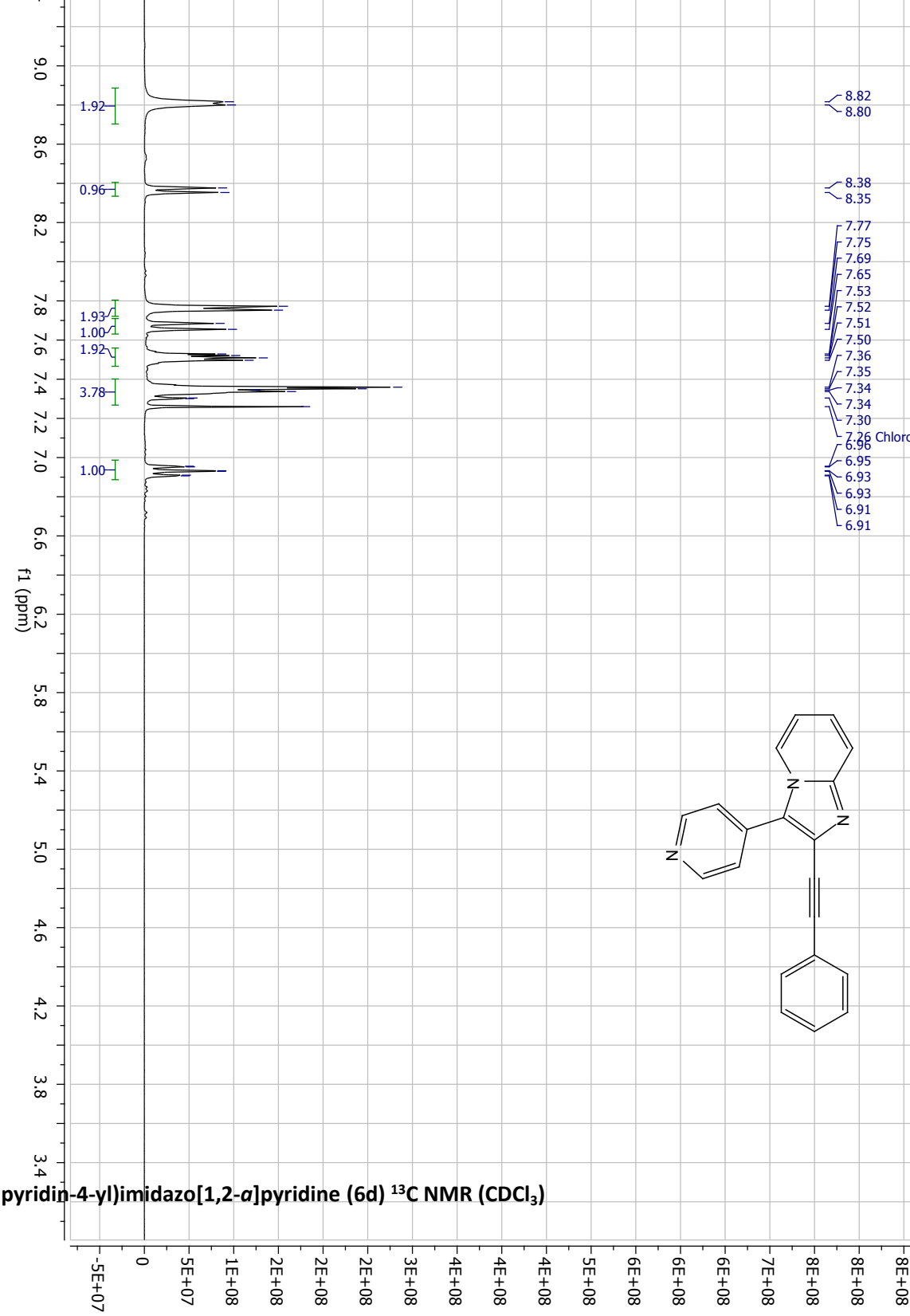
3-methyl-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (6c) ^{1}H NMR ($CDCl_3$)



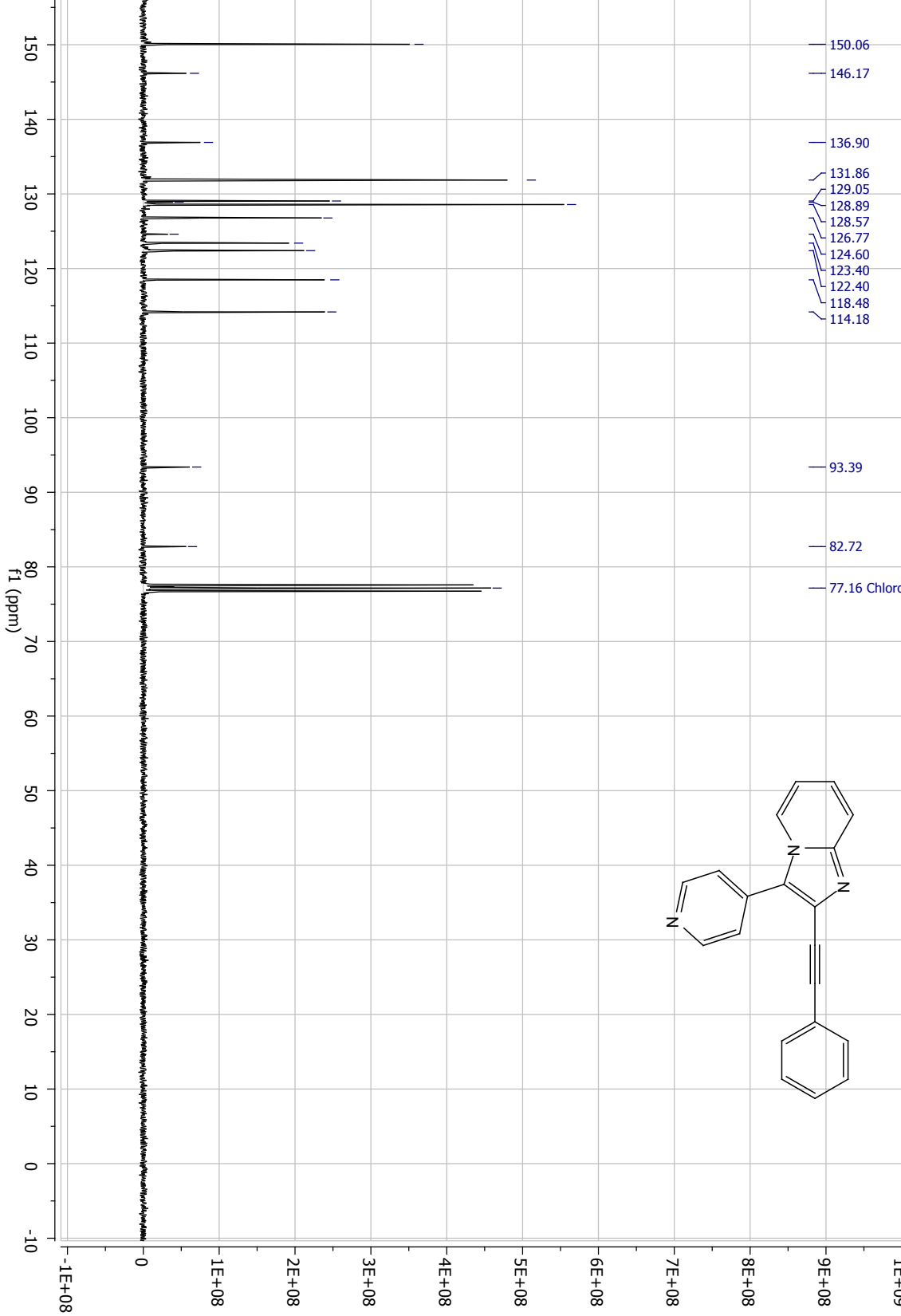
3-methyl-2-(phenylethynyl)imidazo[1,2-*a*]pyridine (6c) ^{13}C NMR ($CDCl_3$)



2-(phenylethynyl)-3-(pyridin-4-yl)imidazo[1,2-*a*]pyridine (6d) ^{1}H NMR ($CDCl_3$)



2-(phenylethynyl)-3-(pyridin-4-yl)imidazo[1,2-*a*]pyridine (6d) ^{13}C NMR ($CDCl_3$)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93.39
82.72
77.16 Chlorc
f1 (ppm)
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140
130
120
110
100
90
80
70
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50
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30
20
10
0
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-1E+08
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1E+08
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4E+08
5E+08
6E+08
7E+08
8E+08
9E+08
N
N
N