ELECTRONIC SUPPORTING INFORMATION

(Pre)association as a Crucial Step for Computational Prediction and Analysis of the Catalytic Activity of σ-Hole Donating Organocatalysts

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^{1}H NMR monitoring of the Groebke–Blackburn–Bienaymé reaction

The 4-tolylaldehyde (51.8 µL, 0.439 mmol), 2-aminopyridine (10.3 mg, 0.110 mmol) and cyclohexyl isocyanide (13.6 µL, 0.110 mmol) were added to the CD_3OD solution of **Cat1**^{OTf}–**Cat4**^{OTf} (18.3 mM, 600 µL, 0.011 mmol) and placed in an NMR tube. For the noncatalyzed reaction, the same quantities of the reactants were added to the CD_3OD (600 µL) and placed in an NMR tube. The NMR tube was sealed, and the obtained homogeneous solution was maintained at 50 °C for 16 h in an NMR spectrometer. The reaction was monitored by measuring the time-dependent integral density of the ipso-cyclohexyl proton group signals in isocyanide and in the product of the reaction.

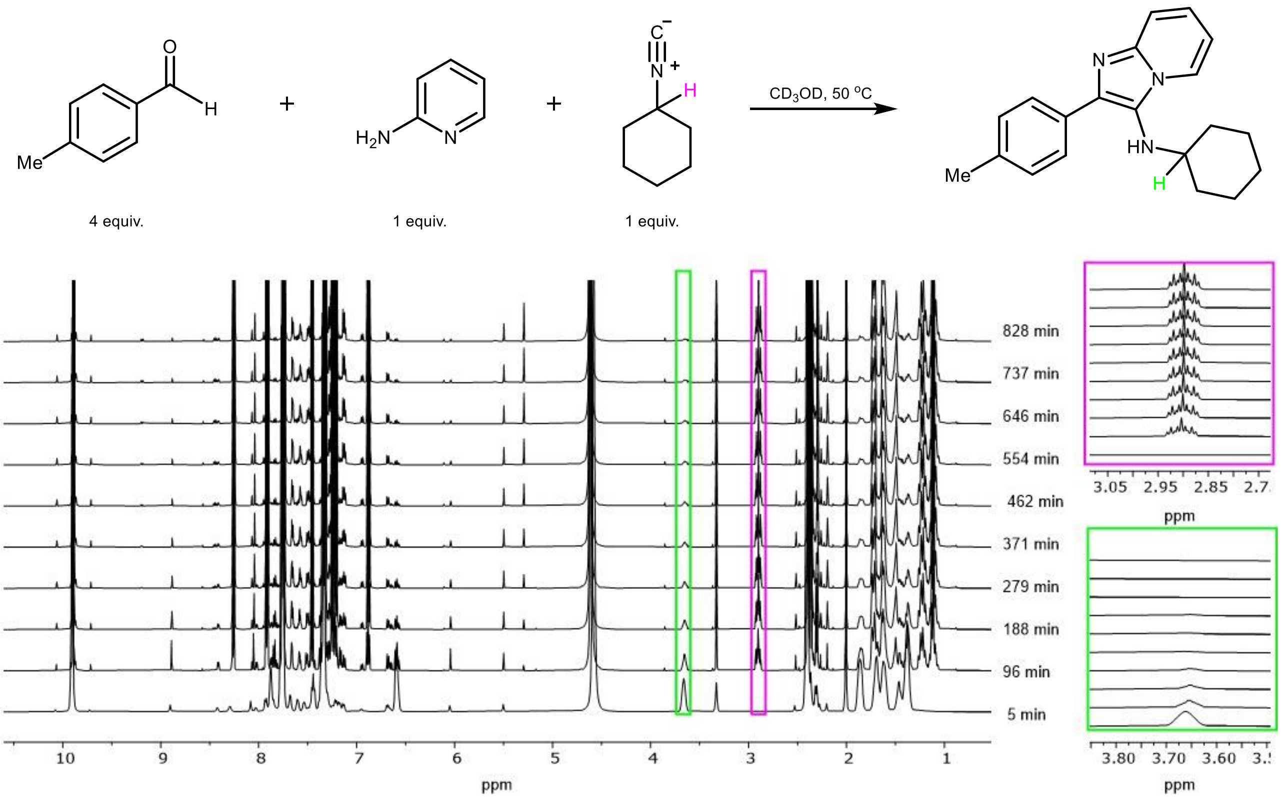


Figure S1. ^{1}H NMR spectra of the monitoring Groebke–Blackburn–Bienaymé reaction with **Cat3**^{OTf} at the different time intervals.

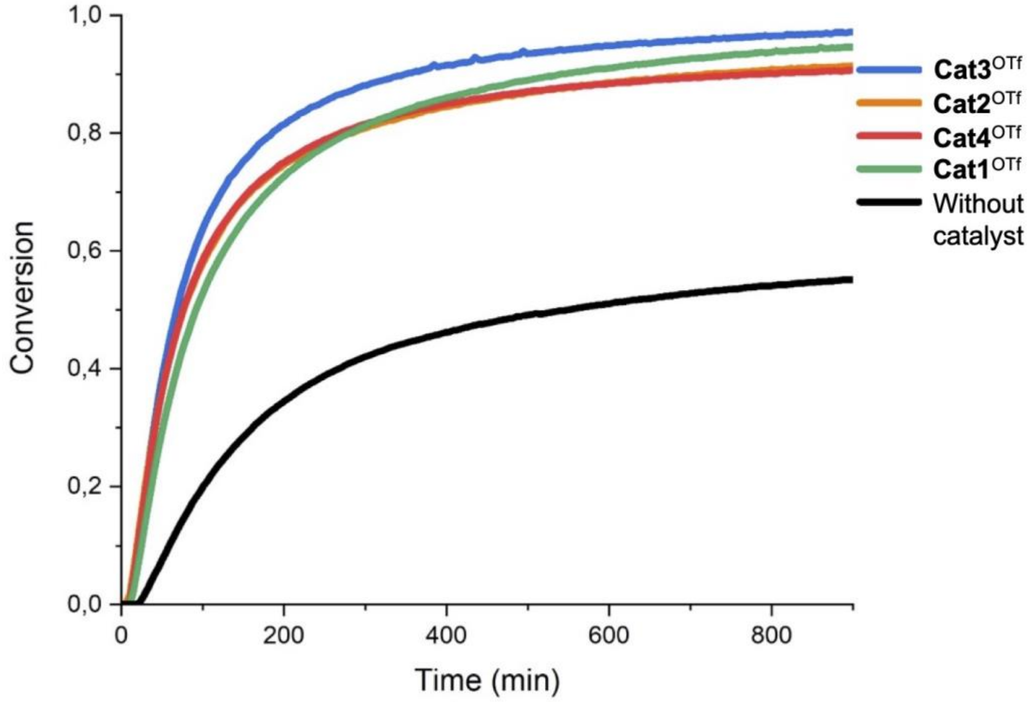


Figure S2. ^{1}H NMR monitoring of the modelled multicomponent reaction in the presence of **Cat1**^{OTf}–**Cat4**^{OTf} and in the absence of the catalyst.

^{1}H NMR Monitoring of the first step of the reaction. The 4-tolylaldehyde (51.8 μL, 0.439 mmol) and 2-aminopyridine (10.3 mg, 0.110 mmol) were added to the CD_3OD solution of **Cat1**^{OTf}–**Cat4**^{OTf} (18.3 mM, 600 μL, 0.011 mmol) and placed in an NMR tube. For the noncatalyzed reaction, the same quantities of the reactants were added to CD_3OD (600 μL) and placed in an NMR tube. The NMR tube was then sealed, and the obtained homogeneous solution was maintained at 50 °C for 100 min in the NMR spectrometer. The reaction was monitored by measuring the time-dependent integral density of the 4-tolylaldehyde and imine proton group signals.

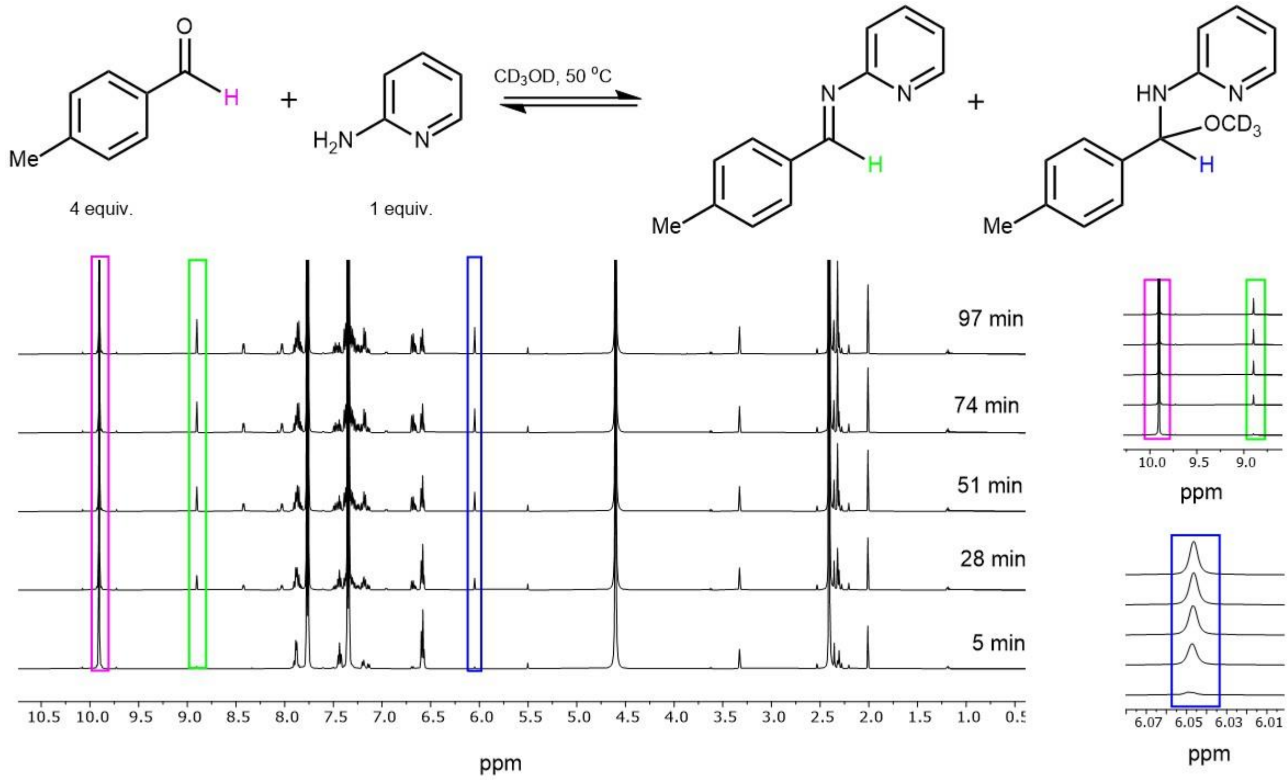


Figure S3. [1]H NMR spectra of the monitoring first step of reaction with **Cat3**^{OTf} at the different time intervals.

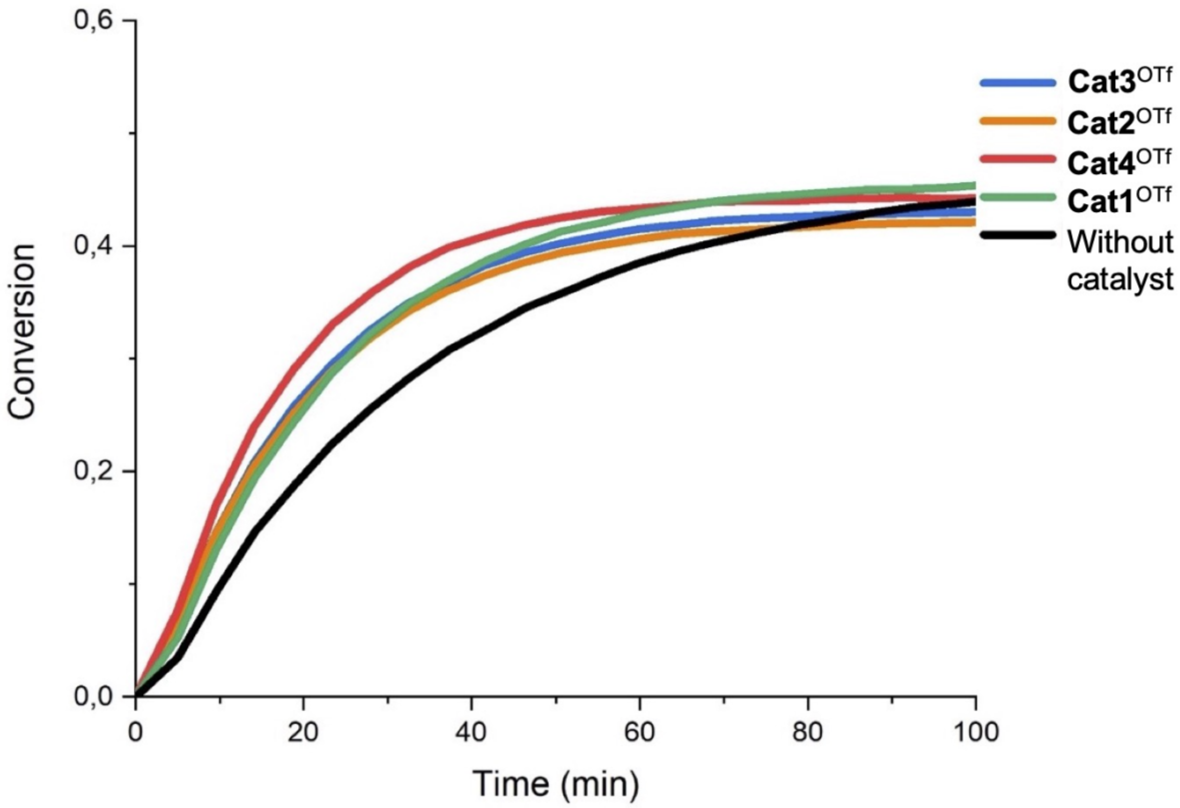


Figure S4. [1]H NMR monitoring of the first step of modelled multicomponent reaction in the presence of **Cat1**^{OTf}–**Cat4**^{OTf} and in the absence of the catalyst.

^{1}H NMR monitoring of the second step of the reaction. The imine (86 mg, 0.439 mmol) and cyclohexyl isocyanide (13.6 μL, 0.110 mmol) were added to the CD_3OD solution of **Cat1**^{OTf}–**Cat4**^{OTf} (18.3 mM, 600 μL, 0.011 mmol) and placed in an NMR tube. For the experiment with 2,6-di-*tert*-butylpyridine, 0.022 mmol of the reagent was added to the reaction mixture containing **Cat3**^{OTf}. For the noncatalyzed reaction, the same quantities of the reactants were added to the CD_3OD (600 μL) and placed in an NMR tube. The NMR tube was sealed, and the obtained homogeneous solution was maintained at 50 °C for 100 min in an NMR spectrometer. The reaction was monitored by measuring the time-dependent integral density of the ipso-cyclohexyl proton group signals in isocyanide and in the product of the reaction.

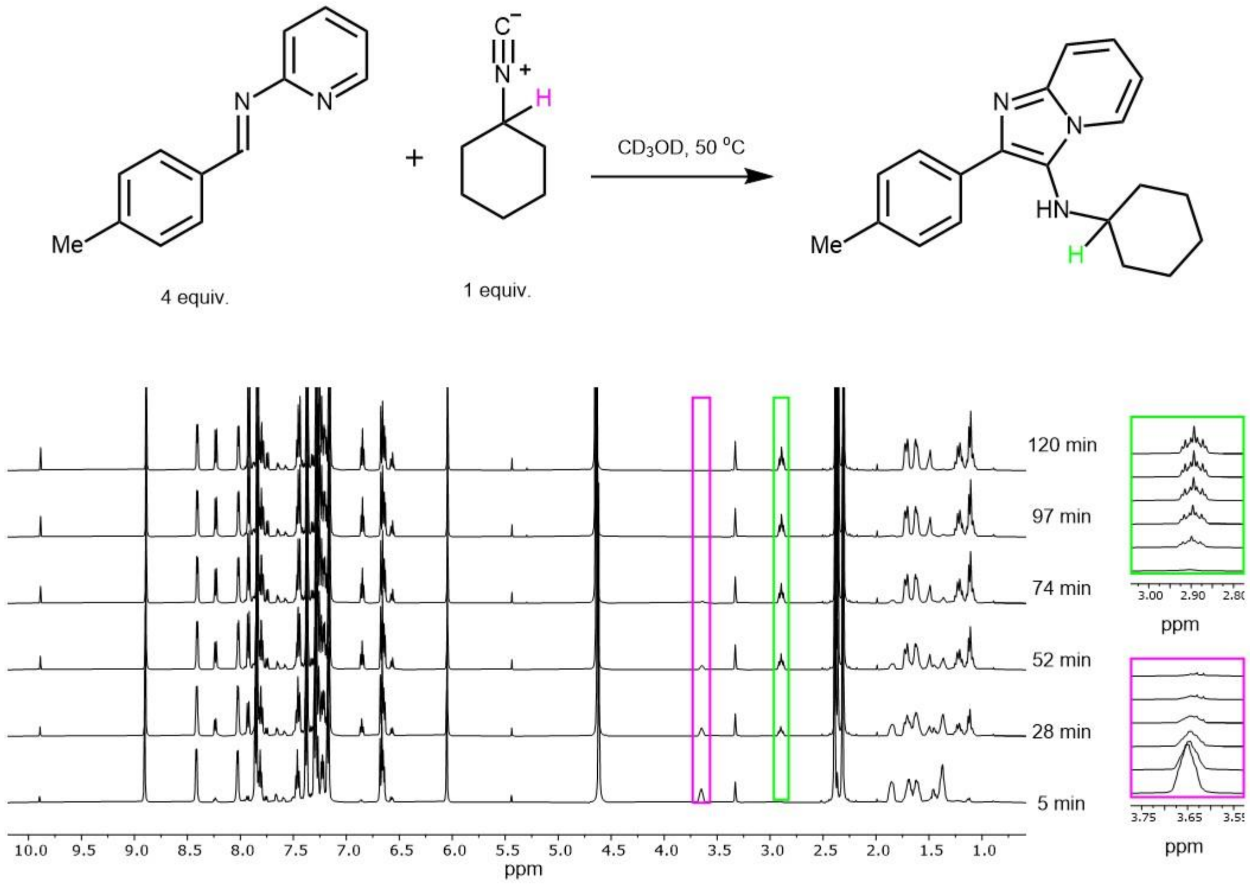


Figure S5. ^{1}H NMR spectra of the monitoring second step of reaction with **Cat3**^{OTf} at the different time intervals.

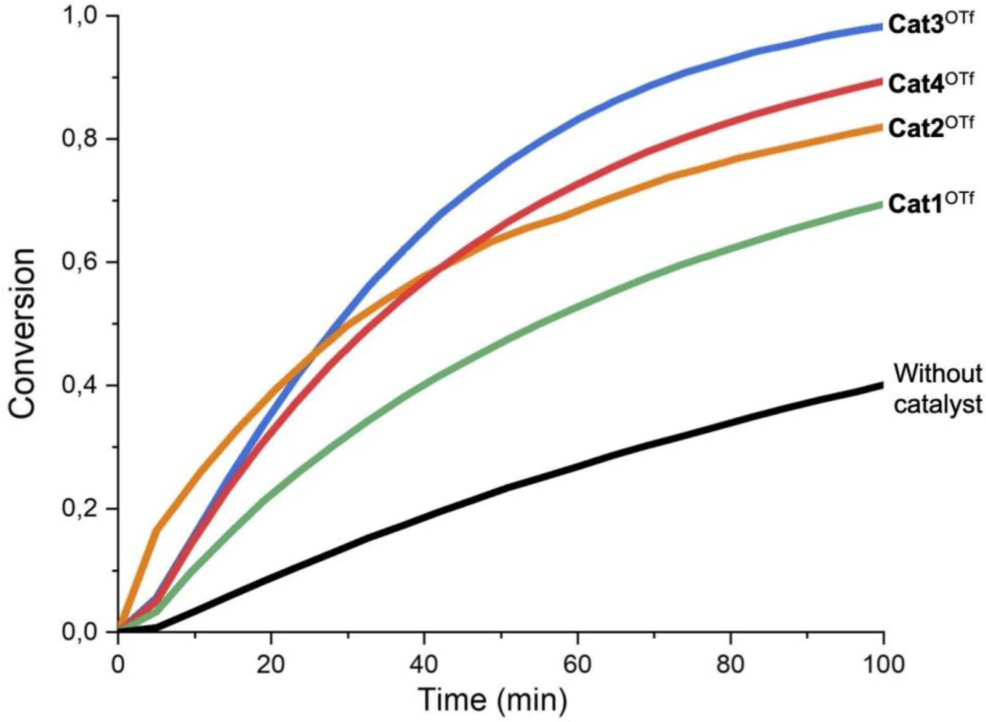


Figure S6. [1]H NMR monitoring of the progress of the second step of the model Groebke–Blackburn–Bienaymé reaction.

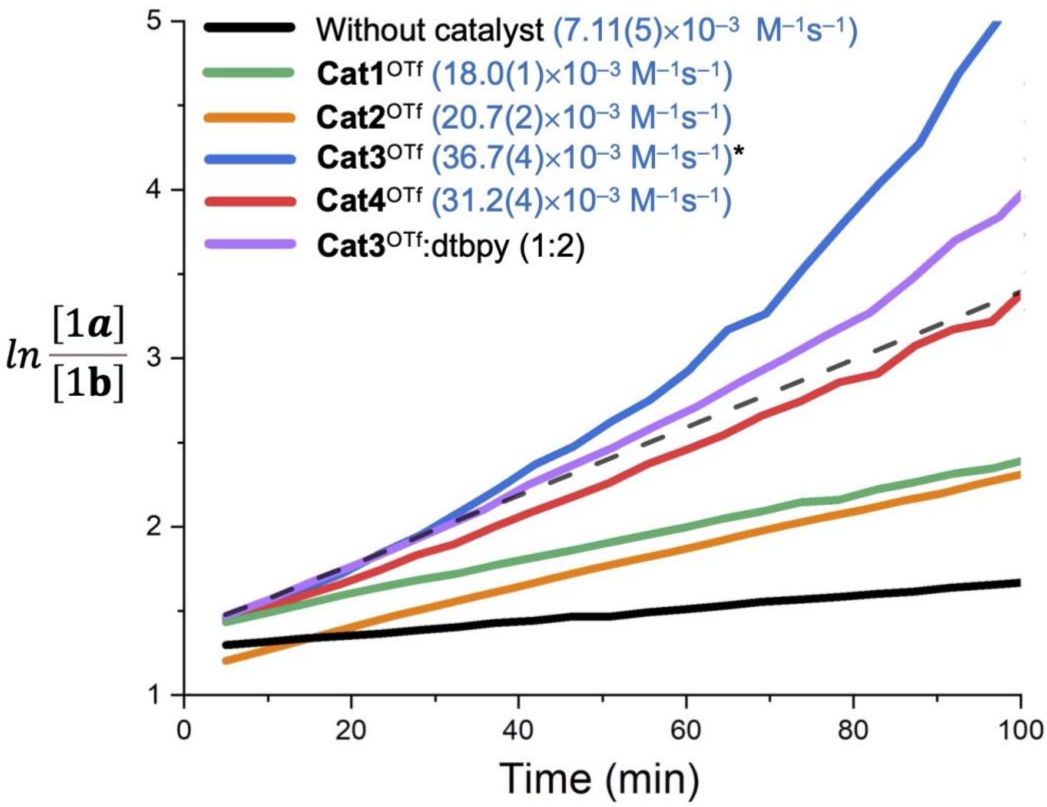
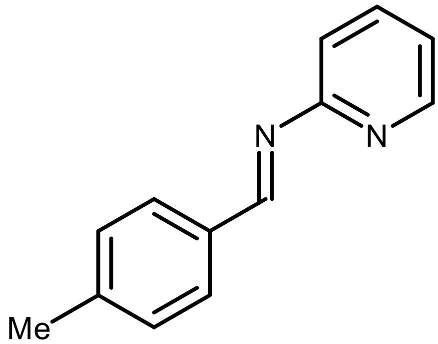


Figure S7. [1]H NMR monitoring of the progress of the second step of the model Groebke–Blackburn–Bienaymé reaction (linearization).

Synthesis of the imine 1a

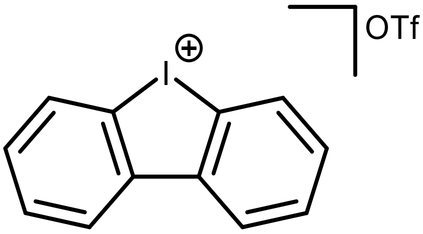
Imine **1a** was synthesized according to the published procedure (DOI: 10.1515/znb-2012-0403). 2-Aminopyridine (2.82 g; 30.00 mmol) was dissolved in dry CH_2Cl_2 (10 mL). Then, 4 Å molecular sieves and 4-methylbenzaldehyde (7.06 mL; 60.00 mmol) were added to the resulting solution and stirred at RT for 24 h. After that the solvent was evaporated *in vacuo* at RT and the residue was crystallized using *n*-hexane, filtered off, washed with *n*-hexane (10 mL) and dried *in vacuo* at 50 °C.



1a. Yield: 51% (2.99 g). M.p.: 60–62 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 9.13 (s, 1H, *H*C=N), 8.52 (dd, $^3J_{HH}$ = 5.0 Hz, $^4J_{HH}$ = 1.9 Hz, 1H, Ar), 7.91 (d, $^3J_{HH}$ = 7.9 Hz, 2H, Ar), 7.77 (td, $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 2.0 Hz, 1H, Ar), 7.35–7.30 (m, 3H, Ar, the signal overlaps with the residual signal of the $CDCl_3$), 7.20–7.17 (m, 1H, Ar), 2.45 (s, 3H, C*H*$_3$). ^{13}C{^{1}H} NMR (101.61 MHz, $CDCl_3$): δ = 162.8, 161.4, 148.9, 142.5, 138.1, 133.4, 129.6, 121.6, 119.7 (Ar) and (H*C*=N); 21.7 (*C*H$_3$). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}N_2$ 197.1073; Found 197.1073.

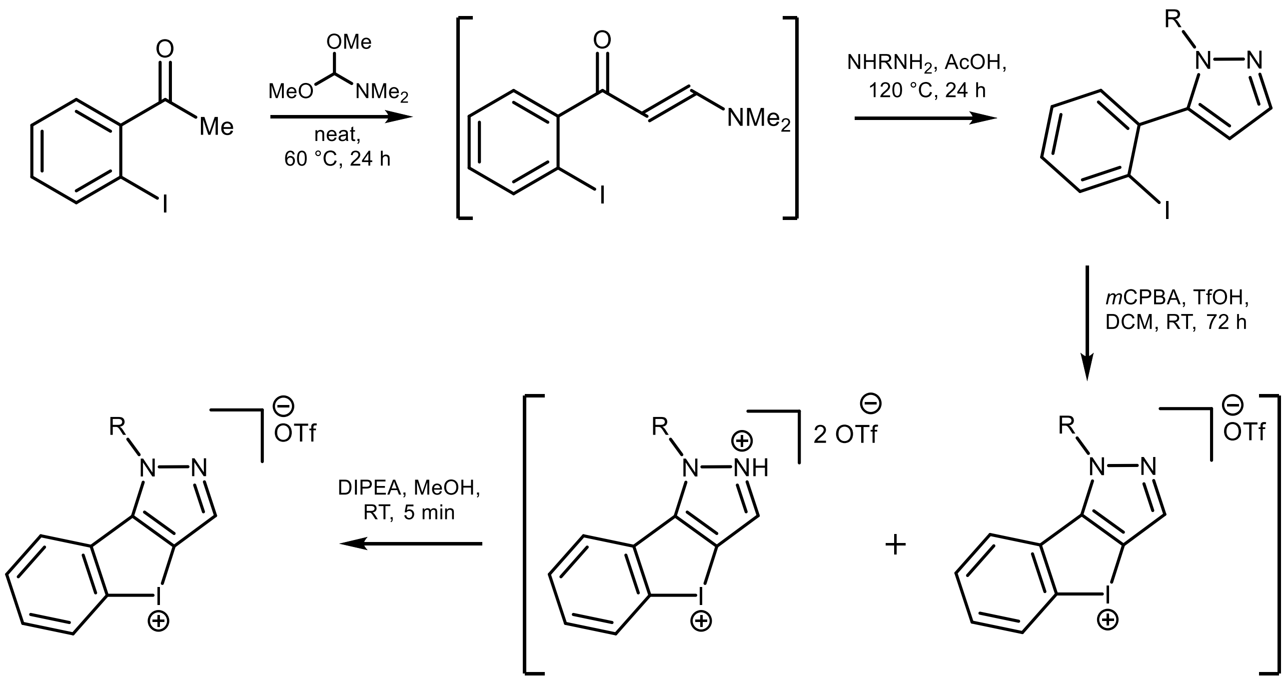
Synthesis of dibenziodolium triflate Cat1^{OTf}

Cat1^{OTf} was synthesized according to published procedure (DOI: 10.1039/d0ra09640g). m-CPBA (77%, 665 mg, 2.96 mmol) and TfOH (0.521 mL, 5.89 mmol) were added to a stirred solution of 2-iodo-1,1'-biphenyl (550 mg, 0.346 mL, 1.97 mmol) in dry CH_2Cl_2 (5 mL) and stirred for 1 h at RT. Then the solvent was evaporated *in vacuo* at RT, and the product was crystallized using Et_2O (10 mL). The precipitate which formed, was stirred for 20 min at RT and filtered off, washed with Et_2O (10 mL), and dried at 50 °C in air.

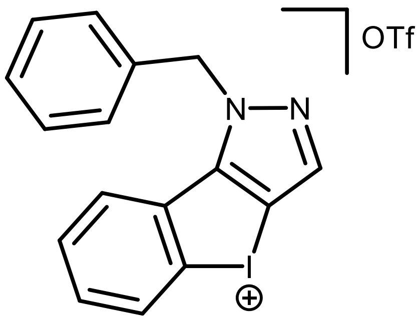


Cat1^{OTf}. Yield: 90% (760 mg). M.p.: 240–242 °C (decomp.). ^{1}H NMR (400.13 MHz, DMSO-d$_6$): δ = 8.37 (dd, $^3J_{HH}$ = 8.0 Hz, $^4J_{HH}$ = 1.5 Hz, 1H, Ar), 8.15 (d, $^3J_{HH}$ = 8.1 Hz, 1H, Ar), 7.79 (t, $^3J_{HH}$ = 7.5 Hz, 1H, Ar), 7.67 (td, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.4 Hz, 1H, Ar). ^{13}C{^{1}H} NMR (101.61 MHz, DMSO-d$_6$): δ = 142.1, 131.5, 131.1, 131.0, 127.4 and 121.9 (Ar); 121.2 (q, $^1J_{CF}$ = 322.3 Hz, *C*F$_3$). HRMS (ESI) *m/z*: [M]$^+$ Calcd for $C_{12}H_8I$ 278.9665; Found 278.9667.

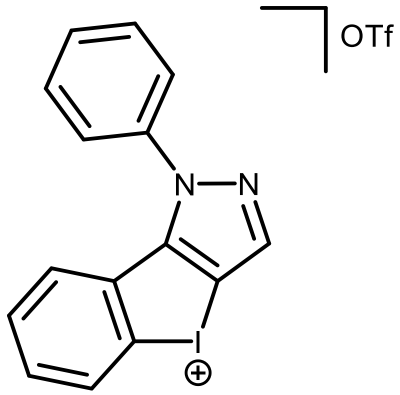
Synthesis and characterization of Cat2^{OTf}–Cat4^{OTf}



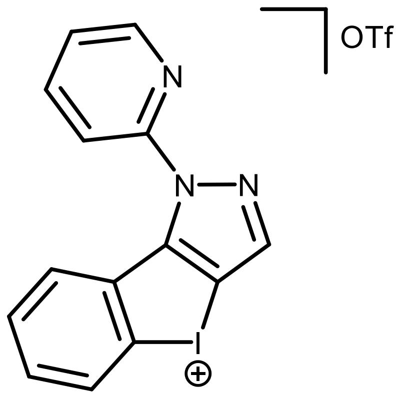
Corresponded compound was synthesized according to a previously published procedure (DOI: 10.1021/acs.orglett.0c02593), with some modifications. 2-Iodoacetophenone (1.00 g; 4.066 mmol) was dissolved in dimethylformamide-dimethylacetal (0.968 g; 8.132 mmol) and stirred at 60 °C for 24 h. After that solution was evaporated *in vacuo* at 60 °C and the residue was dissolved in the solution of relevant hydrazine (4.472 mmol) in 3 mL acetic acid and stirred at 120 °C for 24 h. After that the solvent was evaporated *in vacuo* at 75 °C, and the corresponding pyrazoles was isolated *via* column chromatography (eluent: Hexane/EtOAc 9:1). The residue was dissolved in the solution of triflic acid (3 equiv.) and m-CPBA (1.5 equiv.) in 30 mL of dry dichloromethane. The resulting solution was stirred at RT for 72 h. After that the solvent was evaporated *in vacuo* at 50 °C, and the residue was crystallized using diethyl ether. After that the residue was added to the solution of diisopropylethylamine (1 equiv.) in MeOH (5 mL). The resulting solution was stirred at RT for 5 min and then the solvent was evaporated *in vacuo* at 50 °C and the residue was crystallized using EtOAc, filtered and dried *in vacuo* at 50 °C.



Cat2^{OTf}. Overall yield: 25% (520 mg). M.p.: 200–204 °C (decomp.). ^{1}H NMR (400.13 MHz, DMSO-d_6) δ = 8.29 (d, $^{3}J_{HH}$ = 7.8 Hz, 1H, Ar), 8.15 (d, $^{3}J_{HH}$ = 7.9 Hz, 1H, Ar), 8.03 (s, 1H, Ar), 7.76 (t, $^{3}J_{HH}$ = 7.6 Hz, 1H, Ar), 7.61 (t, $^{3}J_{HH}$ = 7.8 Hz, 1H, Ar), 7.36–7.21 (m, 3H, Ar), 7.20 (d, $^{3}J_{HH}$ = 7.4 Hz, 2H, Ar), 6.00 (s, 2H, C*H*$_2$). ^{13}C{^{1}H} NMR (101.61 MHz, DMSO-d_6) δ = 148.0, 138.2, 136.6, 131.9, 131.2, 130.7, 129.3, 128.4, 128.2, 127.0, 126.7 and 94.08 (Ar); 121.17 (q, $^{1}J_{CF}$ = 322.8 Hz, *C*F$_3$); 55.4 (*C*H$_2$). HRMS (ESI) *m/z*: [M]$^+$ Calcd for $C_{16}H_{12}N_2I$ 359.0045; Found 359.0044.



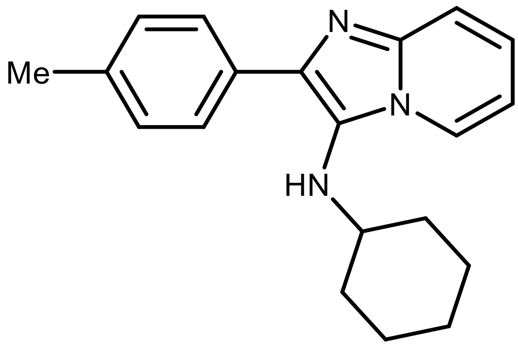
Cat3^{OTf}. Overall yield: 28% (560 mg). M.p.: 220–224 °C (decomp.). ^{1}H NMR (400.13 MHz, DMSO-d_6) δ = 8.32 (d, $^{3}J_{HH}$ = 7.9 Hz, 1H, Ar), 8.19 (s, 1H, Ar), 7.71–7.60 (m, 7H, Ar), 7.24 (dd, $^{3}J_{HH}$ = 7.5 Hz, $^{4}J_{HH}$ = 1.8 Hz, 1H, Ar). ^{13}C{^{1}H} NMR (101.61 MHz, DMSO-d_6) δ = 148.4, 139.3, 139.2, 132.0, 131.1, 131.0, 130.9, 130.5, 128.5, 127.2, 126.9, 125.8, and 95.1 (Ar); 121.1 (q, $^{1}J_{CF}$ = 322.8 Hz, CF_3). HRMS (ESI) m/z: [M]$^{+}$ Calcd for $C_{15}H_{10}N_2I$ 344.9889; Found 344.9883.



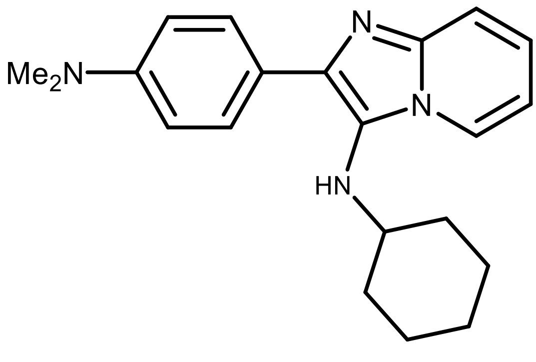
Cat4^{OTf}. Overall yield: 35% (704 mg). M.p.: 221–223 °C (decomp.). ^{1}H NMR (400.13 MHz, DMSO-d_6) δ = 8.73 (d, $^{3}J_{HH}$ = 5.0 Hz, 1H, Ar), 8.43 (d, $^{3}J_{HH}$ = 8.1 Hz, 1H, Ar), 8.34 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, Ar), 8.26 (s, 1H, Ar), 8.23 (t, $^{3}J_{HH}$ = 7.8 Hz, 1H, Ar), 7.92 (d, $^{3}J_{HH}$ = 8.1 Hz, 1H, Ar), 7.77–7.75 (t, $^{3}J_{HH}$ = 7.5 Hz, 1H, Ar), 7.73–7.62 (m, 2H, Ar). ^{13}C{^{1}H} NMR (101.61 MHz, DMSO-d_6) δ = 151.9, 148.7, 148.6, 140.7, 140.1, 131.5, 131.1z, 130.7, 128.9, 128.8, 126.9, 125.2, 119.0 and 97.4 (Ar); 121.15 (q, $^{1}J_{CF}$ = 322.2 Hz, CF_3). HRMS (ESI) m/z: [M]$^{+}$ Calcd for $C_{14}H_9N_3I$ 345.9841; Found 345.9838.

Synthesis and characterization of 1–14

The corresponding isocyanide (0.467 mmol) was added to the mixture of relevant aldehyde (0.701 mmol), 2-aminopyridine (43.9 mg, 0.467 mmol) and **Cat3**^{OTf} (23 mg, 0.047 mmol) in MeOH (2 mL). The resulting solution was stirred at 50 °C for 16 h in air. After that the solvent was evaporated *in vacuo* at 50 °C, and the corresponding compound was isolated *via* column chromatography (eluent: *n*-hexane/EtOAc, gradient from 33 to 100%). After that the solvent was evaporated *in vacuo* at 50 °C, the residue was crystallized using hexane and dried at 60 °C in air.

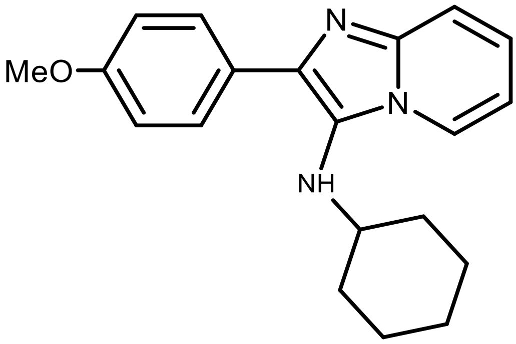


1. Yield: 95% (136 mg). R_f = 0.22 (Hexane/EtOAc, 1:1). M.p.: 160–162 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.10 (d, $^3J_{HH}$ = 6.7 Hz, 1H, C_5H_4N), 7.95 (d, $^3J_{HH}$ = 8.1 Hz, 2H, C_6H_4–Me), 7.55 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C_5H_4N), 7.26 (d, $^3J_{HH}$ = 7.9 Hz, 2H, C_6H_4–Me, the signal overlaps with the residual signal of the $CDCl_3$), 7.11 (t, $^3J_{HH}$ = 7.8 Hz, 1H, C_5H_4N), 6.75 (t, $^3J_{HH}$ = 6.7 Hz, 1H, C_5H_4N), 3.15 (d, br, $^3J_{HH}$ = 5.0 Hz, 1H, N*H*), 2.97 (m, 1H, NH–C*H*), 2.40 (s, 3H, Me), 1.87–1.76 (m, 2H, Cy), 1.75–1.64 (m, 2H, Cy), 1.62–1.52 (m, 1H, Cy), 1.32–1.09 (m, 5H, Cy). $^{13}C\{^1H\}$ NMR (101.61 MHz, $CDCl_3$): δ = 141.4, 137.0, 136.5, 131.5, 129.2, 126.9, 124.7, 123.8, 122.7, 117.2 and 111.5 (Ar); 56.9 (NH–*C*H); 34.2, 25.7 and 24.8 (Cy); 21.3 (Me). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{24}N_3$ 306.1965; Found 306.1956.

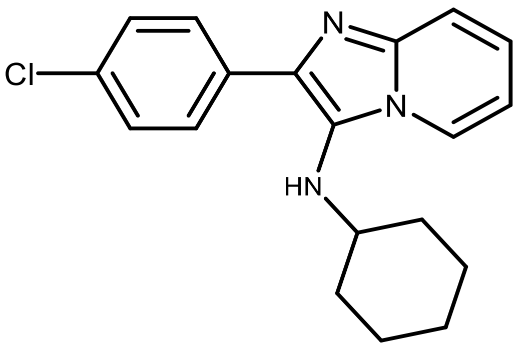


2. Yield: 84 % (131 mg). R_f = 0.47 (EtOAc). M.p.: 174–176 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.13 (d, $^3J_{HH}$ = 6.8 Hz, 1H, C_5H_4N), 7.97 (d, $^3J_{HH}$ = 8.9 Hz, 2H, C_6H_4–NMe_2), 7.57 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C_5H_4N), 7.20 – 7.14 (m, 1H, C_5H_4N), 6.82 (d, $^3J_{HH}$ = 8.9 Hz, 2H,

C_6H_4–NMe$_2$), 6.77 (t, $^3J_{HH}$ = 6.4 Hz, 1H, C_5H_4N), 3.18 (s, br, 1H, N*H*), 3.02 (s, 7H, $(CH_3)_2$ and NH–C*H*), 1.89 – 1.79 (m, 2H, Cy), 1.76 – 1.65 (m, 2H, Cy), 1.65 – 1.54 (m, 1H, Cy), 1.37 – 1.12 (m, 5H, Cy). $^{13}C\{^1H\}$ NMR (101.61 MHz, $CDCl_3$): δ = 149.8, 141.1, 136.7, 127.9, 123.7, 123.5, 122.6, 122.1, 116.6, 112.3 and 111.4 (Ar); 56.8 (NH–*C*H); 40.4 ($(CH_3)_2$); 34.2 (Cy), 25.8 and 24.8 (Cy). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{27}N_4$ 335.2230; Found 335.2235.

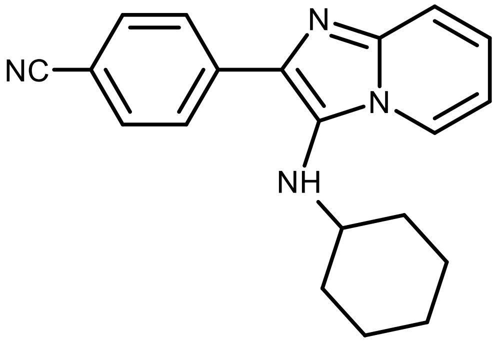


3. Yield: 86 % (129 mg). R_f = 0.35 (Hexane/EtOAc, 1:1). M.p.: 151–152 °C. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 8.07 (d, $^3J_{HH}$ = 6.9 Hz, 1H, C_5H_4N), 7.99 (d, $^3J_{HH}$ = 8.3 Hz, 2H, C_6H_4–OCH_3), 7.52 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C_5H_4N), 7.09 (t, $^3J_{HH}$ = 7.8 Hz, 1H, C_5H_4N), 6.98 (d, $^3J_{HH}$ = 8.3 Hz, 2H, C_6H_4–OCH_3), 6.74 (t, $^3J_{HH}$ = 6.7 Hz, 1H, C_5H_4N), 3.85 (s, 3H, C_6H_4–OCH_3), 3.09 (d, br, $^3J_{HH}$ = 4.8 Hz, 1H, N*H*), 3.02 – 2.87 (m, 1H, NH–C*H*), 1.89 – 1.74 (m, 2H, Cy), 1.74 – 1.64 (m, 2H, Cy), 1.61 – 1.51 (m, 1H, Cy), 1.19 (m, 5H, Cy). $^{13}C\{^1H\}$ NMR (101.61 MHz, $CDCl_3$): δ = 159.0, 141.4, 136.6, 128.3, 127.1, 124.1, 123.7, 122.6, 117.1, 113.9 and 111.4 (Ar); 56.8 and 55.2 (NH–*C*H and O*C*H$_3$); 34.2, 25.8 and 24.8 (Cy). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{24}N_3O$ 322.1914; Found 322.1914.

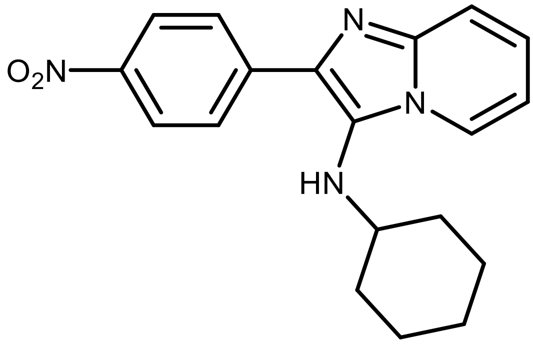


4. Yield: 90 % (137 mg). R_f = 0.27 (Hexane/EtOAc, 1:1). M.p.: 185–187 °C. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 8.04 (d, $^3J_{HH}$ = 6.9 Hz, 1H, C_5H_4N), 8.01 (d, $^3J_{HH}$ = 8.6 Hz, 2H, C_6H_4–Cl), 7.51 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C_5H_4N), 7.38 (d, $^3J_{HH}$ = 8.6 Hz, 2H, C_6H_4–Cl), 7.14 – 7.10 (m, 1H, C_5H_4N), 6.76 (td, $^3J_{HH}$ = 6.7 Hz, $^4J_{HH}$ = 1.2 Hz, 1H, C_5H_4N), 3.09 (d, $^3J_{HH}$ = 4.8 Hz, 1H, N*H*), 2.99 – 2.86 (m, 1H, NH–C*H*), 1.83 – 1.73 (m, 2H, Cy), 1.72 – 1.63

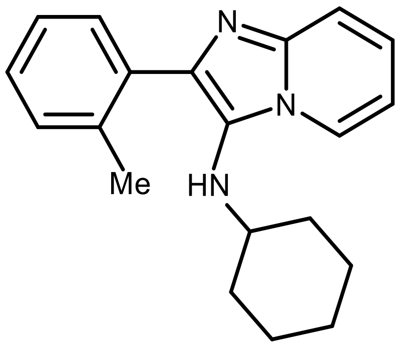
(m, 2H, Cy), 1.61 – 1.51 (m, 1H, Cy), 1.29 – 1.09 (m, 5H, Cy). $^{13}C\{^{1}H\}$ NMR (101.61 MHz, $CDCl_3$): δ = 141.5, 135.5, 133.0, 132.9, 128.6, 128.2, 124.9, 124.2, 122.7, 117.3 and 111.8 (Ar); 56.8 (NH–*C*H); 34.2, 25.7 and 24.8 (Cy). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}N_3Cl$ 326.1419; Found 326.1413.



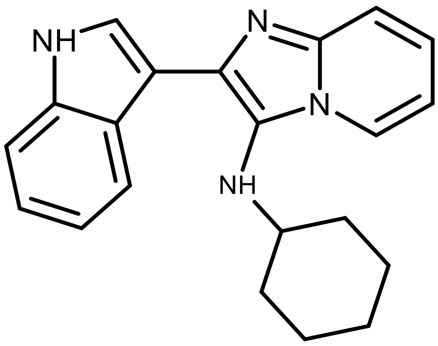
5. Yield: 96 % (143 mg). R_f = 0.34 (Hexane/EtOAc, 1:1). M.p.: 179–181 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.28 (d, $^{3}J_{HH}$ = 8.0 Hz, 2H, C_6H_4–CN), 8.10 (d, $^{3}J_{HH}$ = 6.9 Hz, 1H, C_5H_4N), 7.72 (d, $^{3}J_{HH}$ = 8.1 Hz, 2H, C_6H_4–CN), 7.59 (d, $^{3}J_{HH}$ = 9.1 Hz, 1H, C_5H_4N), 7.25 – 7.19 (m, 1H, C_5H_4N), 6.86 (t, $^{3}J_{HH}$ = 6.8 Hz, 1H, C_5H_4N), 3.16 (s, 1H, N*H*), 3.06 – 2.90 (m, 1H, NH–C*H*), 1.89 – 1.79 (m, 2H, Cy), 1.78 – 1.67 (m, 2H, Cy), 1.67 – 1.59 (m, 1H, Cy), 1.40 – 1.01 (m, 5H, Cy). $^{13}C\{^{1}H\}$ NMR (101.61 MHz, $CDCl_3$): δ = 141.8, 138.7, 134.3, 132.3, 127.3, 126.2, 125.1, 122.8, 119.2, 117.6, 112.4 and 110.5 (Ar and *C*N); 57.0, 34.3, 25.6 and 24.8 (Cy). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{21}N_4$ 317.1761; Found 317.1761.



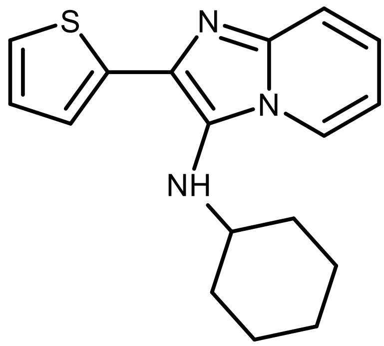
6. Yield: 92% (144 mg). R_f = 0.48 (Hexane/EtOAc, 1:1). M.p.: 210–211 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.35 (d, $^{3}J_{HH}$ = 8.7 Hz, 2H, C_6H_4–NO_2), 8.29 (d, $^{3}J_{HH}$ = 8.7 Hz, 2H, C_6H_4–NO_2), 8.11 (d, $^{3}J_{HH}$ = 6.9 Hz, 1H, C_5H_4N), 7.60 (d, $^{3}J_{HH}$ = 9.1 Hz, 1H, C_5H_4N), 7.23 (t, $^{3}J_{HH}$ = 9.1, $^{3}J_{HH}$ = 6.6 Hz, 1H, C_5H_4N), 6.88 (t, $^{3}J_{HH}$ = 6.8 Hz, 1H, C_5H_4N), 3.25 (d, $^{3}J_{HH}$ = 5.1 Hz, 1H, N*H*), 3.07 – 2.91 (m, 1H, NH–C*H*), 1.91 – 1.81 (m, 2H, Cy), 1.78 – 1.68 (m, 2H, Cy), 1.66 – 1.56 (m, 1H, Cy), 1.37 – 1.10 (m, 5H, Cy). $^{13}C\{^{1}H\}$ NMR (101.61 MHz, $CDCl_3$): δ = 146.6, 141.8, 140.5, 133.8, 127.3, 126.6, 125.5, 123.9, 122.8, 117.6 and 112.6 (Ar); 57.1 (NH–*C*H); 34.3, 25.6 and 24.8 (Cy). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}N_4O_2$ 337.1659; Found 337.1661.



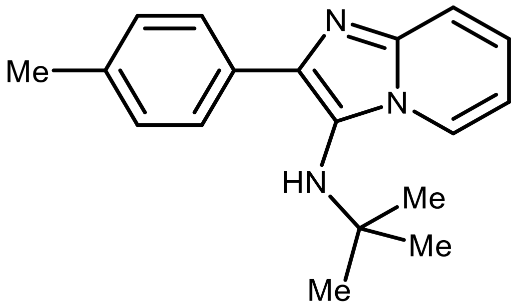
7. Yield: 93 % (132 mg). R_f = 0.21 (Hexane/EtOAc, 1:1). M.p.: 114–116 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.13 (d, $^3J_{HH}$ = 6.8 Hz, 1H, C_5H_4N), 7.55 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C_5H_4N), 7.36 (d, $^3J_{HH}$ = 6.9 Hz, 1H, C_6H_4–CH_3), 7.31 – 7.29 (m, 2H, C_6H_4–CH_3), 7.28 – 7.21 (m, 1H, C_6H_4–CH_3), 7.18 – 7.09 (m, 1H, C_5H_4N), 6.81 (t, $^3J_{HH}$ = 6.7 Hz, 1H, C_5H_4N), 3.06 (d, $^3J_{HH}$ = 6.6 Hz, 1H, N*H*), 2.85 – 2.63 (m, 1H, NH–C*H*), 2.35 (s, 3H, CH_3), 1.74 – 1.65 (m, 2H, Cy), 1.64 – 1.55 (m, 2H, Cy), 1.54 – 1.41 (m, 1H, Cy), 1.19 – 0.94 (m, 5H, Cy). ^{13}C{^{1}H} NMR (101.61 MHz, $CDCl_3$): δ = 141.0, 137.4, 137.1, 133.7, 130.3, 130.2, 128.0, 125.8, 125.5, 123.4, 122.8, 117.3 and 111.5 (Ar); 56.3, 33.8, 25.6 and 24.6 (Cy); 20.1 (CH_3). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{24}N_3$ 306.1965; Found 306.1969.



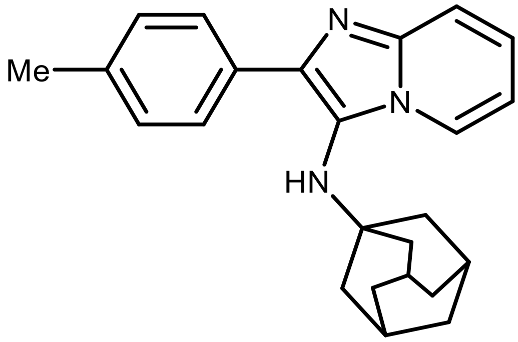
8. Yield: 86 % (133 mg). R_f = 0.45 (EtOAc). M.p.: 266–267 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6): δ = 11.25 (s, 1H, N*H*(Ar)), 8.61 (d, $^3J_{HH}$ = 7.9 Hz, 1H, Ar), 8.29 (d, $^3J_{HH}$ = 6.8 Hz, 1H, Ar), 8.03 (s, 1H, Ar), 7.49 (d, $^3J_{HH}$ = 9.0 Hz, 1H, Ar), 7.43 (d, $^3J_{HH}$ = 7.9 Hz, 1H), 7.25 – 6.99 (m, 3H, Ar), 6.86 (t, $^3J_{HH}$ = 6.7 Hz, 1H, Ar), 4.66 (d, $^3J_{HH}$ = 5.6 Hz, 1H, N*H*–CH(Cy)), 2.96 – 2.88 (m, 1H, NH–C*H*(Cy)), 1.93 – 0.92 (m, 10H, Cy). ^{13}C{^{1}H} NMR (101.61 MHz, DMSO-d_6): δ = 141.0, 136.4, 134.8, 126.8, 124.1, 124.0, 123.1, 122.8, 122.6, 121.8, 119.5, 116.6, 111.7, 111.4 and 109.8 (Ar); 56.3 (NH–*C*H(Cy)); 34.2, 26.0 and 25.0 (Cy). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{23}N_4$ 331.1917; Found 331.1919.



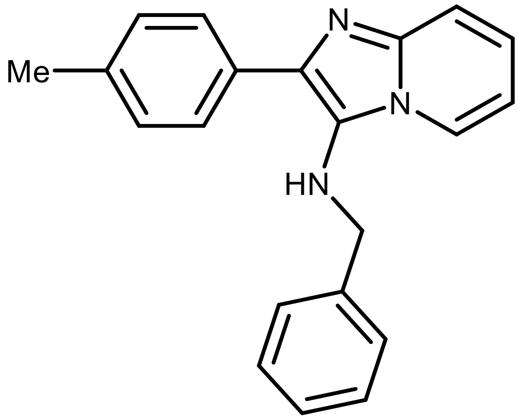
9. Yield: 70 % (123 mg). R_f = 0.26 (Hexane/EtOAc, 1:1). M.p.: 161–163 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.11 (d, $^3J_{HH}$ = 6.8 Hz, 1H, Ar), 7.64 (d, $^3J_{HH}$ = 3.6 Hz, 1H, Ar), 7.55 (d, $^3J_{HH}$ = 9.0 Hz, 1H, Ar), 7.34 (d, $^3J_{HH}$ = 5.1 Hz, 1H, Ar), 7.20 – 7.11 (m, 2H, Ar), 6.80 (t, $^3J_{HH}$ = 6.8 Hz, 1H, Ar), 3.17 – 3.03 (m, 2H, N*H*–CH and NH–C*H*), 1.95 – 1.83 (m, 2H, Cy), 1.82 – 1.69 (m, 2H, Cy), 1.68 – 1.61 (m, 1H, Cy), 1.47 – 1.08 (m, 5H, Cy). ^{13}C{^{1}H} NMR (101.61 MHz, $CDCl_3$): δ = 141.6, 136.9, 132.6, 127.6, 124.8, 124.4, 124.1, 124.0, 122.8, 117.0 and 111.8 (Ar); 57.1, 34.3, 25.8 and 24.9 (Cy). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{20}N_3S$ 298.1372; Found 298.1378.



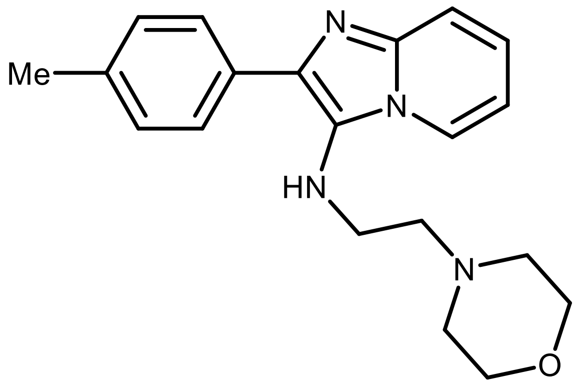
10. Yield: 60 % (77 mg). R_f = 0.40 (Hexane/EtOAc, 1:1). M.p.: 153–154 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.21 (d, $^3J_{HH}$ = 6.9 Hz, 1H, C_5H_4N), 7.82 (d, $^3J_{HH}$ = 8.1 Hz, 2H, C_6H_4–CH_3), 7.54 (d, $^3J_{HH}$ = 9.1 Hz, 1H, C_5H_4N), 7.23 (d, $^3J_{HH}$ = 7.9 Hz, 2H, C_6H_4–CH_3), 7.14 – 7.08 (m, 1H, C_5H_4N), 6.74 (t, $^3J_{HH}$ = 6.8 Hz, 1H, C_5H_4N), 3.13 (s, br, 1H, N*H*), 2.39 (s, 3H, C_6H_4–CH_3), 1.04 (s, 12H, $C(CH_3)_3$). ^{13}C{^{1}H} NMR (101.61 MHz, $CDCl_3$): δ = 141.9, 139.5, 137.0, 132.3, 129.0, 128.0, 123.9, 123.5, 123.3, 117.2 and 111.2 (Ar); 56.4 ($C(CH_3)_3$); 30.3 ($C(CH_3)_3$); 21.3 (C_6H_4–CH_3). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{23}N_3$ 280.1808; Found 280.1809.



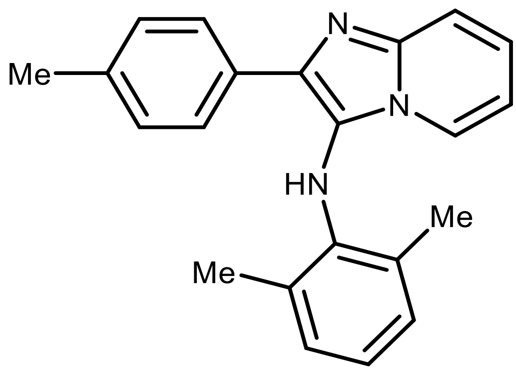
11. Yield: 77 % (128 mg). R_f = 0.39 (Hexane/EtOAc, 1:1). M.p.: 179–181 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.23 (d, $^3J_{HH}$ = 6.8 Hz, 1H, C_5H_4N), 7.86 (d, $^3J_{HH}$ = 8.0 Hz, 2H, C_6H_4–CH_3), 7.52 (d, $^3J_{HH}$ = 8.9 Hz, 1H, C_5H_4N), 7.22 (d, $^3J_{HH}$ = 8.2 Hz, 2H, C_6H_4–CH_3), 7.08 (t, $^3J_{HH}$ = 7.4 Hz, 1H, C_5H_4N), 6.71 (t, $^3J_{HH}$ = 6.8 Hz, 1H, C_5H_4N), 3.10 (s, br, 1H, N*H*), 2.38 (s, 3H, C_6H_4–CH_3), 1.92 (s, 3H, Ad), 1.67 – 1.39 (m, 12H, Ad). $^{13}C\{^1H\}$ NMR (101.61 MHz, $CDCl_3$): δ = 141.9, 139.4, 136.9, 132.3, 128.9, 128.0, 123.8, 123.6, 122.2, 117.1 and 111.1 (Ar); 56.6 (NH–C_{Ad}); 43.9, 36.2 and 29.7 (Ad); 21.3 (C_6H_4–CH_3). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{28}N_3$ 358.2278; Found 358.2278.



12. Yield: 63 % (93 mg). R_f = 0.37 (Hexane/EtOAc, 1:1). M.p.: 98–99 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.97 (d, $^3J_{HH}$ = 6.8 Hz, 1H, C_5H_4N), 7.91 (d, $^3J_{HH}$ = 8.1 Hz, 2H, Ar), 7.56 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C_5H_4N), 7.46 – 7.22 (m, 7H, Ar), 7.12 (m, 1H, C_5H_4N), 6.72 (t, $^3J_{HH}$ = 6.7 Hz, 1H, C_5H_4N), 4.19 (d, $^3J_{HH}$ = 6.2 Hz, 2H, CH_2), 3.58 – 3.46 (m, 1H, N*H*), 2.42 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (101.61 MHz, $CDCl_3$): δ = 141.5, 139.1, 137.2, 136.2, 131.3, 129.4, 128.7, 128.2, 127.6, 126.9, 125.4, 123.9, 122.3, 117.3 and 111.6 (Ar); 52.4 (CH_2); 21.3 (CH_3). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{20}N_3$ 314.1652; Found 314.1660.



13. Yield: 76% (119 mg). R_f = 0.15 (MeOH/$CHCl_3$, 1:9). M.p.: 128–129 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.14 (d, $^3J_{HH}$ = 6.8 Hz, 1H, C_5H_4N), 7.89 (d, $^3J_{HH}$ = 8.1 Hz, 2H, C_6H_4–CH_3), 7.58 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C_5H_4N), 7.26 (d, $^3J_{HH}$ = 7.9 Hz, 2H, C_6H_4–CH_3), 7.18 – 7.14 (m, 1H, C_5H_4N), 6.82 (td, $^3J_{HH}$ = 6.7, $^4J_{HH}$ = 1.1 Hz, 1H, C_5H_4N), 4.04 (d, $^3J_{HH}$ = 6.0 Hz, 1H, N*H*), 3.72 (t, $^3J_{HH}$ = 4.6 Hz, 4H, O–($CH_2)_2$), 3.14 – 3.02 (m, 2H, NH–CH_2), 2.59 – 2.53 (m, 2H, N–CH_2), 2.44 (t, $^3J_{HH}$ = 4.6 Hz, 4H, N–($CH_2)_2$), 2.41 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (101.61 MHz, $CDCl_3$): δ = 141.0, 137.3, 134.5, 131.0, 129.4, 126.9, 126.3, 124.1, 122.5, 117.2 and 111.8 (Ar); 67.0 (O–($CH_2)_2$), 58.3 (N–($CH_2)_2$); 53.7 (N–CH_2); 44.0 (NH–CH_2); 21.3 (CH_3). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{25}N_4O$ 337.2023; Found 337.2024.



14. Yield: 63 % (96 mg). R_f = 0.35 (Hexane/EtOAc, 2:1). M.p.: 187–189 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.02 (d, $^3J_{HH}$ = 7.9 Hz, 2H, Ar), 7.60 – 7.53 (m, 2H, Ar), 7.19 – 7.09 (m, 3H, Ar), 6.99 (d, $^3J_{HH}$ = 7.5 Hz, 2H, Ar), 6.81 (t, $^3J_{HH}$ = 7.5 Hz, 1H, Ar), 6.66 (t, $^3J_{HH}$ = 6.8 Hz, 1H, Ar), 5.45 (s, br, 1H, N*H*), 2.36 (s, 3H, C_6H_4–CH_3), 2.02 (s, 6H, C_6H_3–($CH_3)_2$). ^{13}C{^{1}H} NMR (101.61 MHz, $CDCl_3$): δ = 141.2, 140.4, 137.5, 137.2, 130.8, 129.9, 129.1, 126.9, 125.3, 124.1, 122.3, 120.9, 120.5, 117.4 and 112.1 (Ar); 21.3 (C_6H_4–CH_3); 18.6 (C_6H_3–($CH_3)_2$). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{22}N_3$ 328.1808; Found 328.1810

Spectra of 1a, Cat1^{OTf}–Cat4^{OTf}, and 1–14

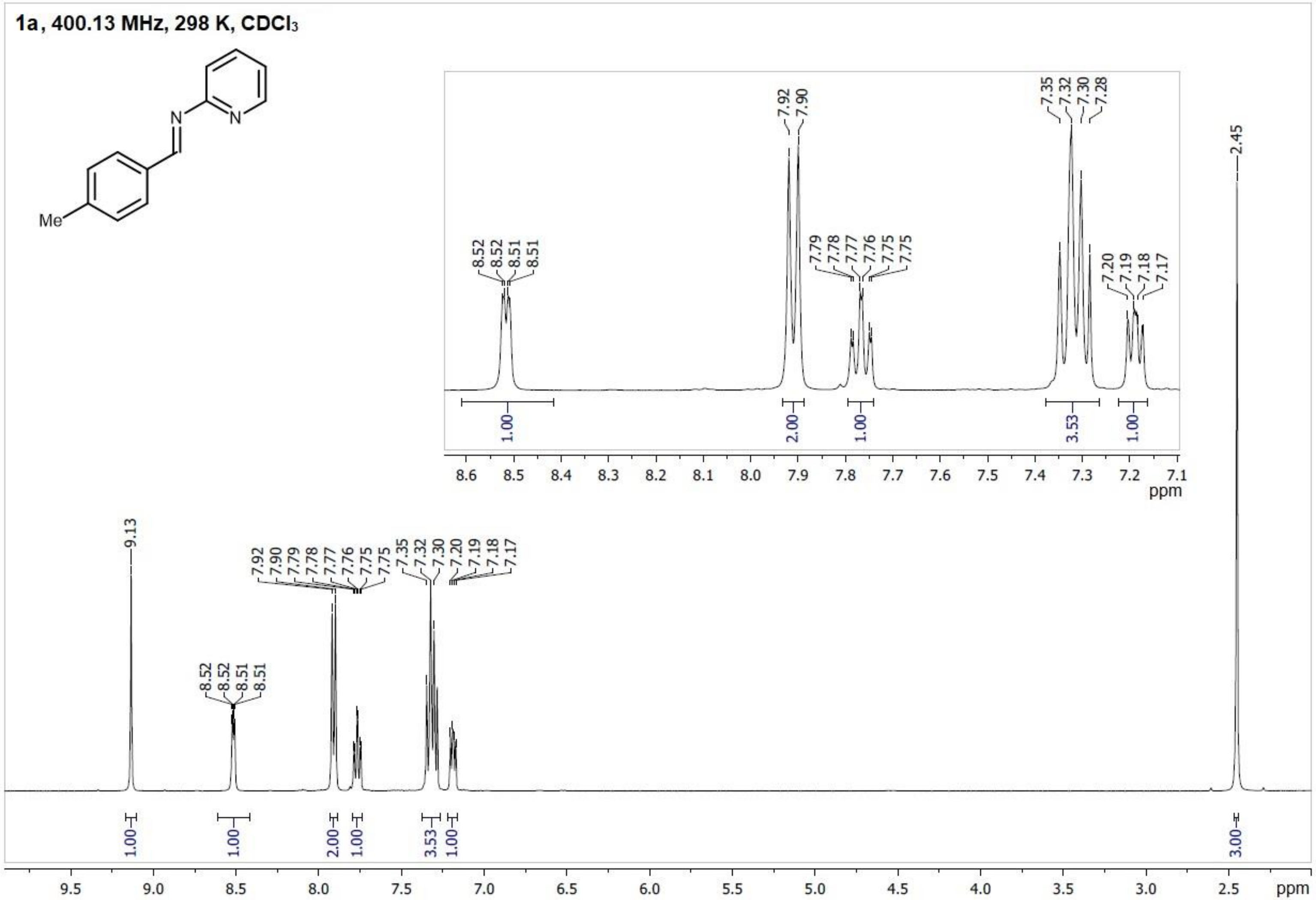


Figure S8. ^{1}H NMR spectrum of the imine **1a**.

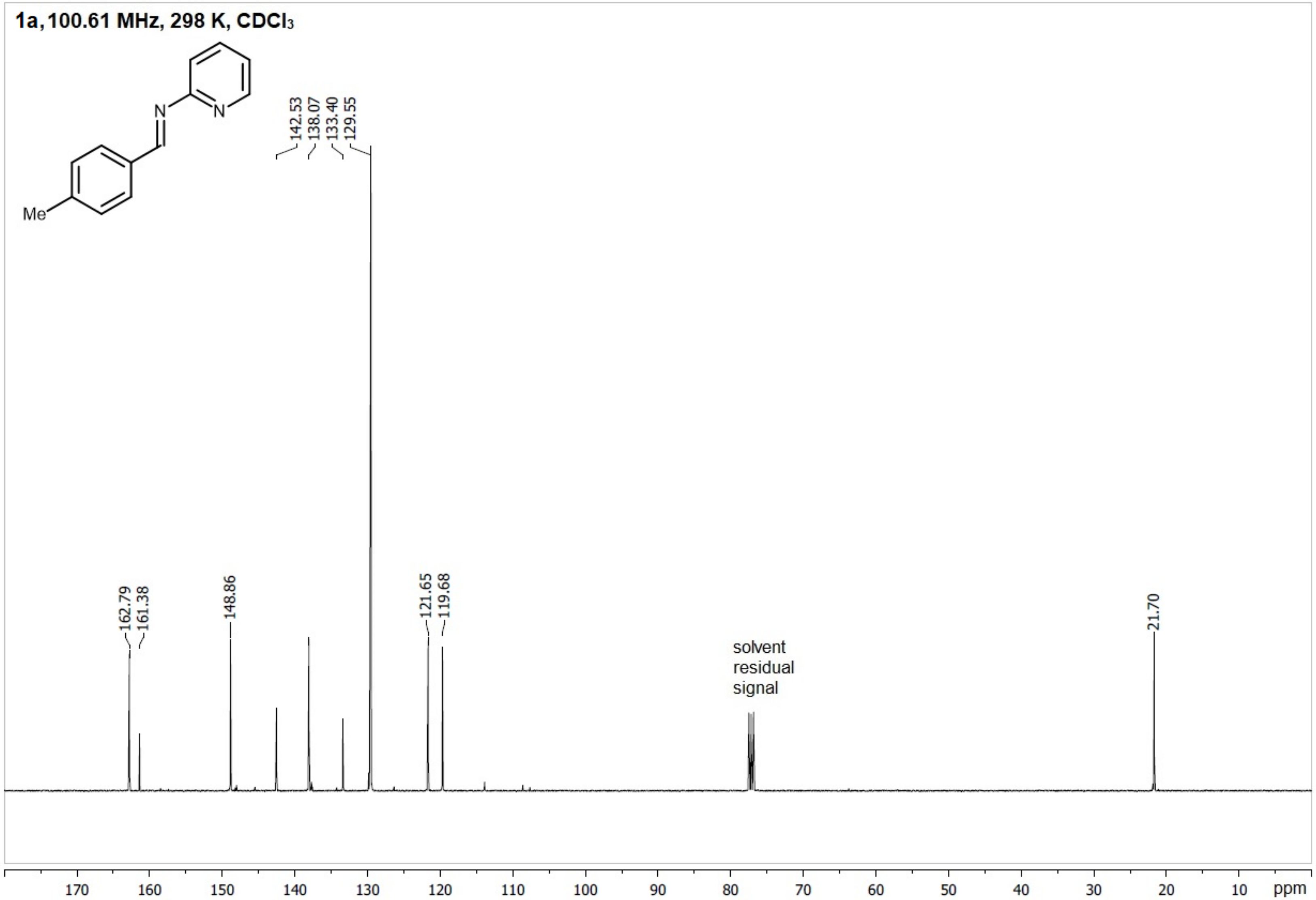


Figure S9. $^{13}C\{^1H\}$ NMR spectrum of the imine **1a**.

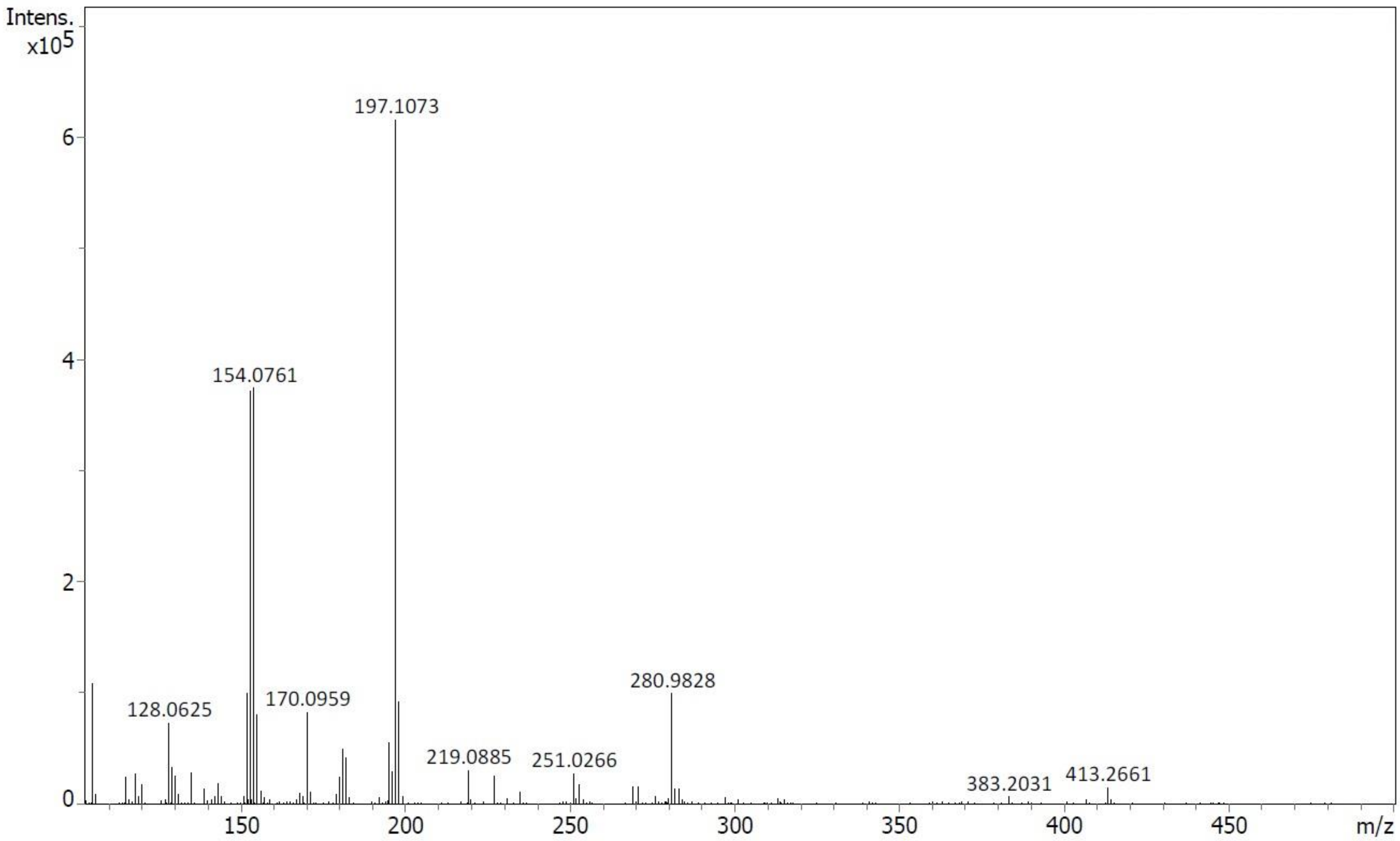


Figure S10. HRESI$^+$-MS of the imine **1a**.

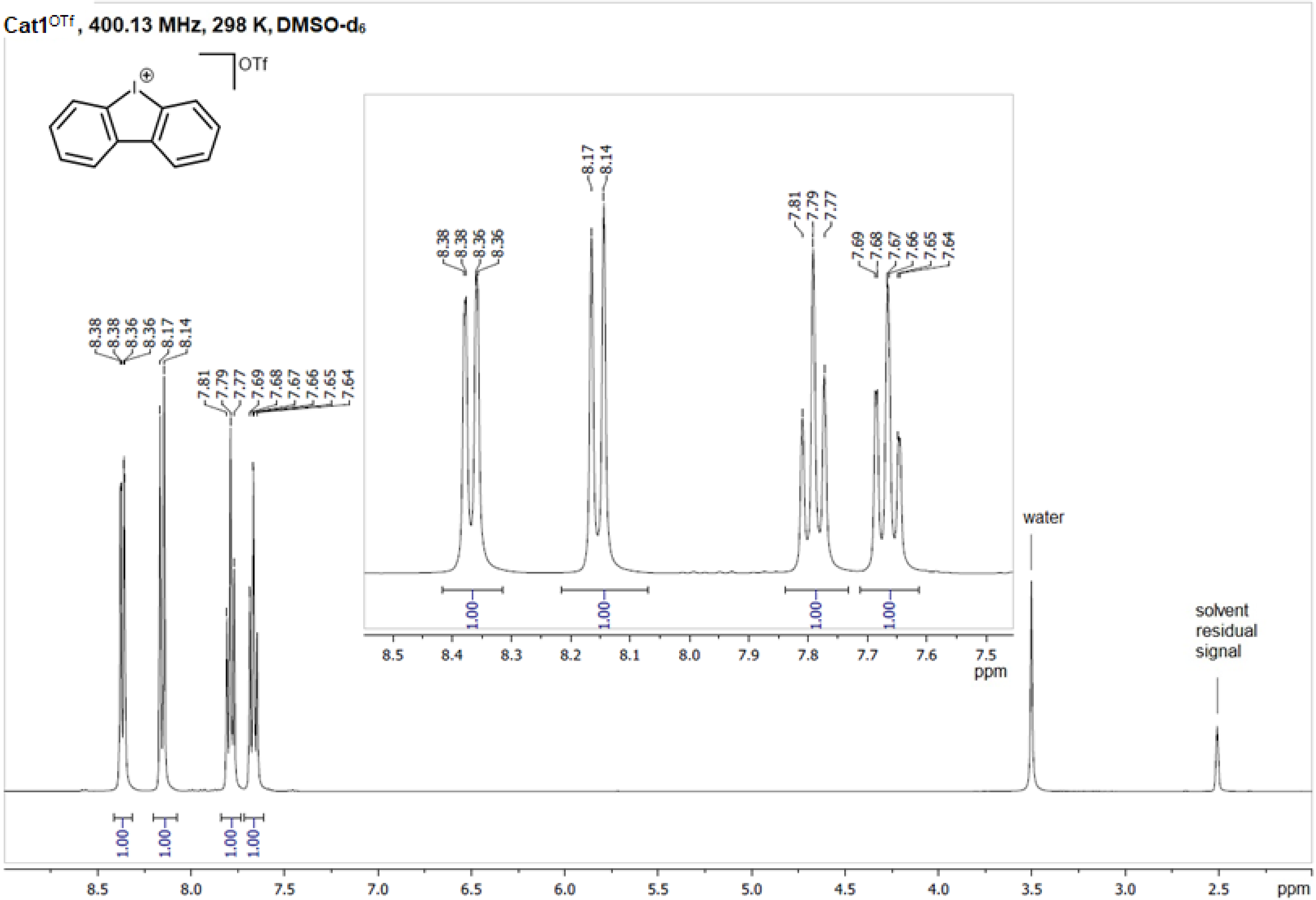


Figure S11. ^{1}H NMR spectrum of **Cat1**^{OTf}.

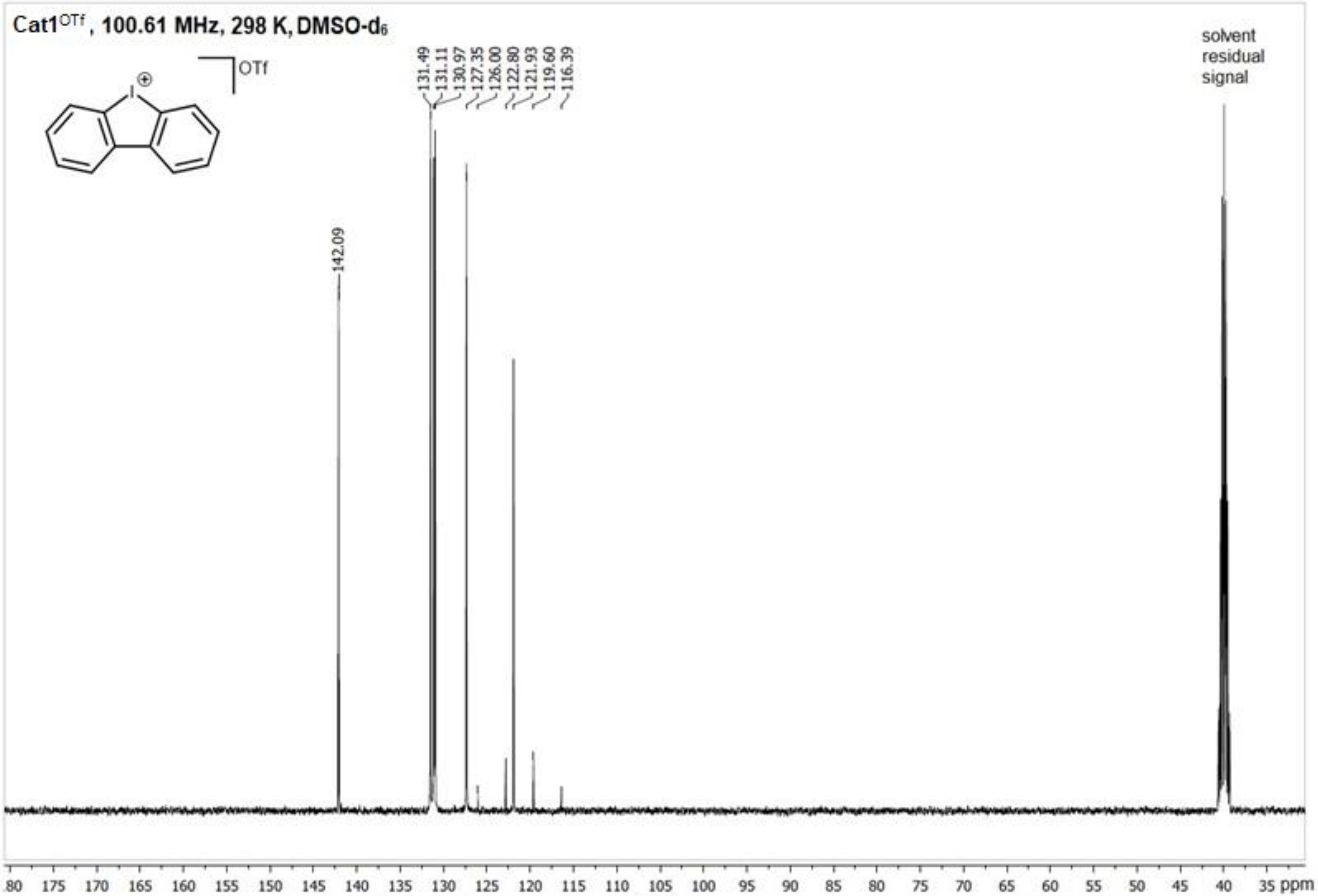


Figure S12. $^{13}C\{^{1}H\}$ NMR spectrum of **Cat1**^{OTf}.

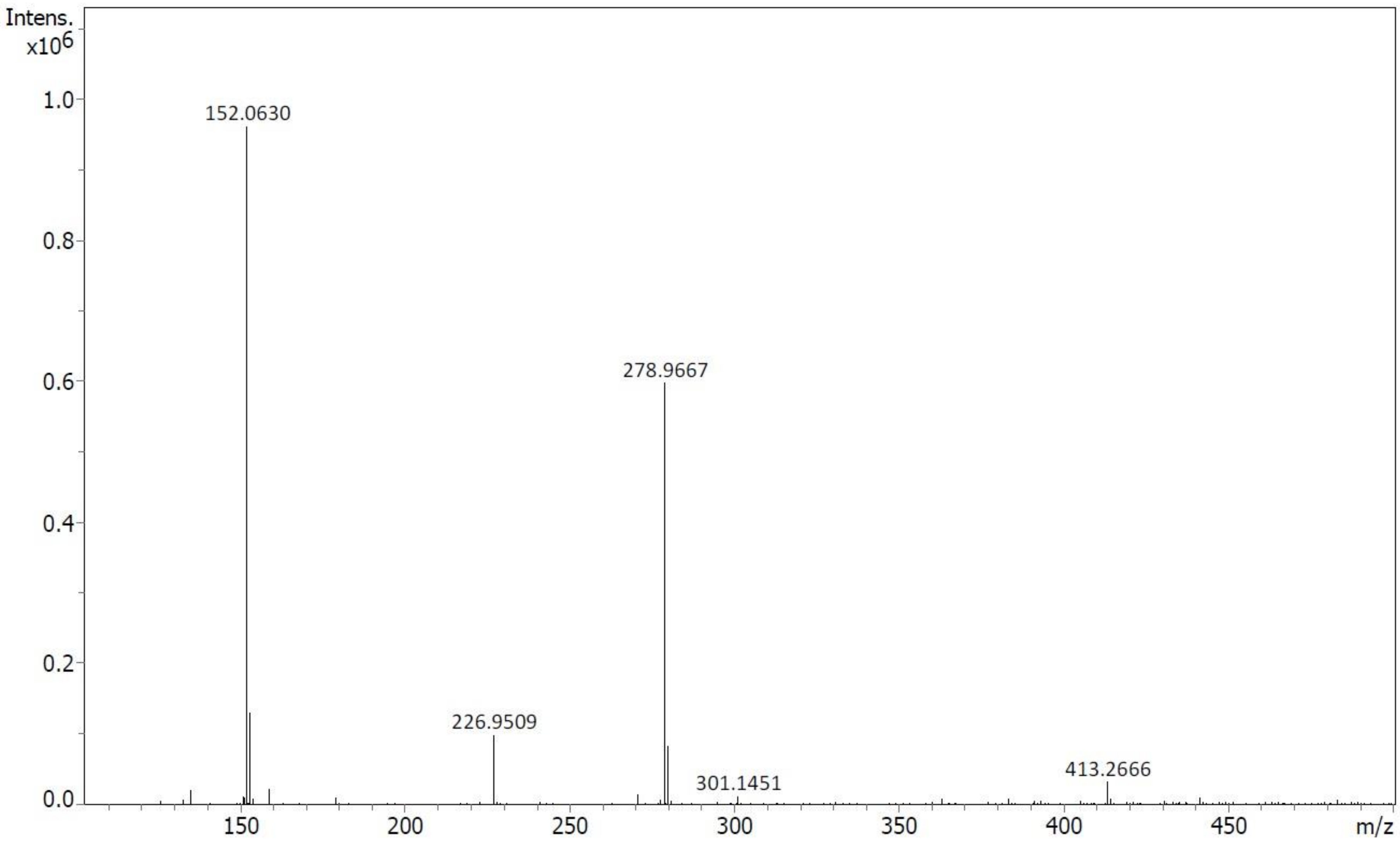


Figure S13. HRESI^{+}-MS of **Cat1**^{OTf}.

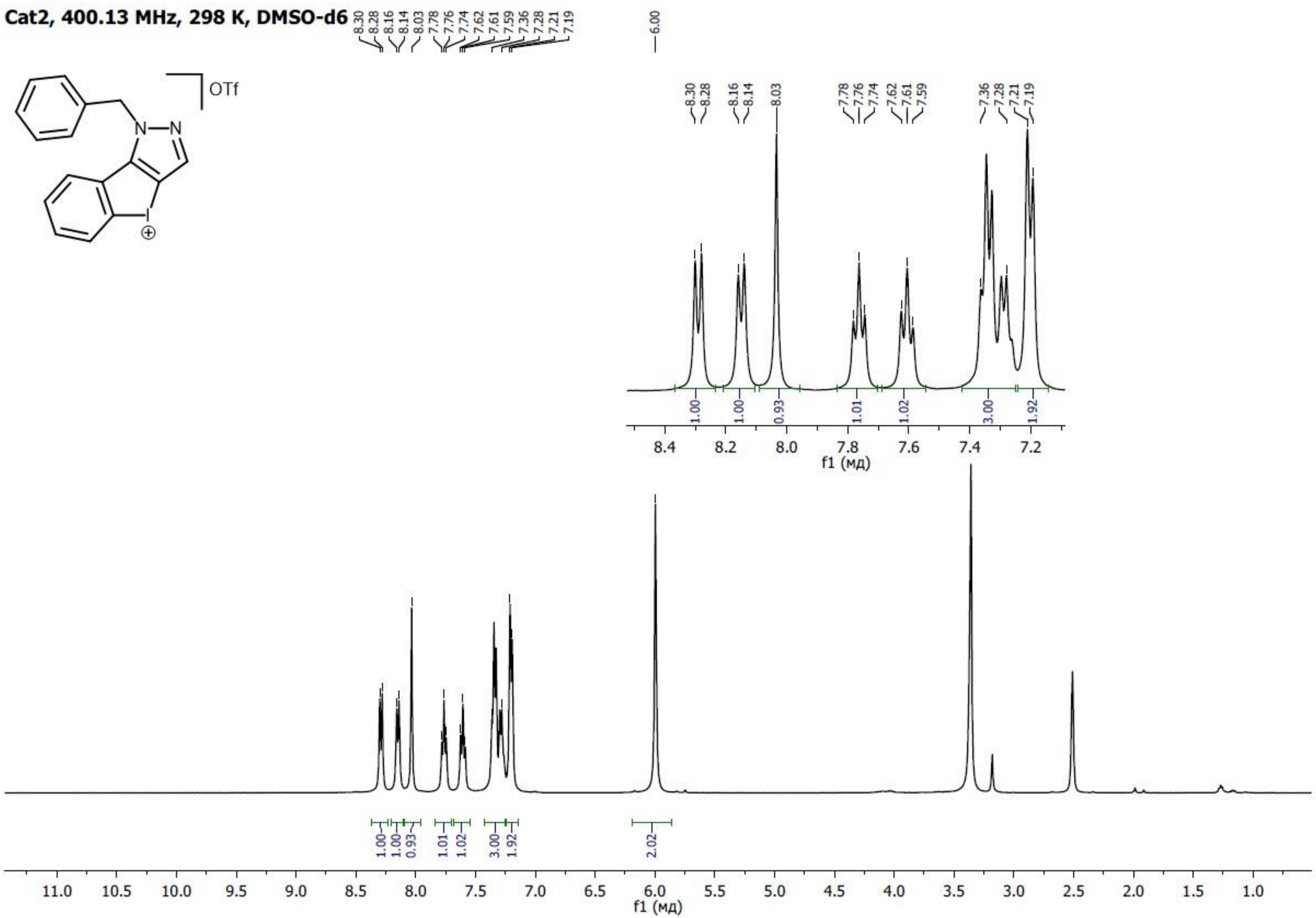


Figure S14. ^{1}H NMR spectrum of **Cat2**^{OTf}.

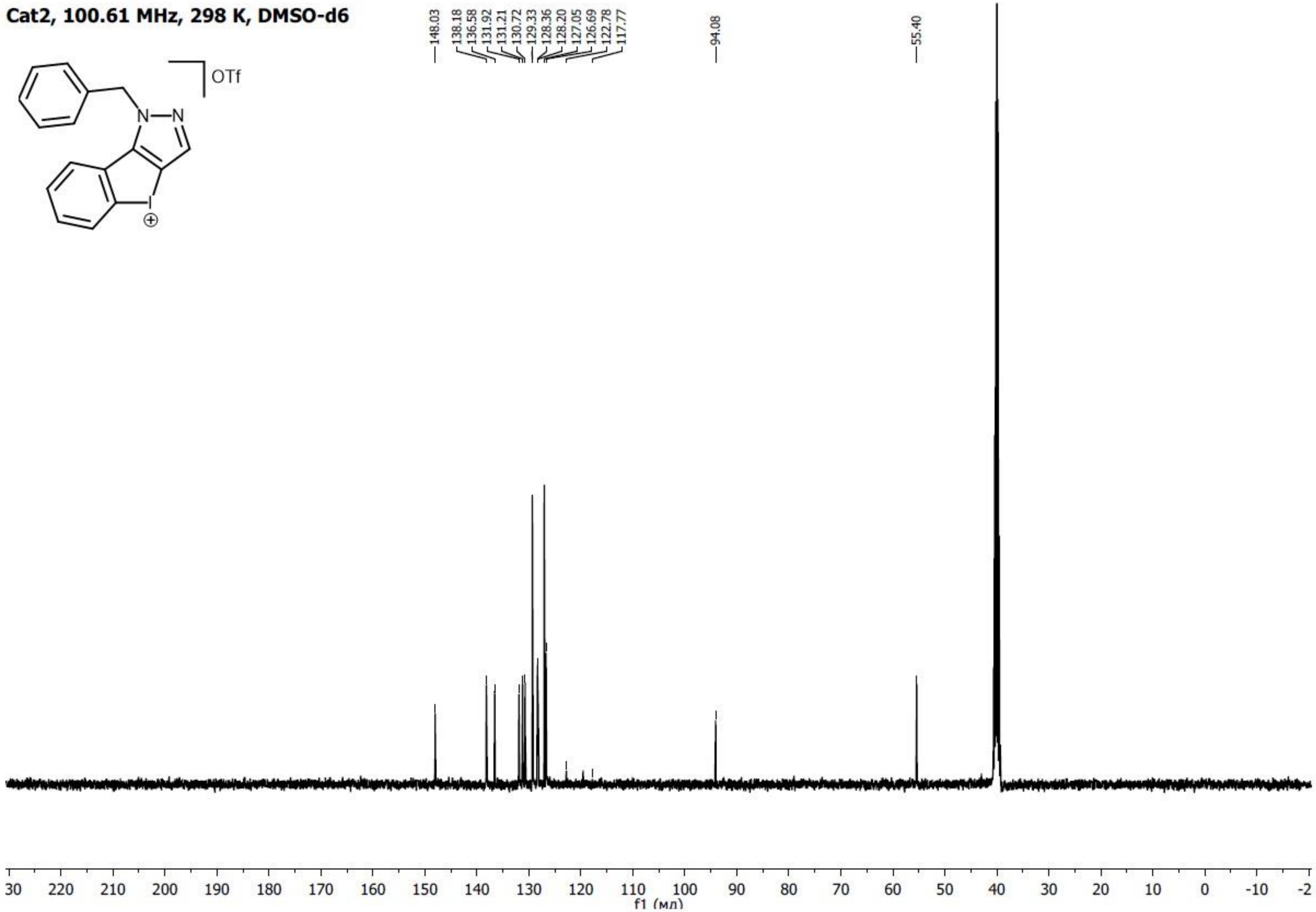


Figure S15. ^{13}C NMR spectrum of **Cat2**^{OTf}.

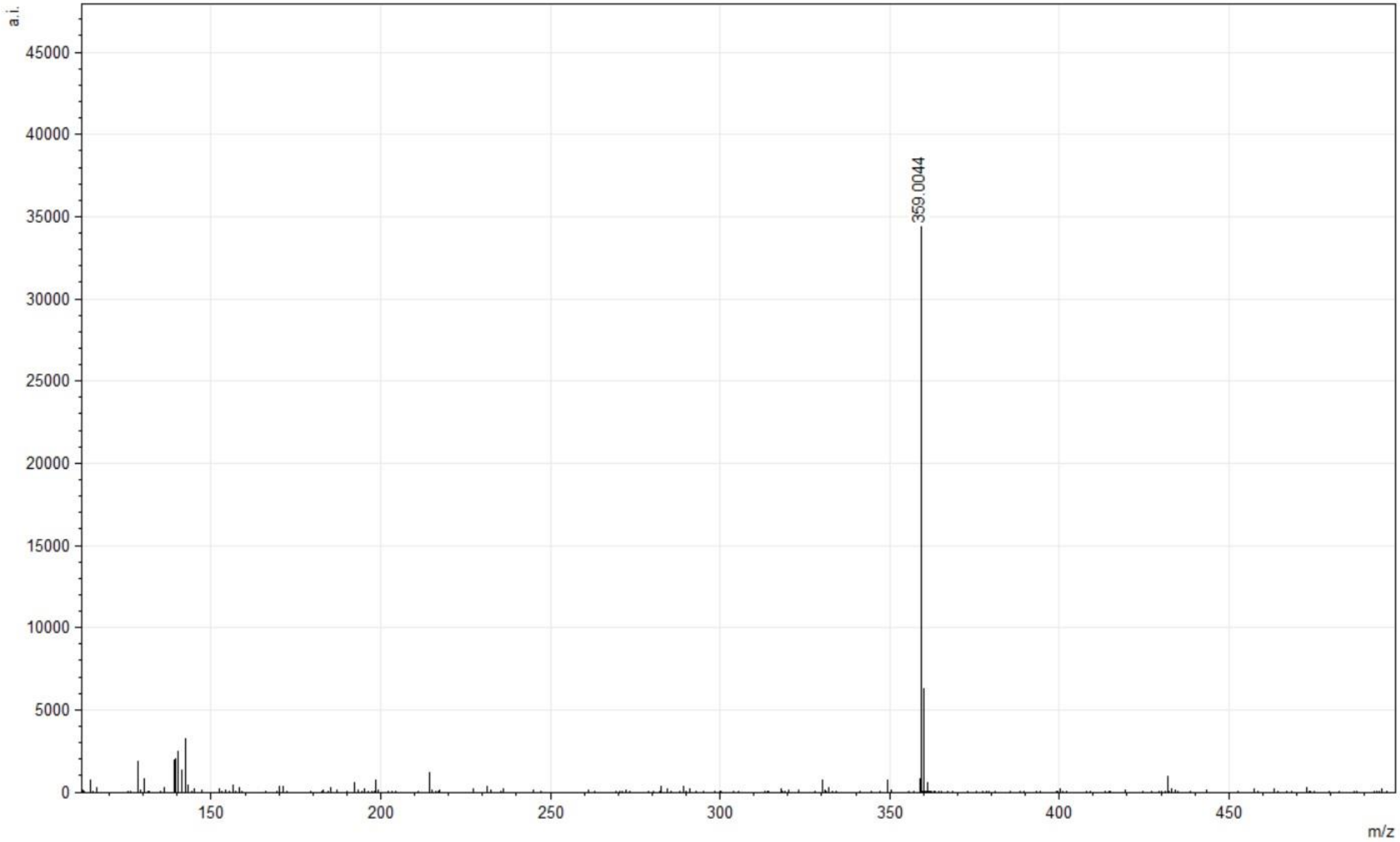


Figure S16. HRESI$^+$-MS of **Cat2**^{OTf}.

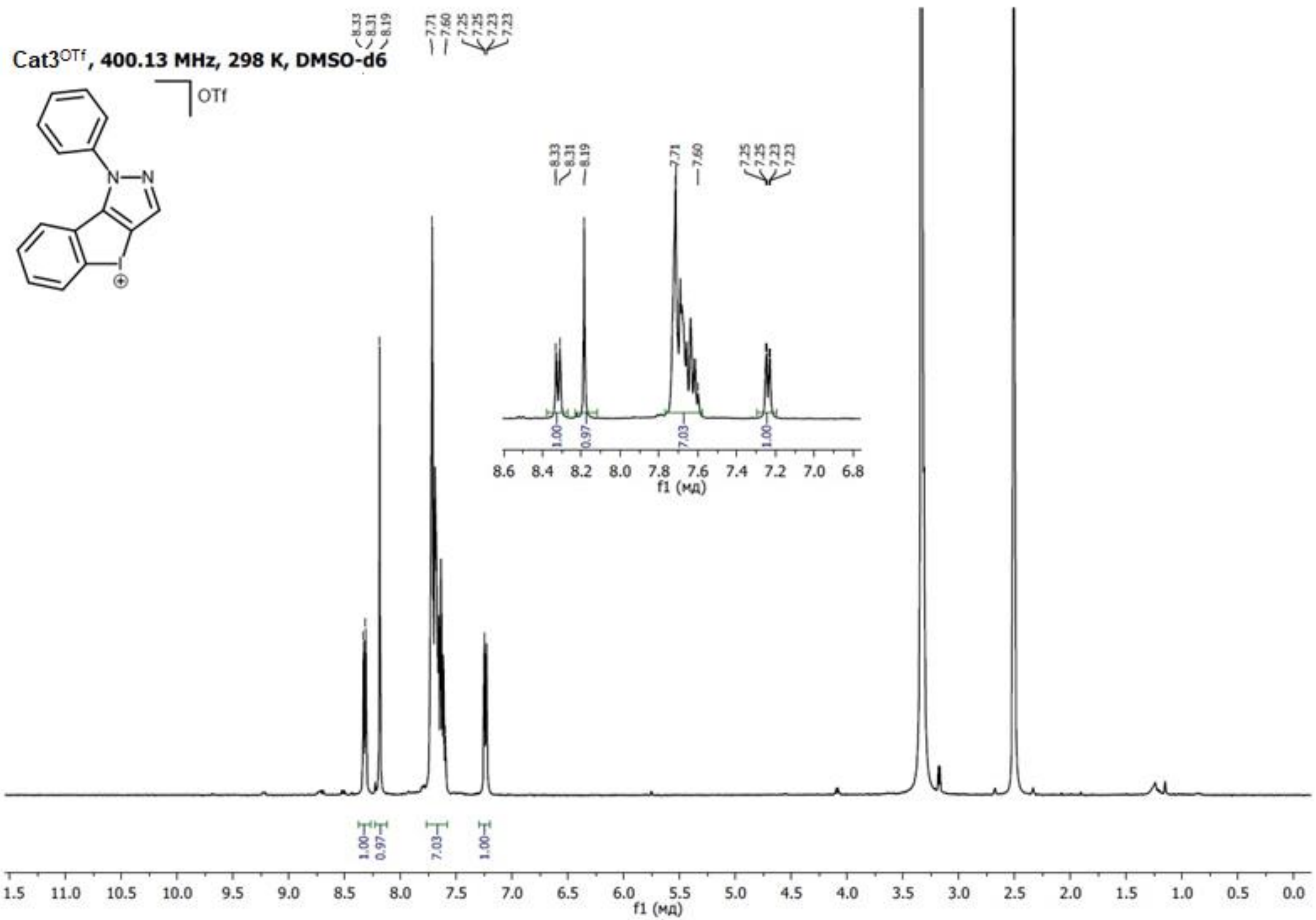


Figure S17. ^{1}H NMR spectrum of **Cat3**^{OTf}.

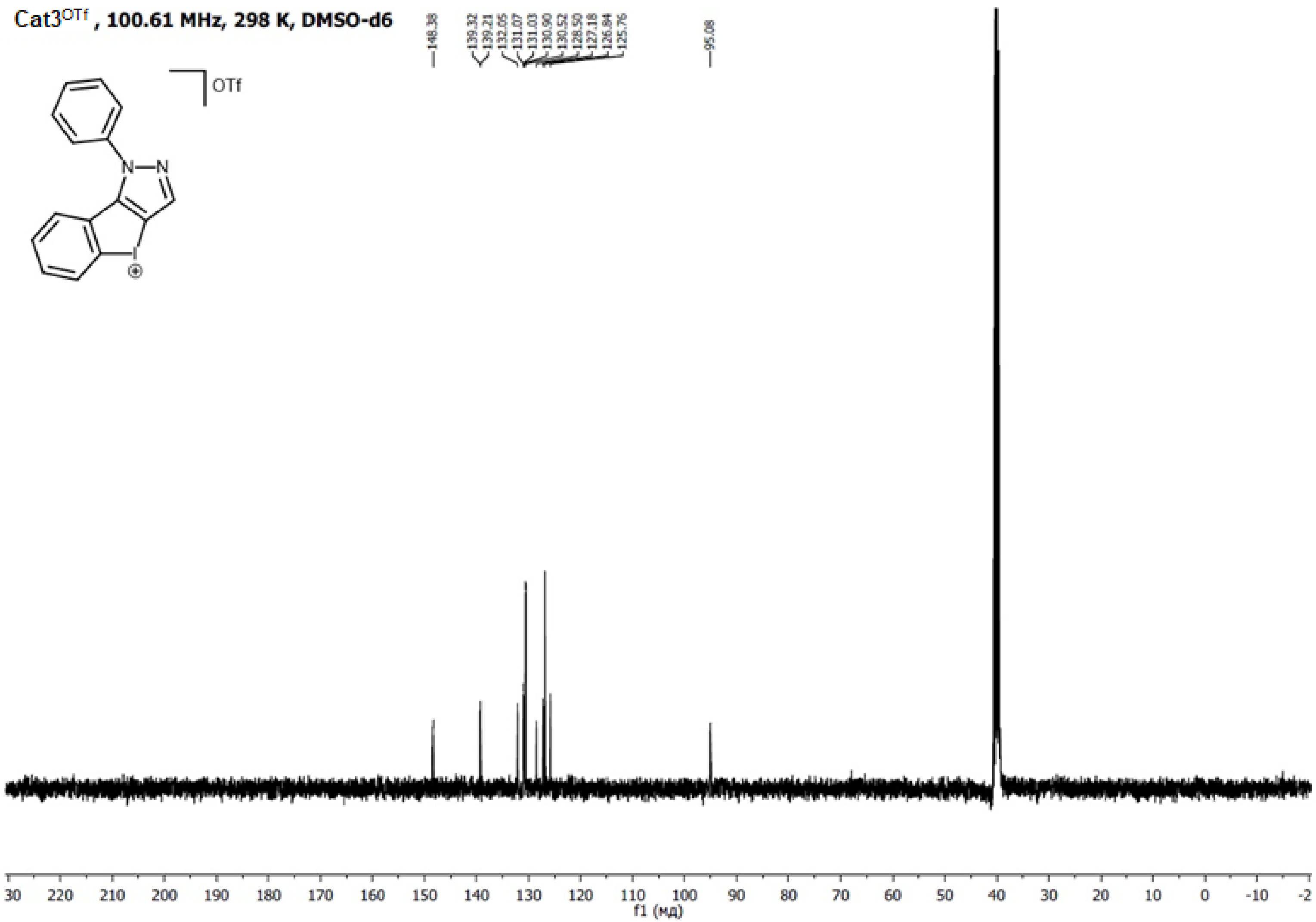


Figure S18. ^{13}C NMR spectrum of **Cat3**^{OTf}.

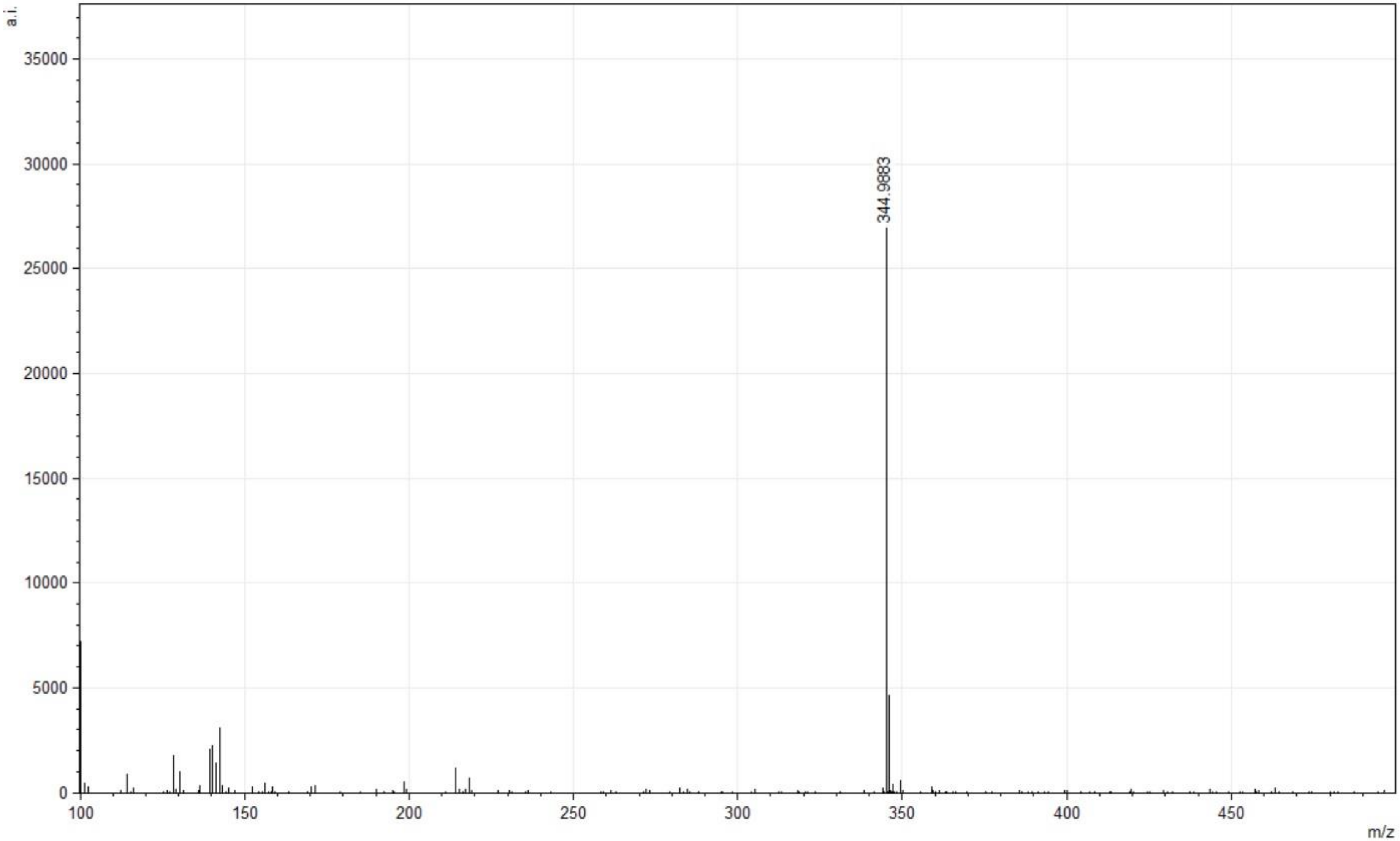


Figure S19. HRESI+-MS of **Cat3**^{OTf}.

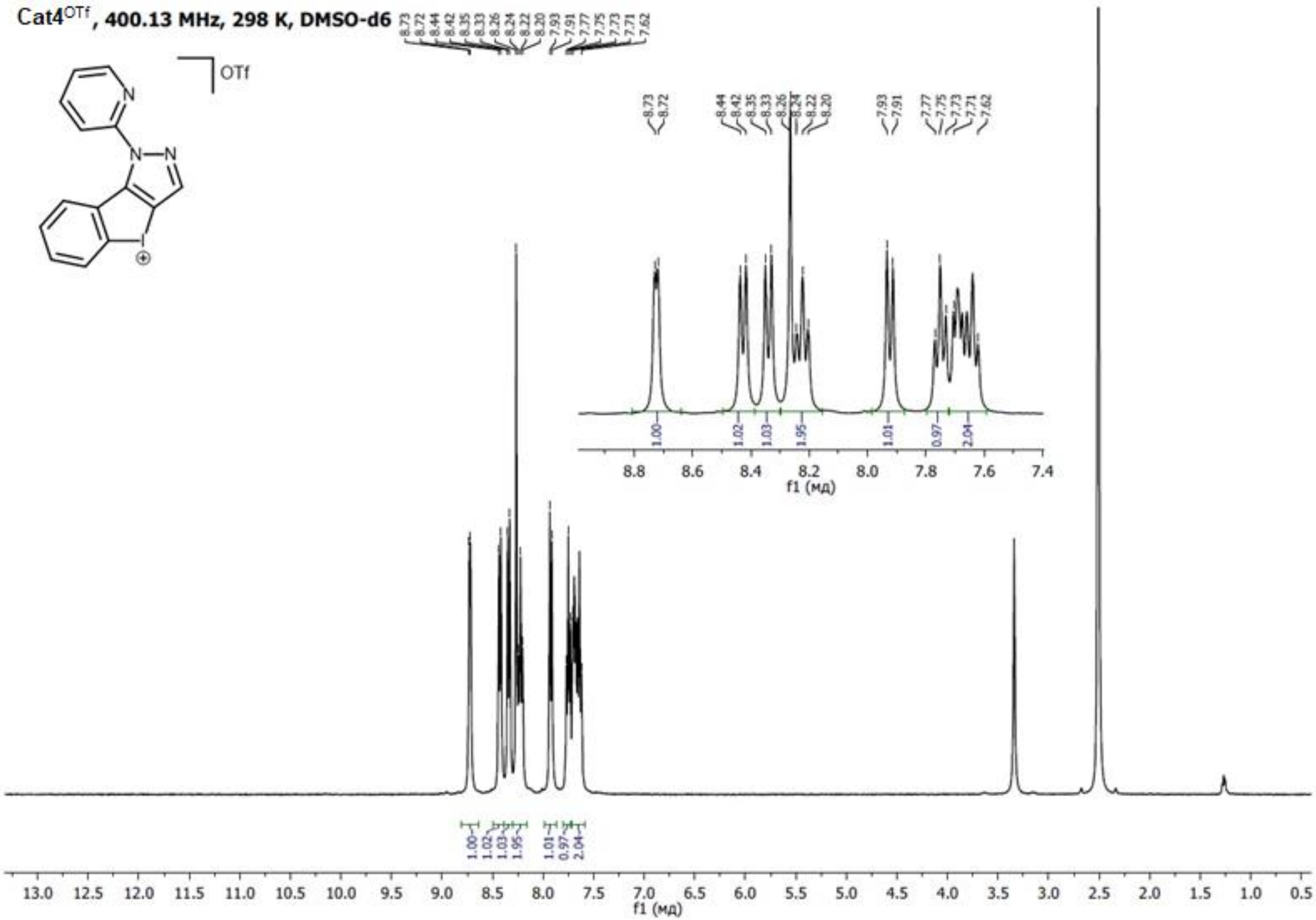


Figure S20. ^{1}H NMR spectrum of **Cat4**^{OTf}.

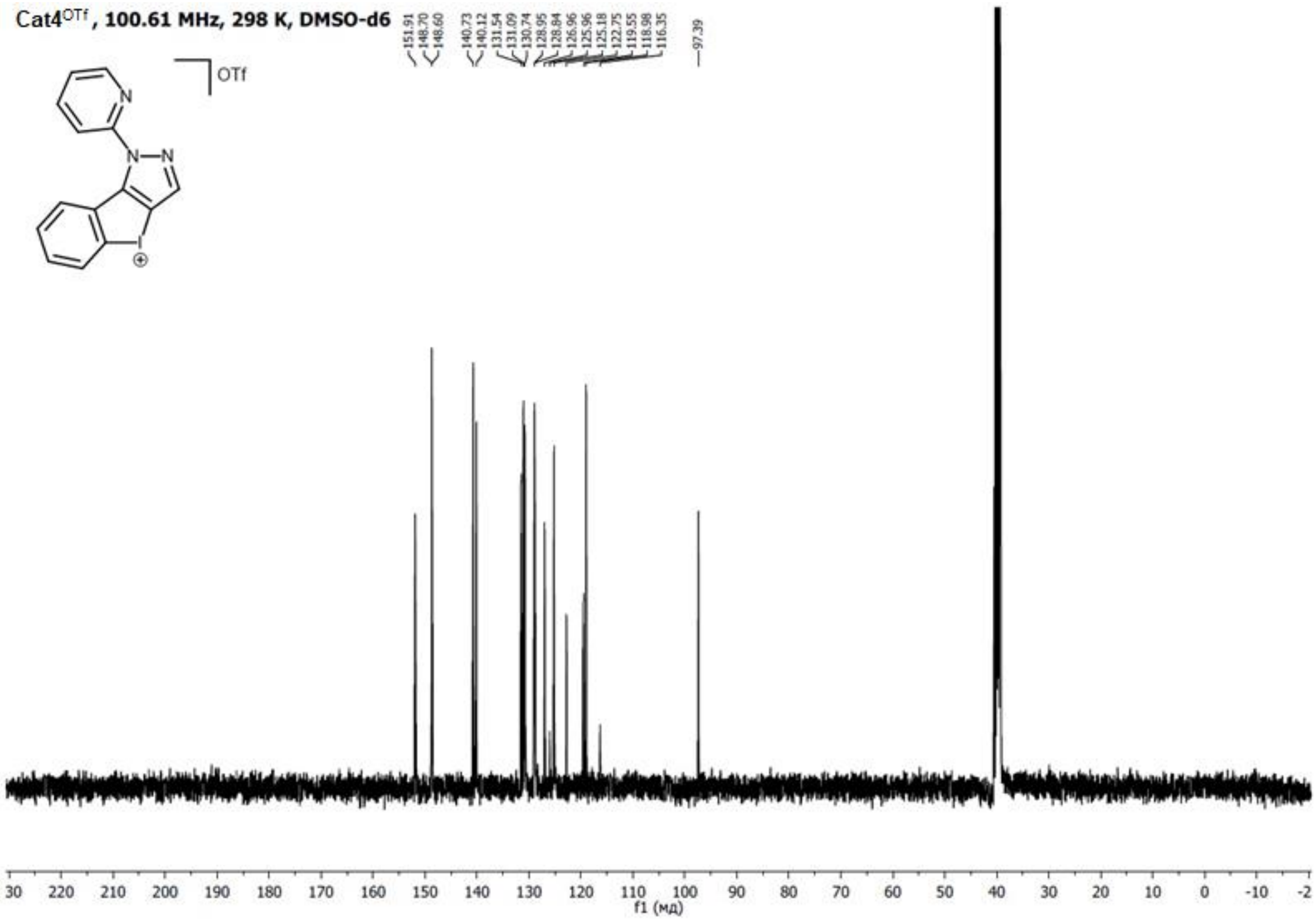


Figure S21. ^{13}C NMR spectrum of **Cat4**^{OTf}.

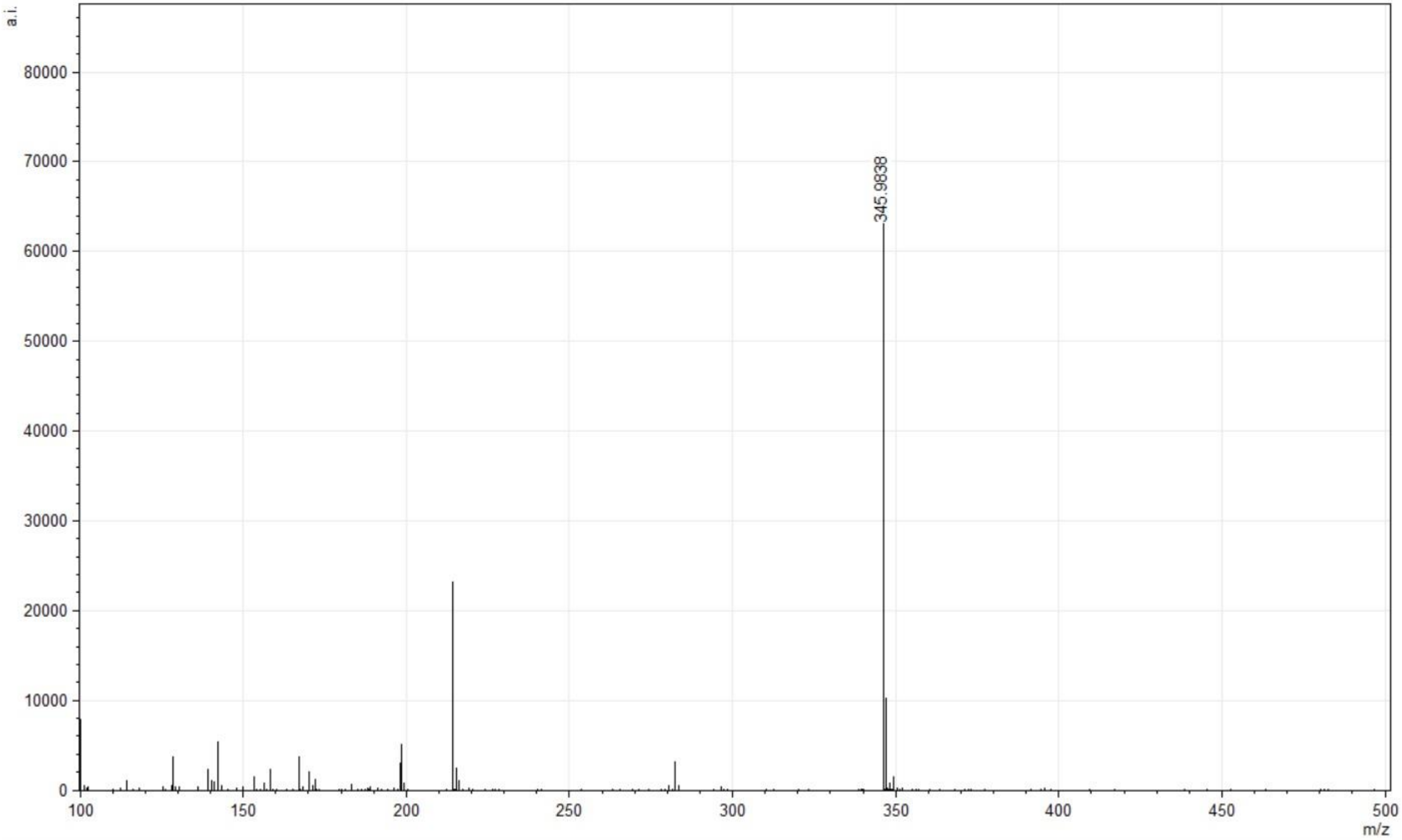


Figure S22. HRESI$^+$-MS of **Cat4**^{OTf}.

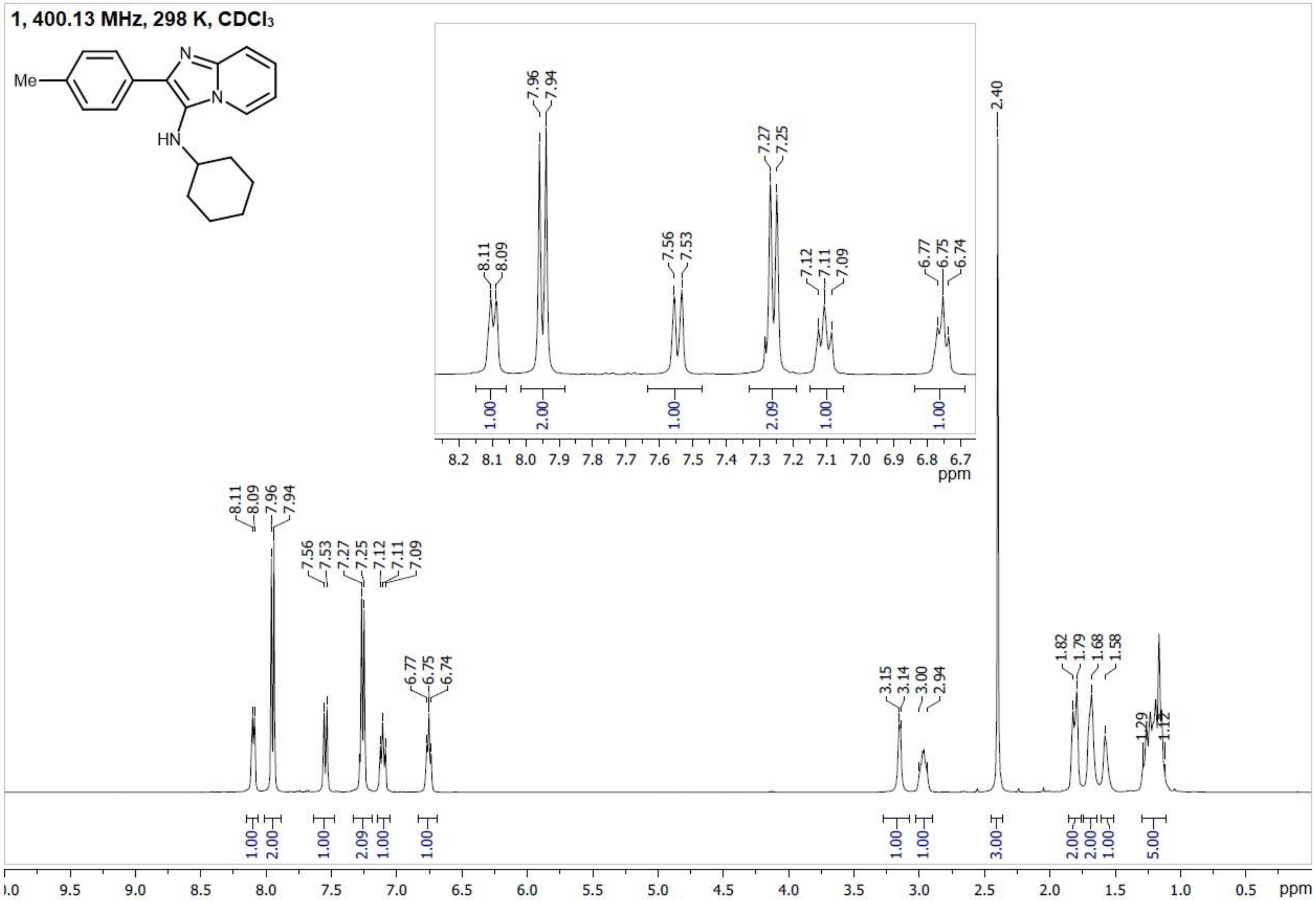


Figure S23. ^{1}H NMR spectrum of **1**.

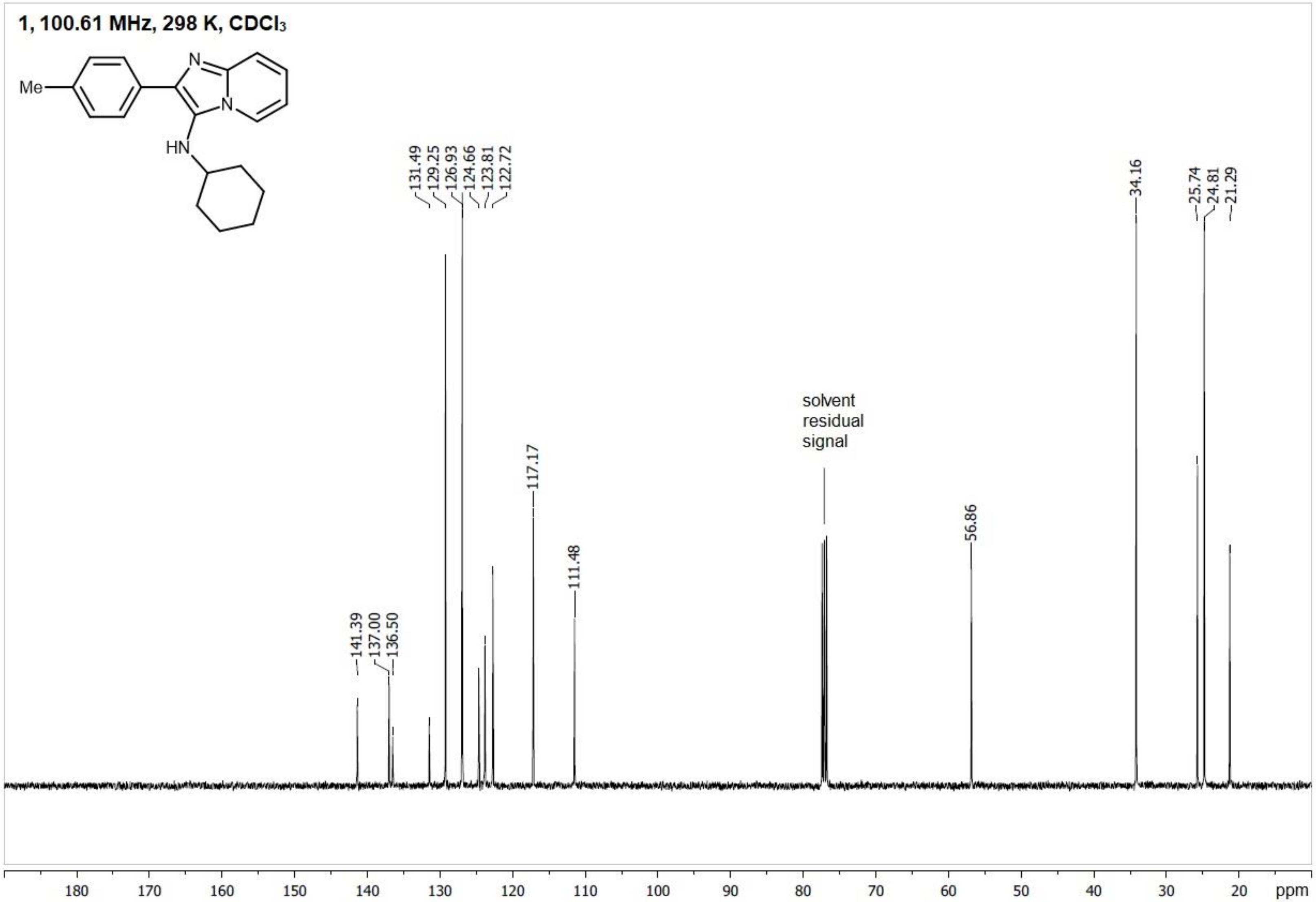


Figure S24. $^{13}C\{^{1}H\}$ NMR spectrum of **1**.

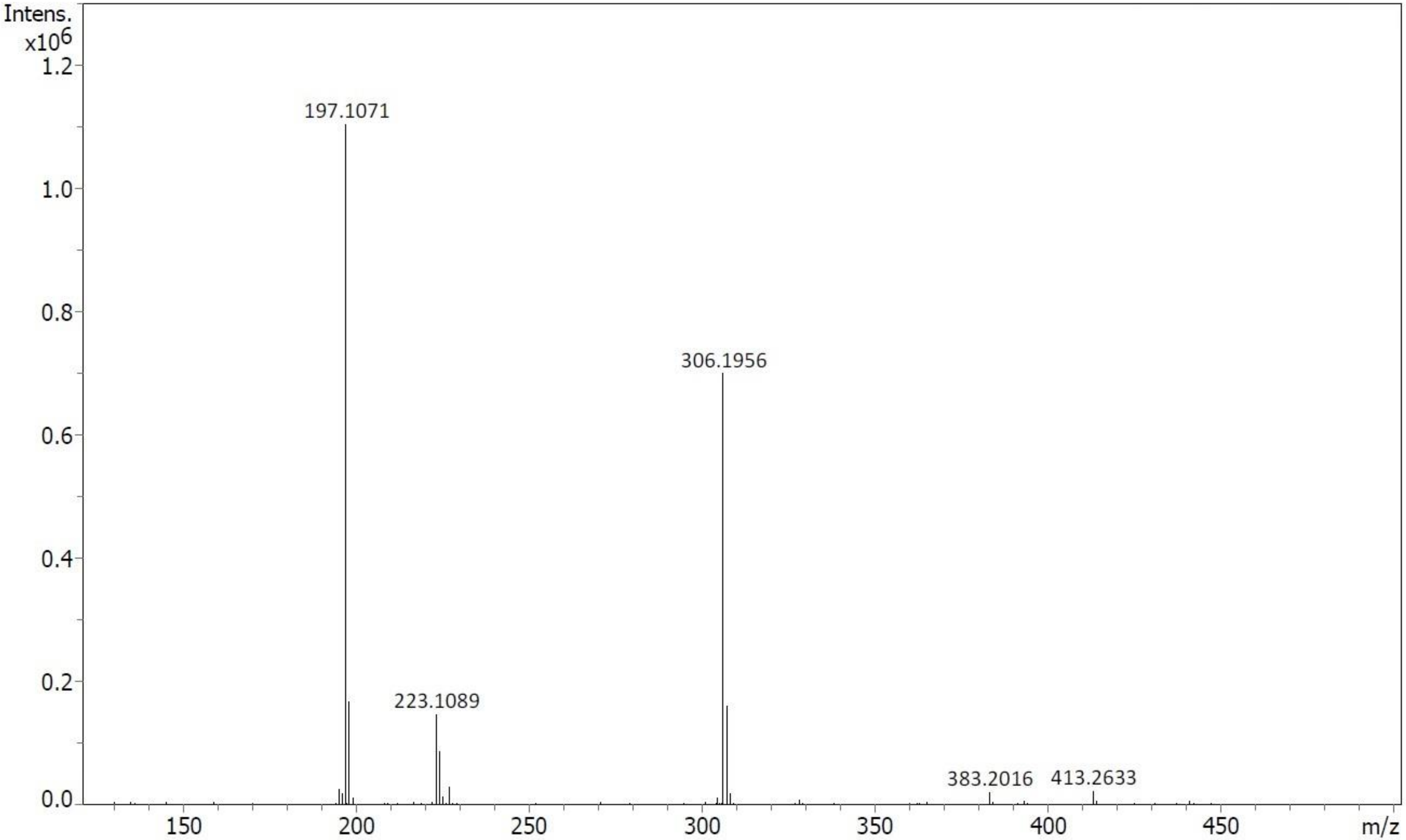


Figure S25. HRESI$^+$-MS of **1**.

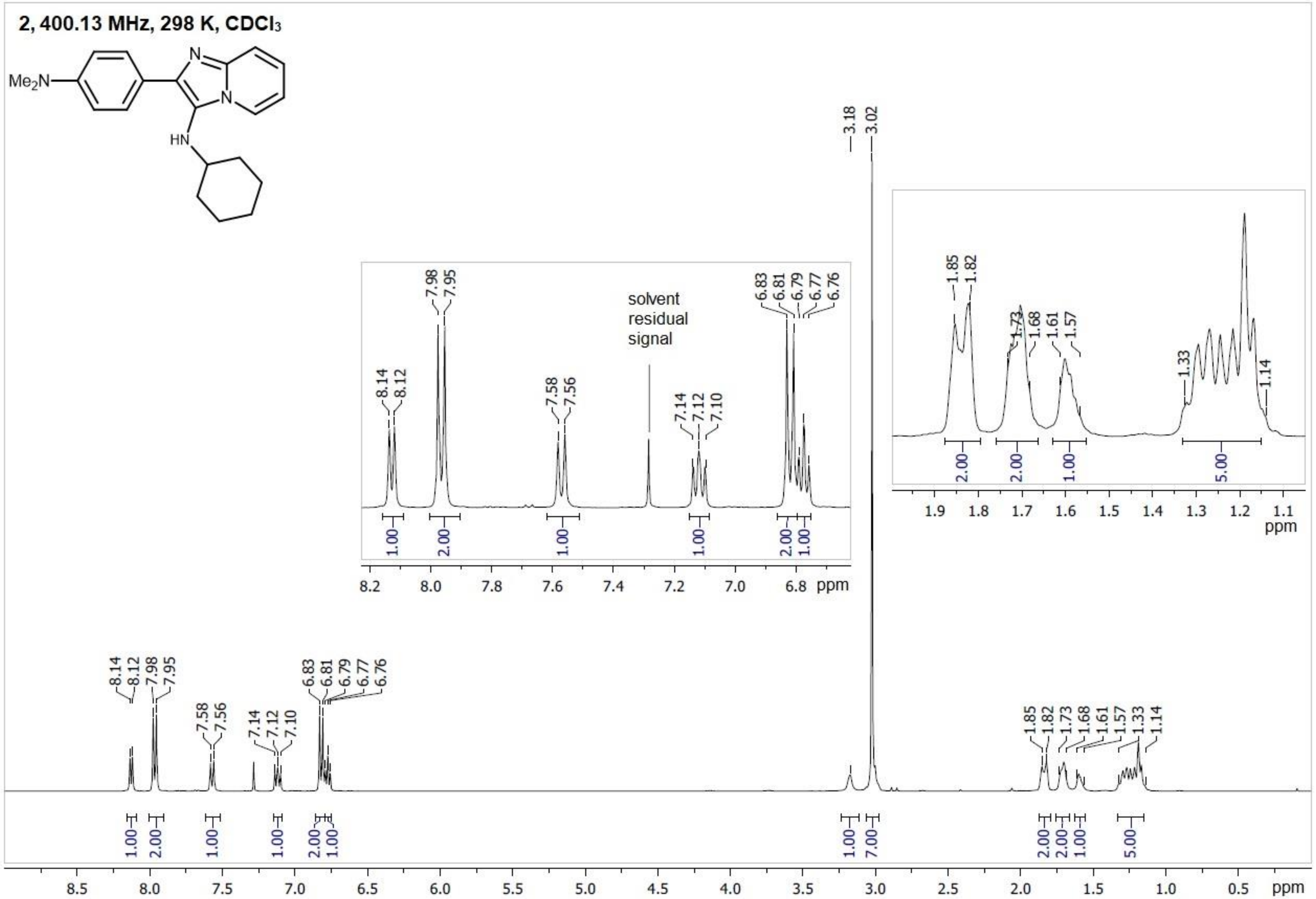


Figure S26. ^{1}H NMR spectrum of **2.**

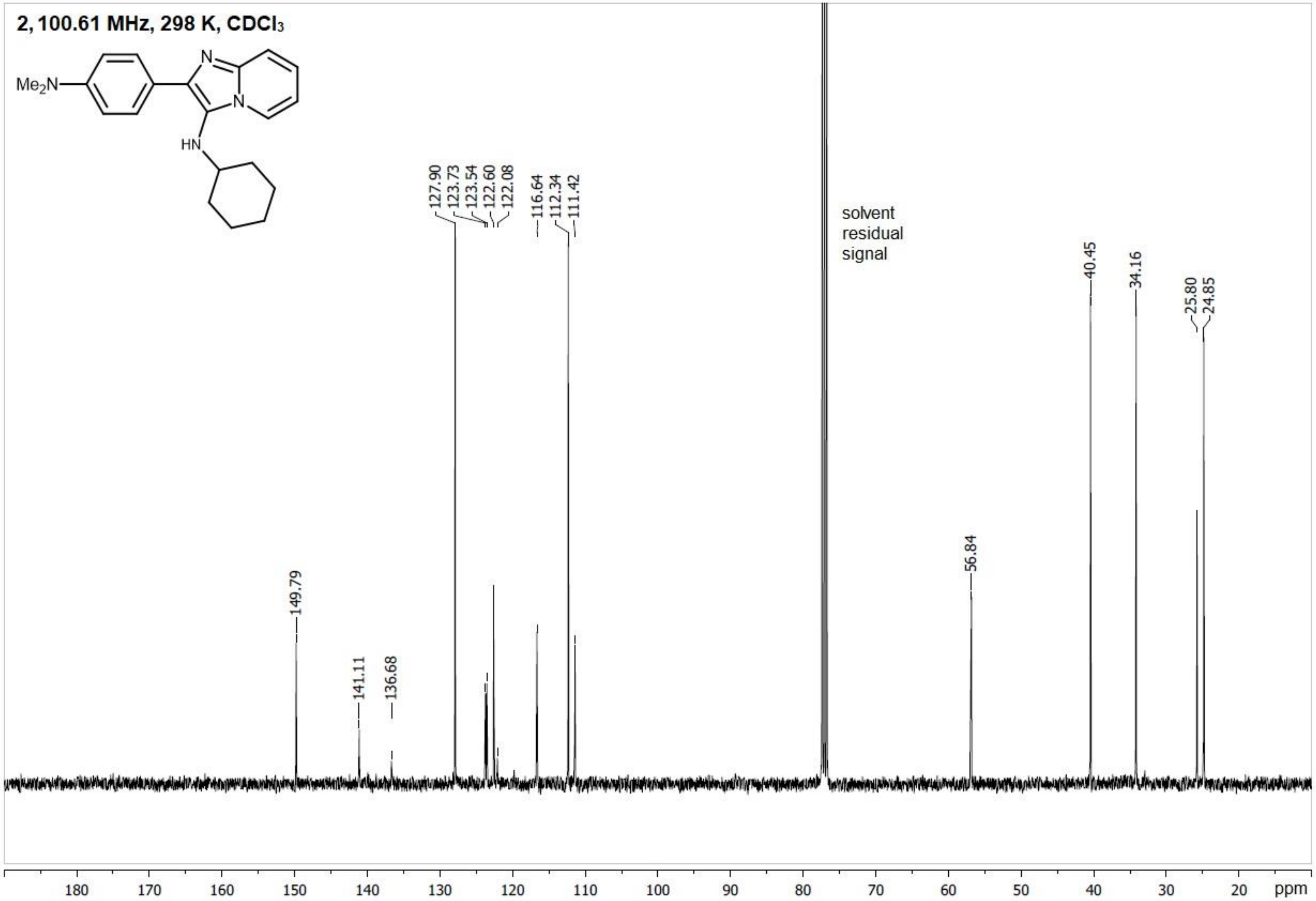


Figure S27. $^{13}C\{^1H\}$ NMR spectrum of **2**.

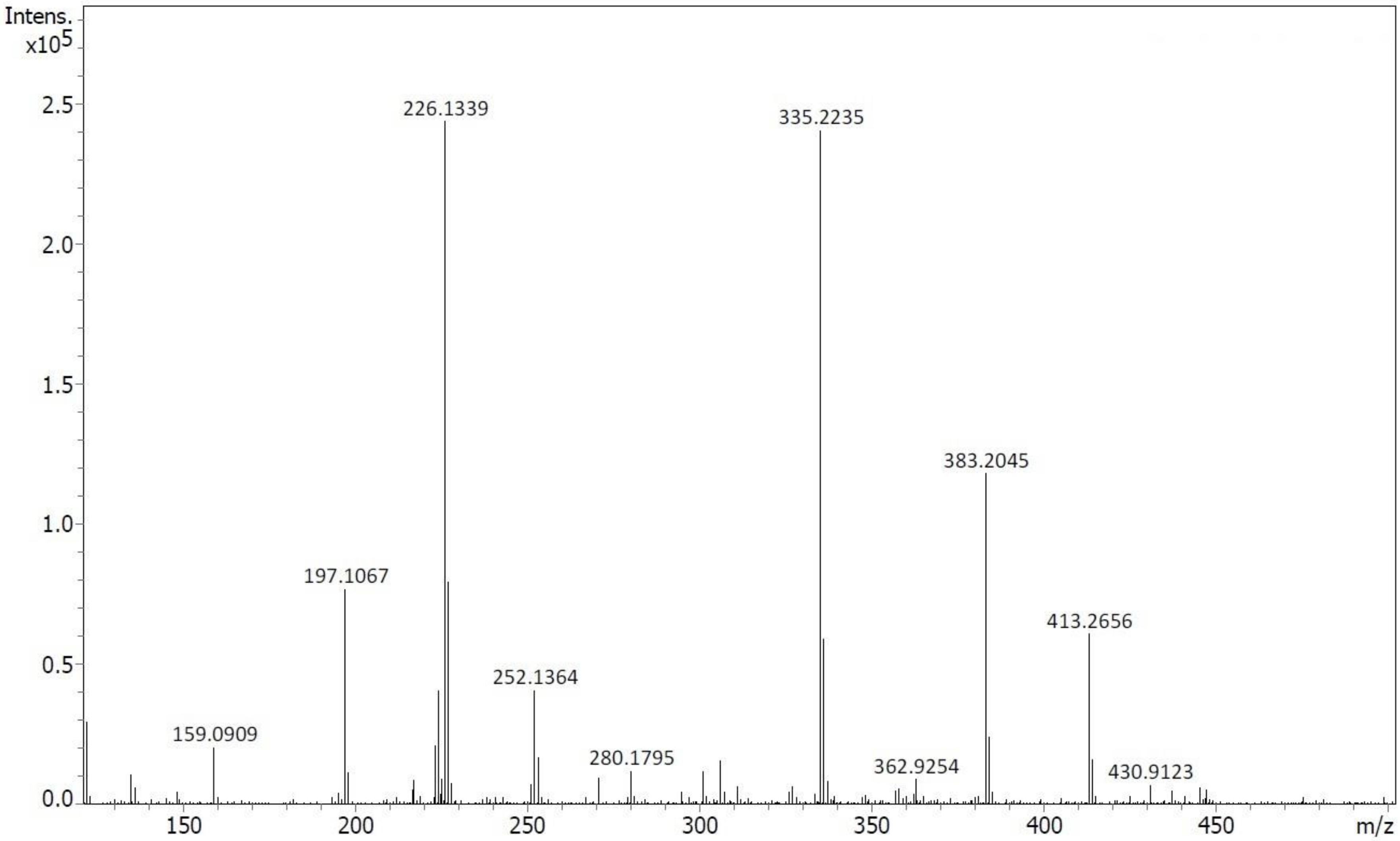


Figure S28. HRESI$^+$-MS of **2**.

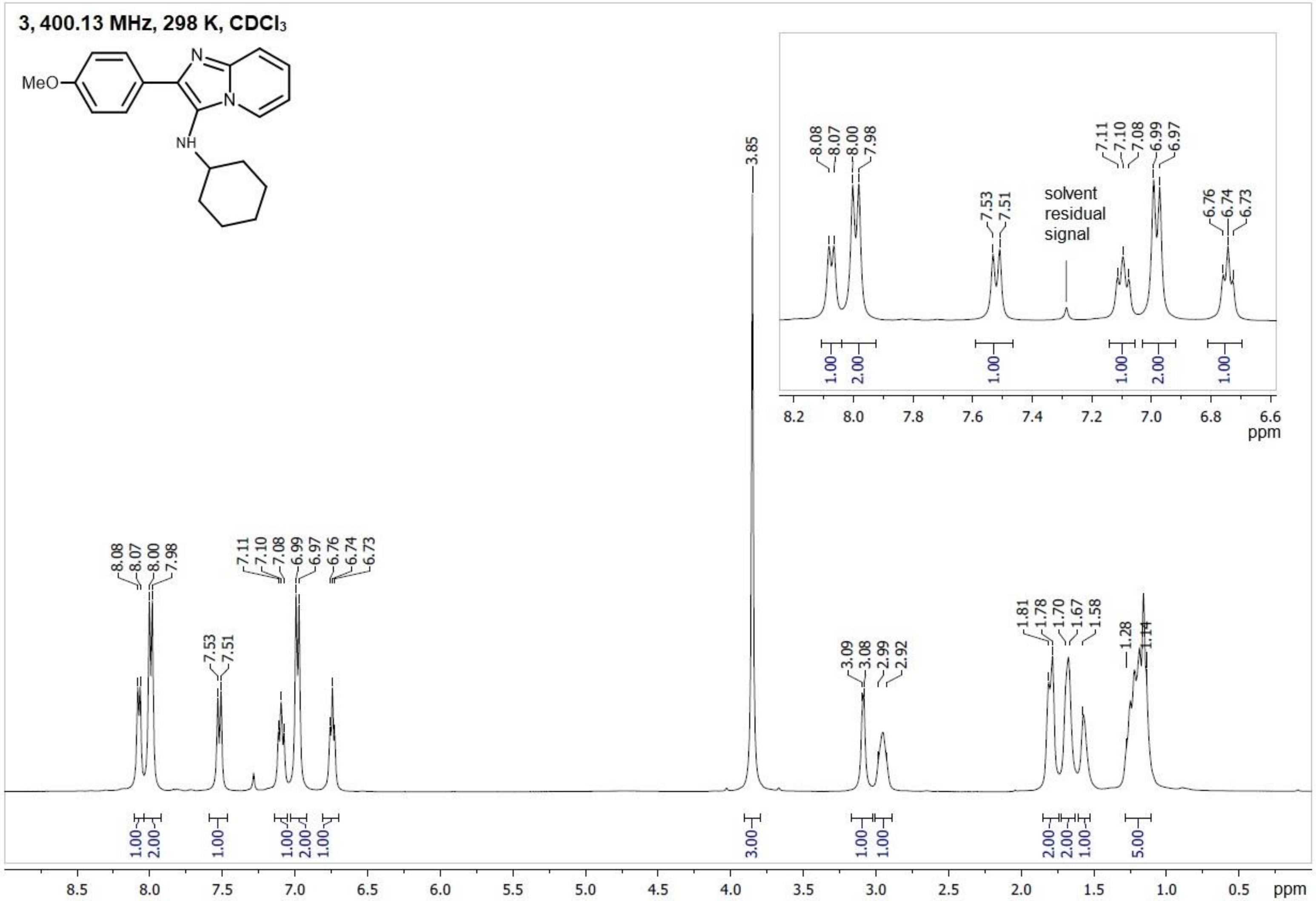


Figure S29. ^{1}H NMR spectrum of **3.**

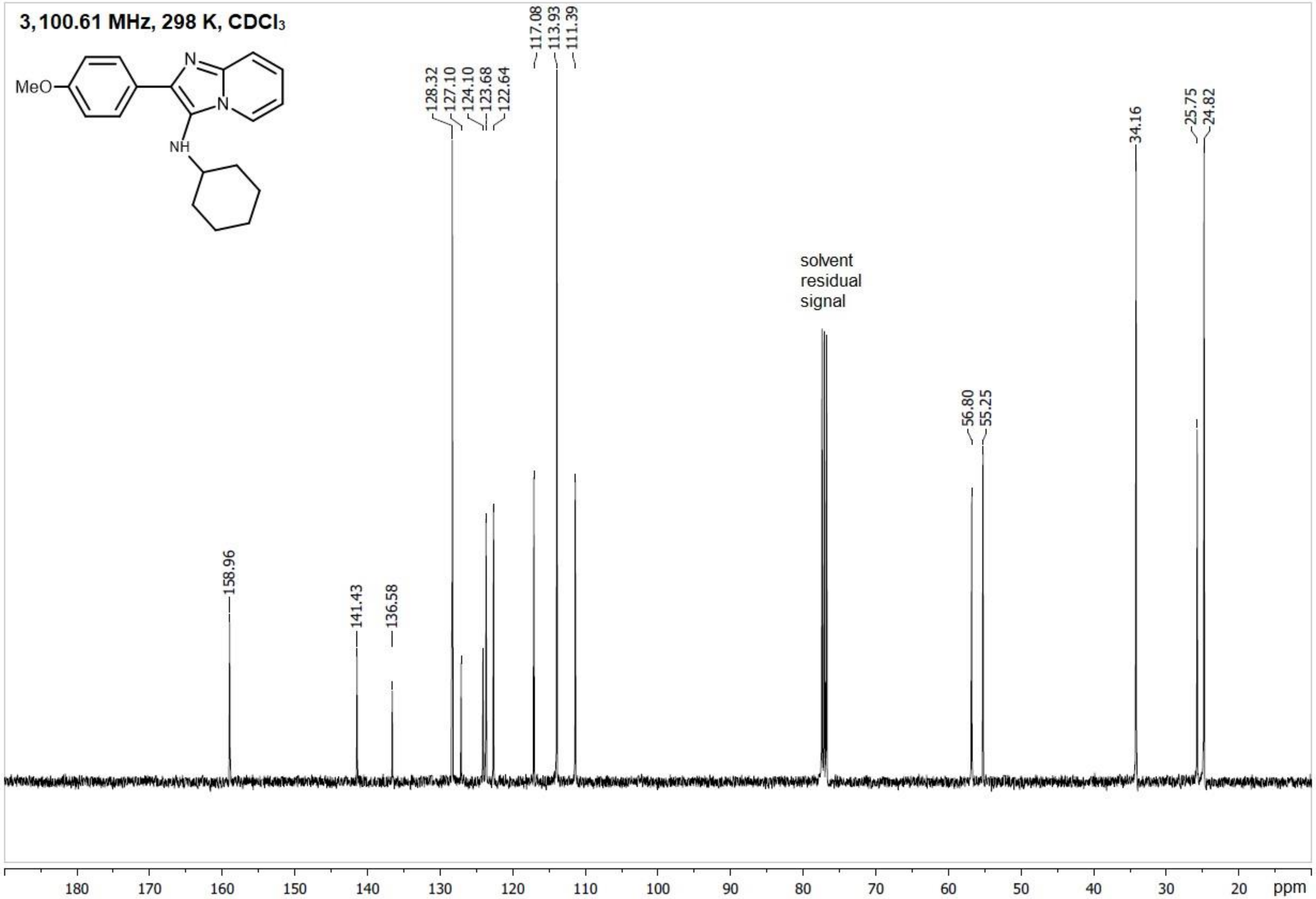


Figure S30. $^{13}C\{^1H\}$ NMR spectrum of **3**.

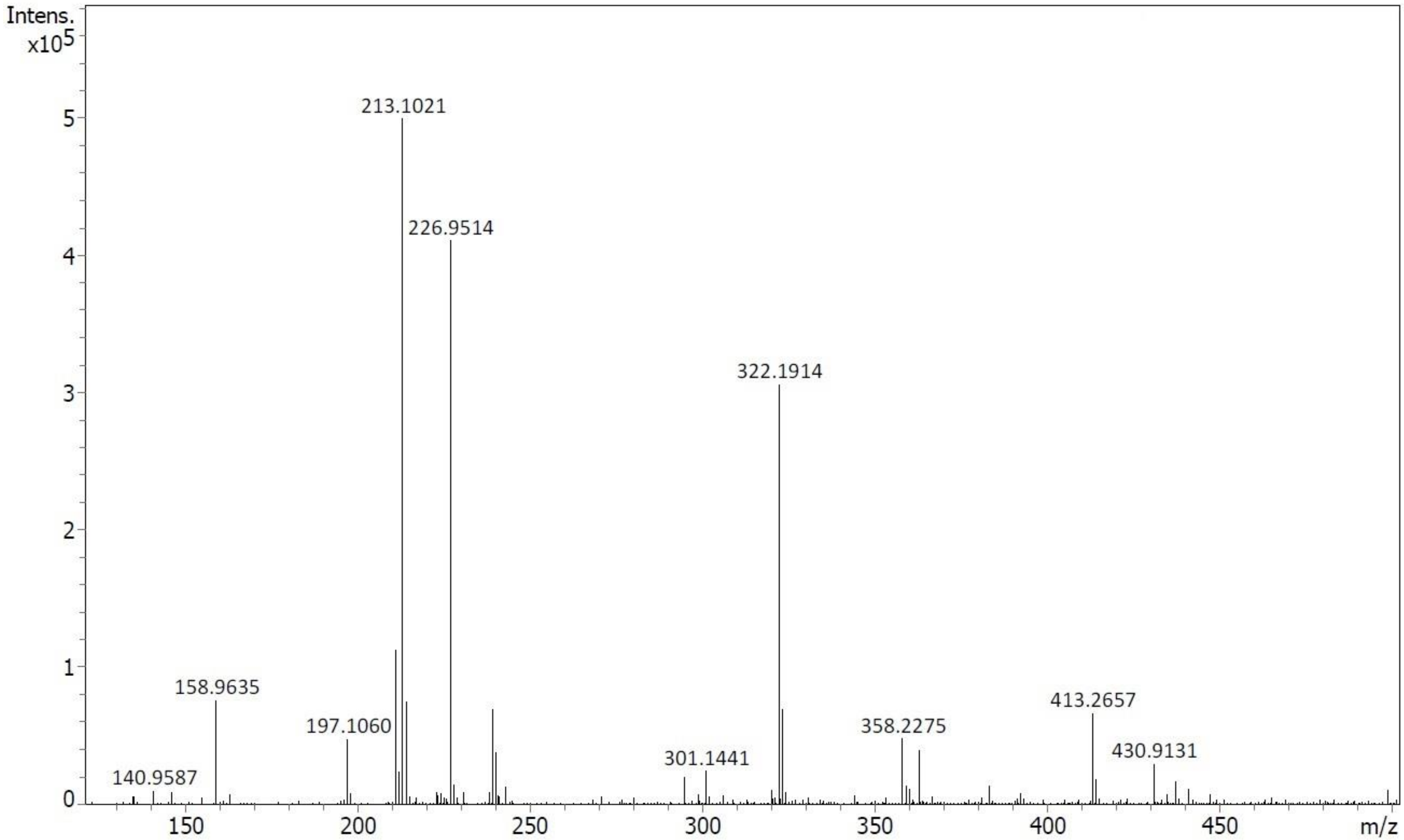


Figure S31. HRESI$^+$-MS of **3**.

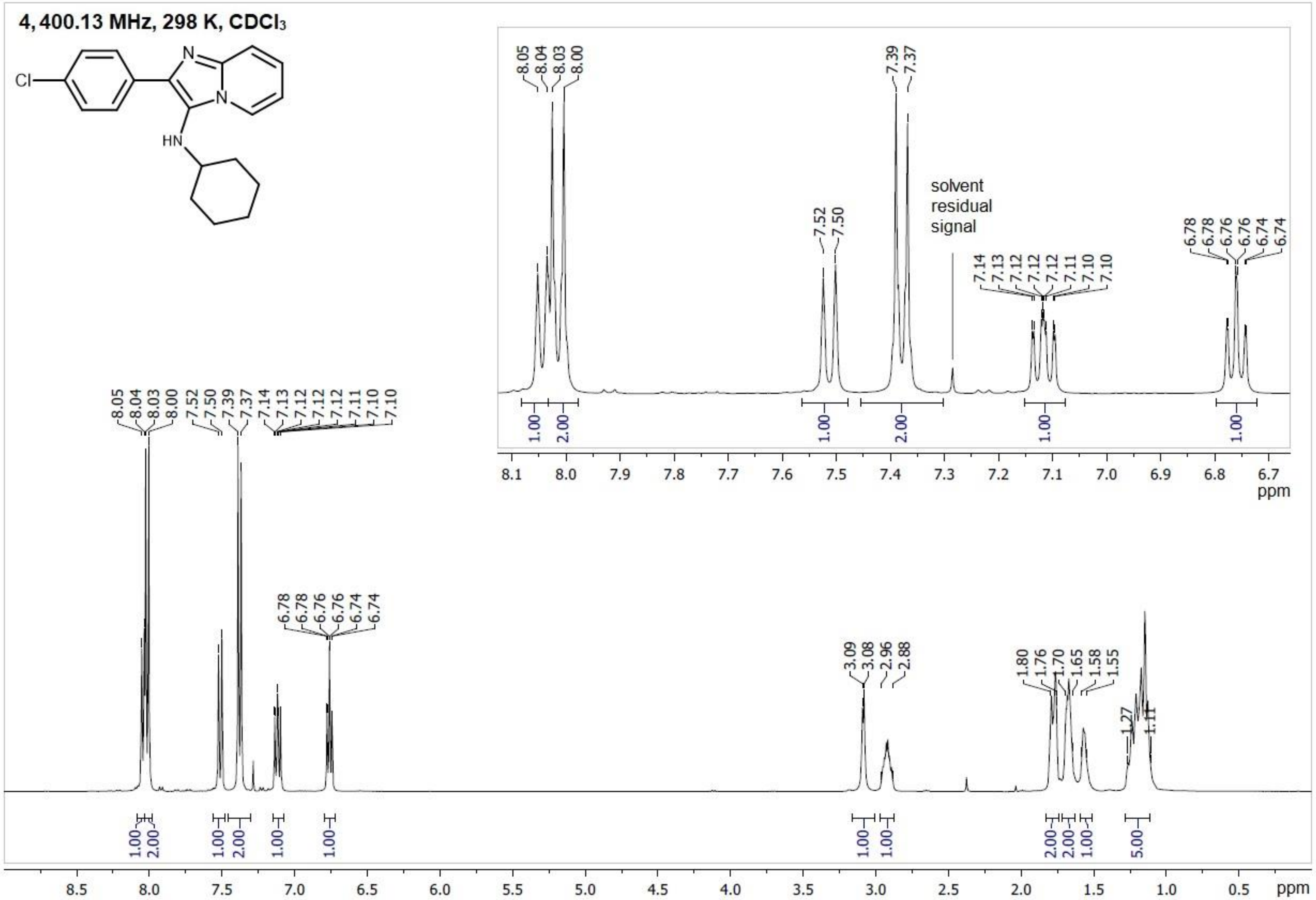


Figure S32. ^{1}H NMR spectrum of **4**.

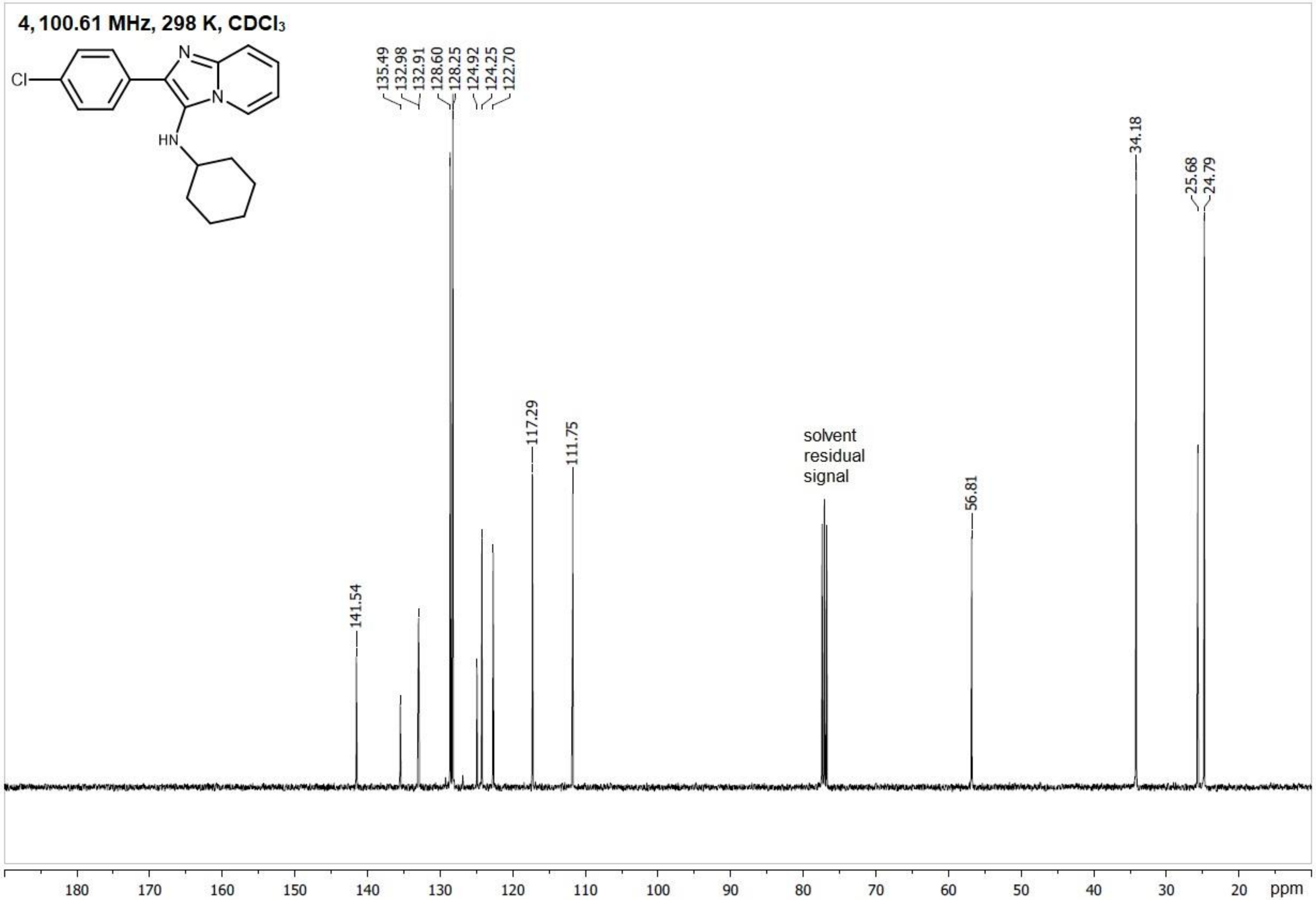


Figure S33. $^{13}C\{^1H\}$ NMR spectrum of **4**.

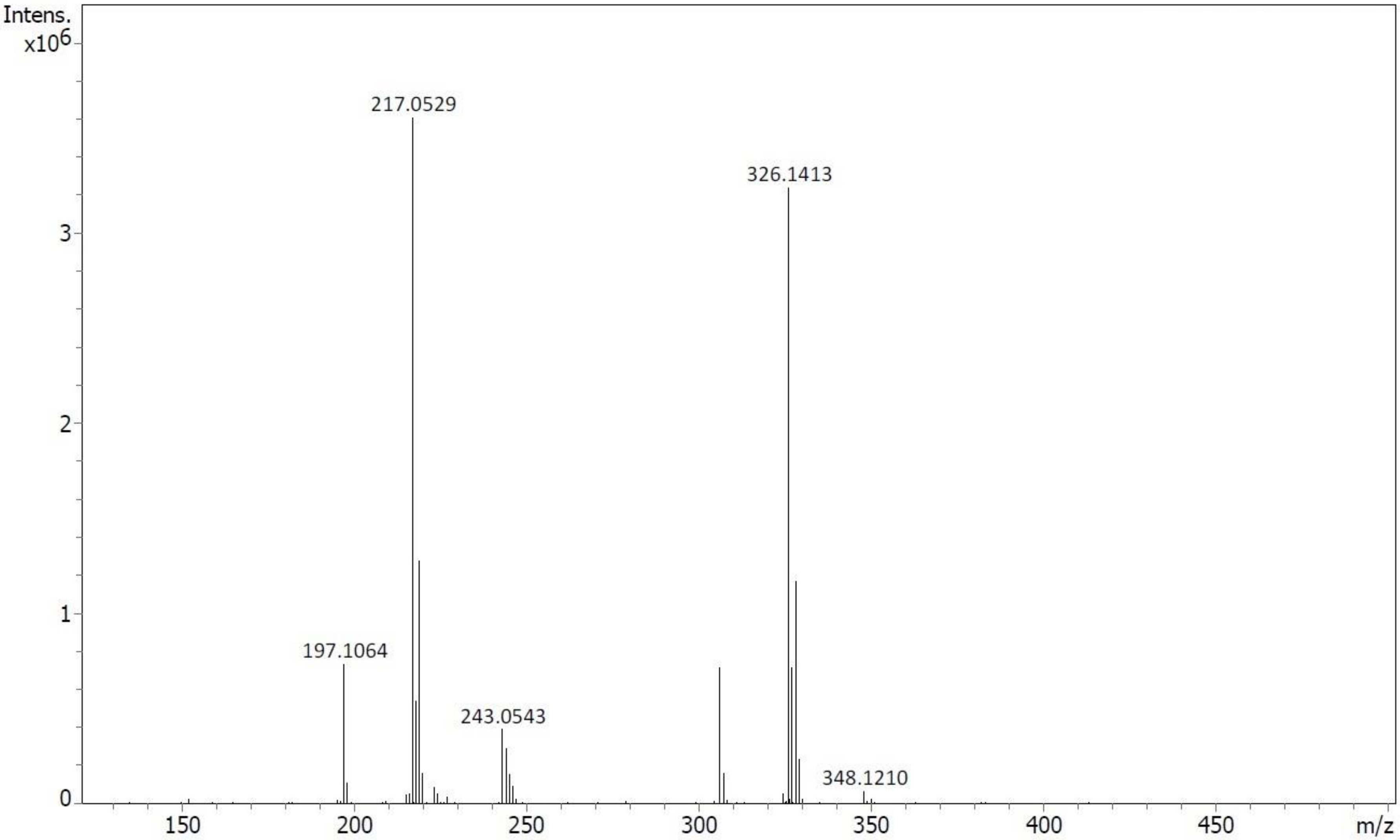


Figure S34. HRESI$^+$-MS of **4**.

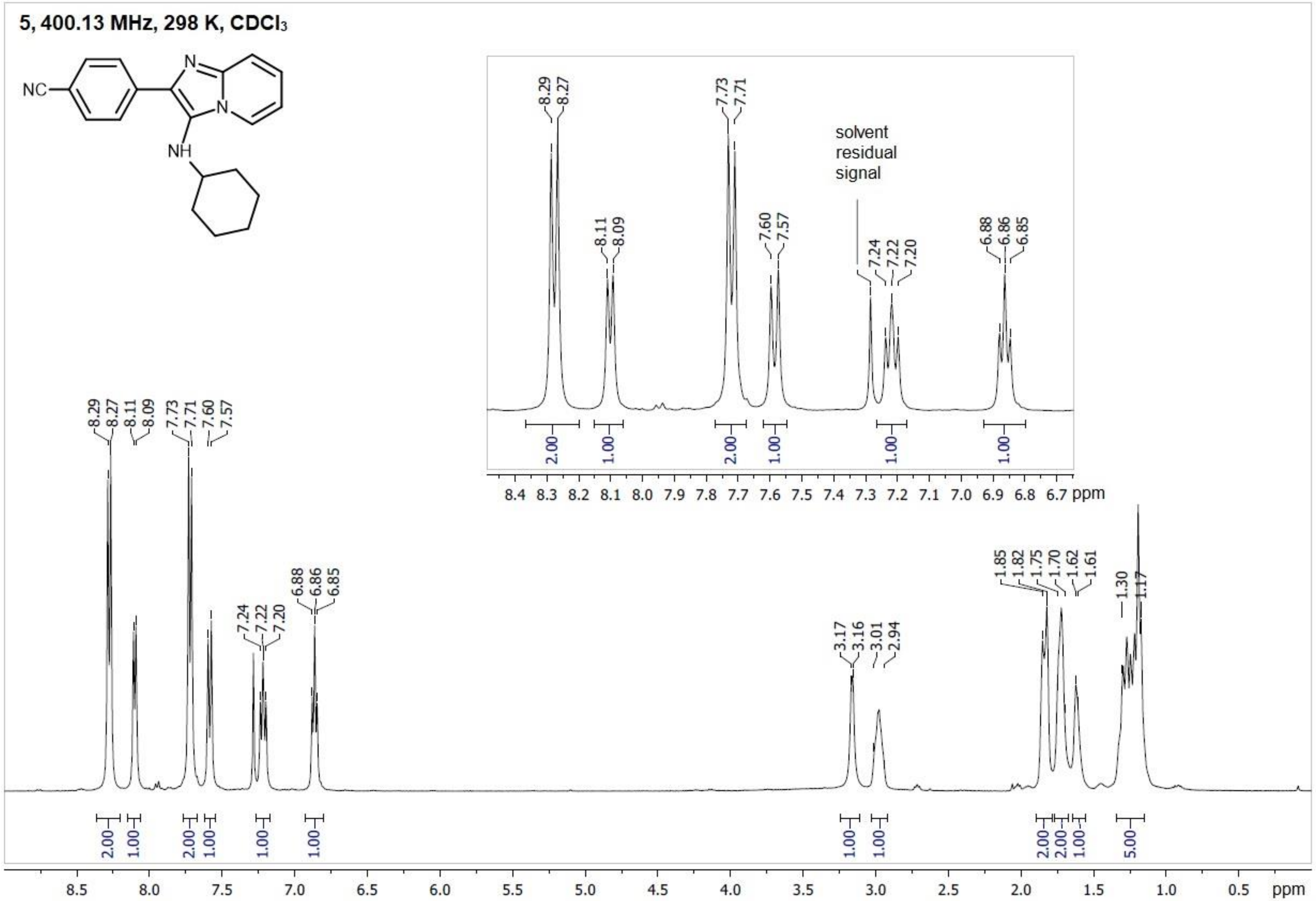


Figure S35. ^{1}H NMR spectrum of **5**.

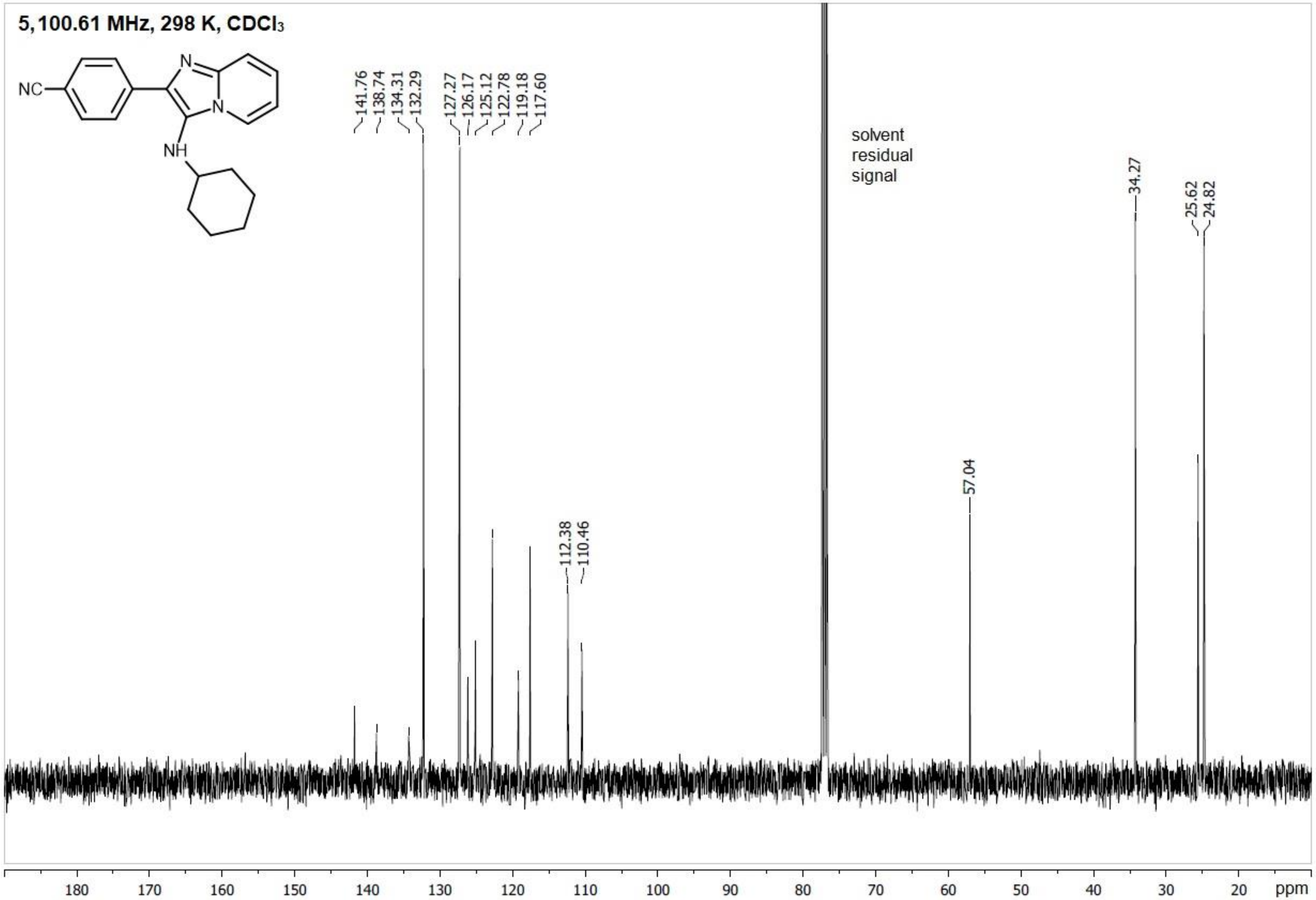


Figure S36. $^{13}C\{^{1}H\}$ NMR spectrum of **5**.

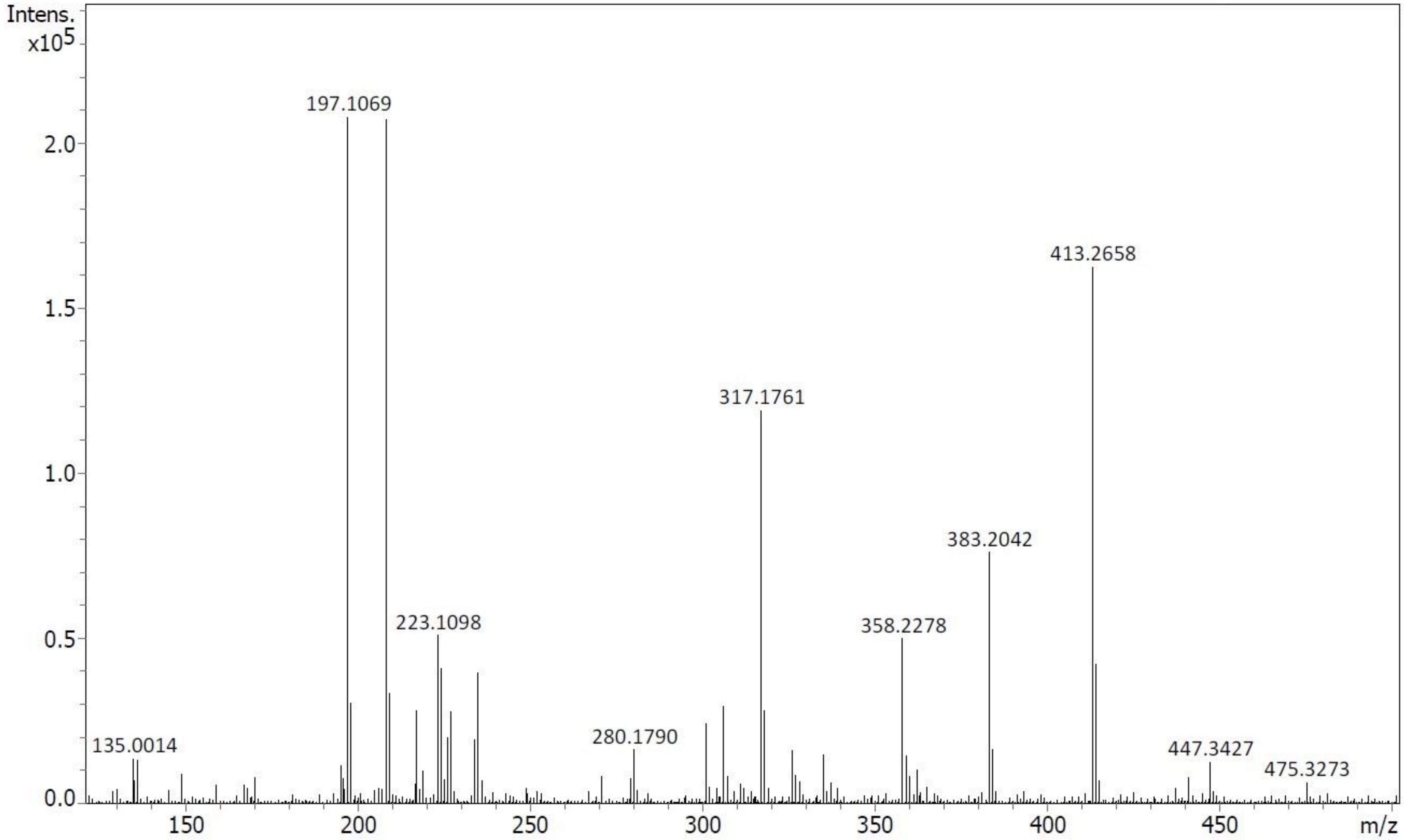


Figure S37. HRESI$^+$-MS of **5**.

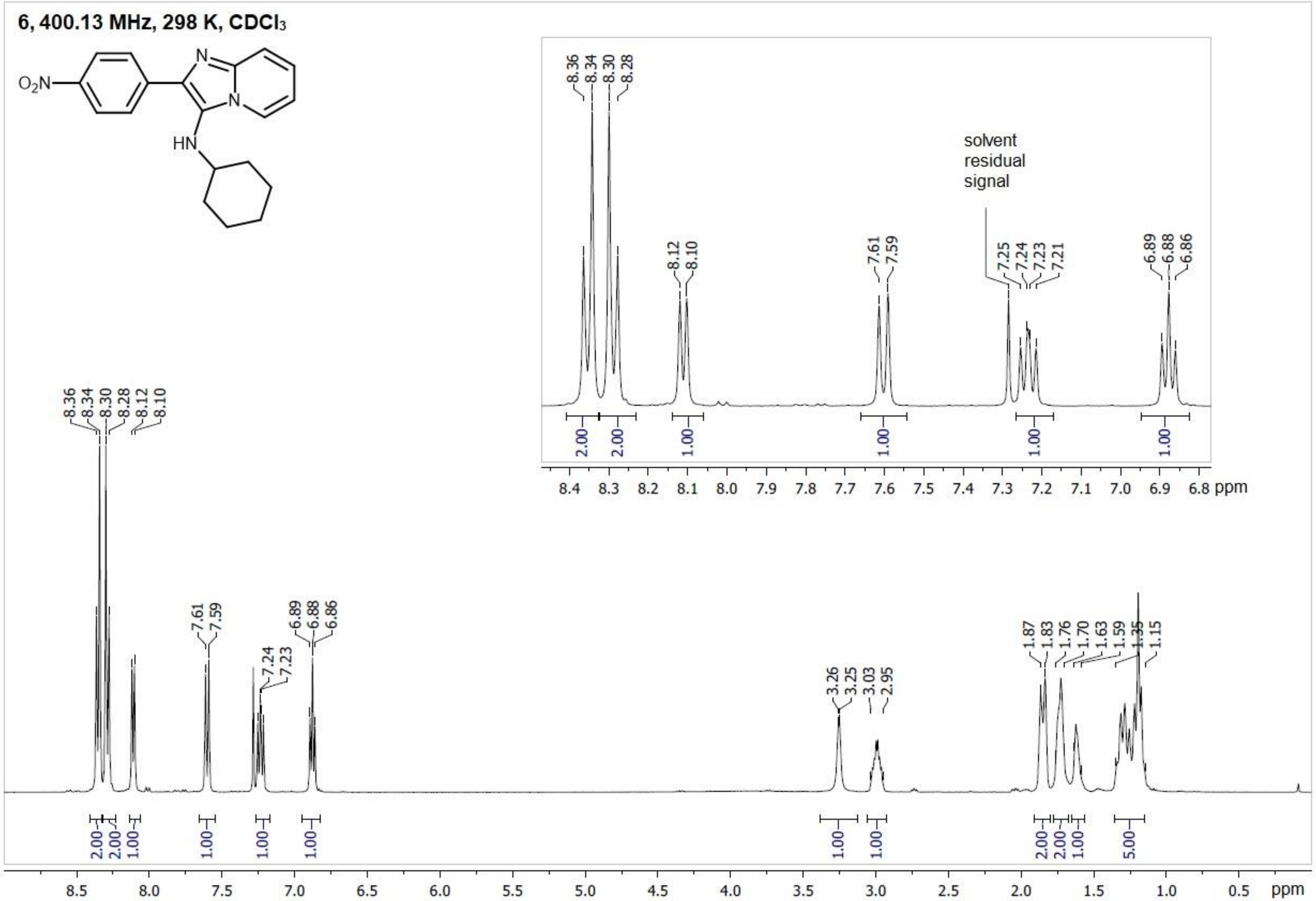


Figure S38. ^{1}H NMR spectrum of **6**.

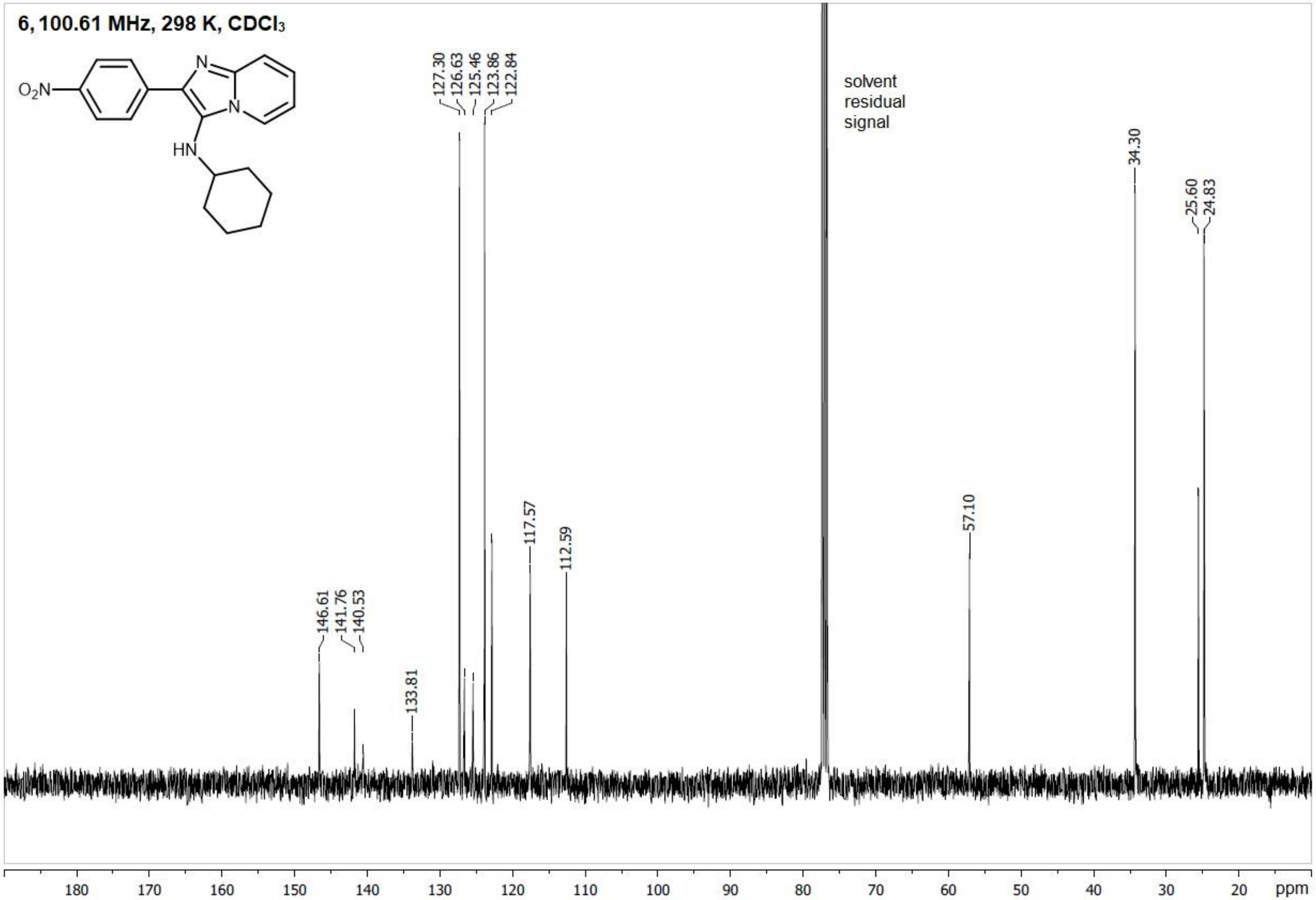


Figure S39. $^{13}C\{^{1}H\}$ NMR spectrum of **6**.

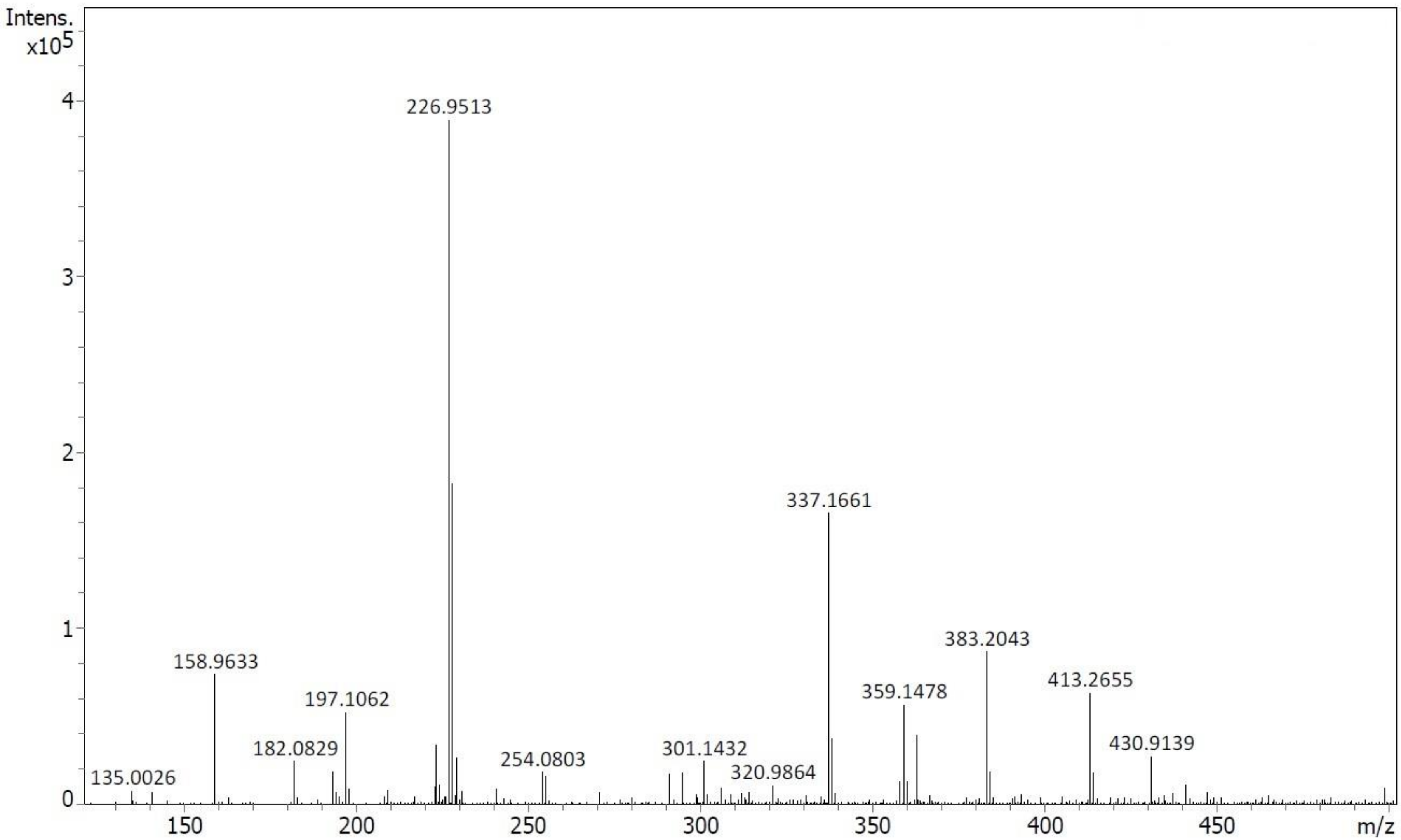


Figure S40. HRESI$^+$-MS of **6**.

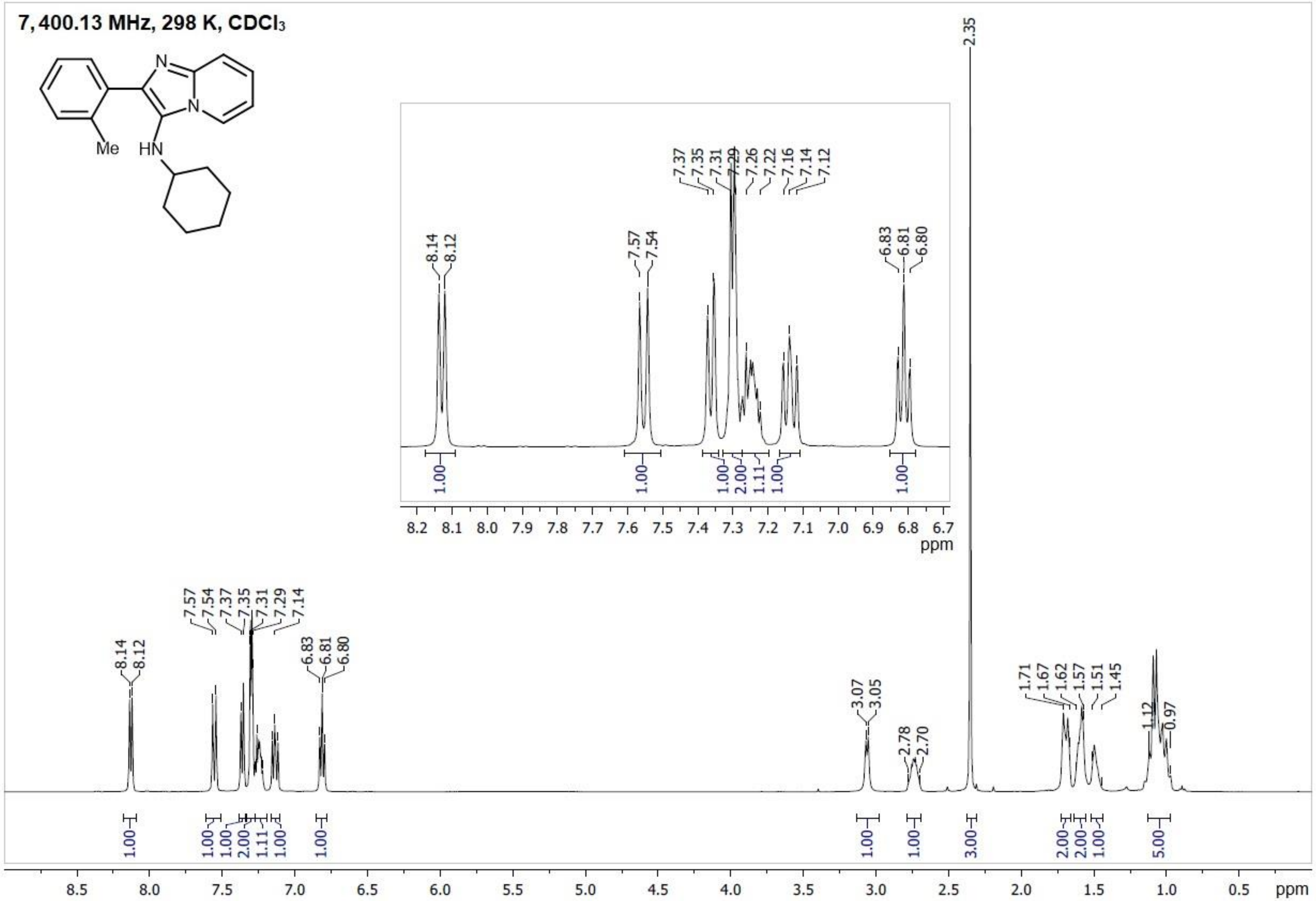


Figure S41. ^{1}H NMR spectrum of **7**.

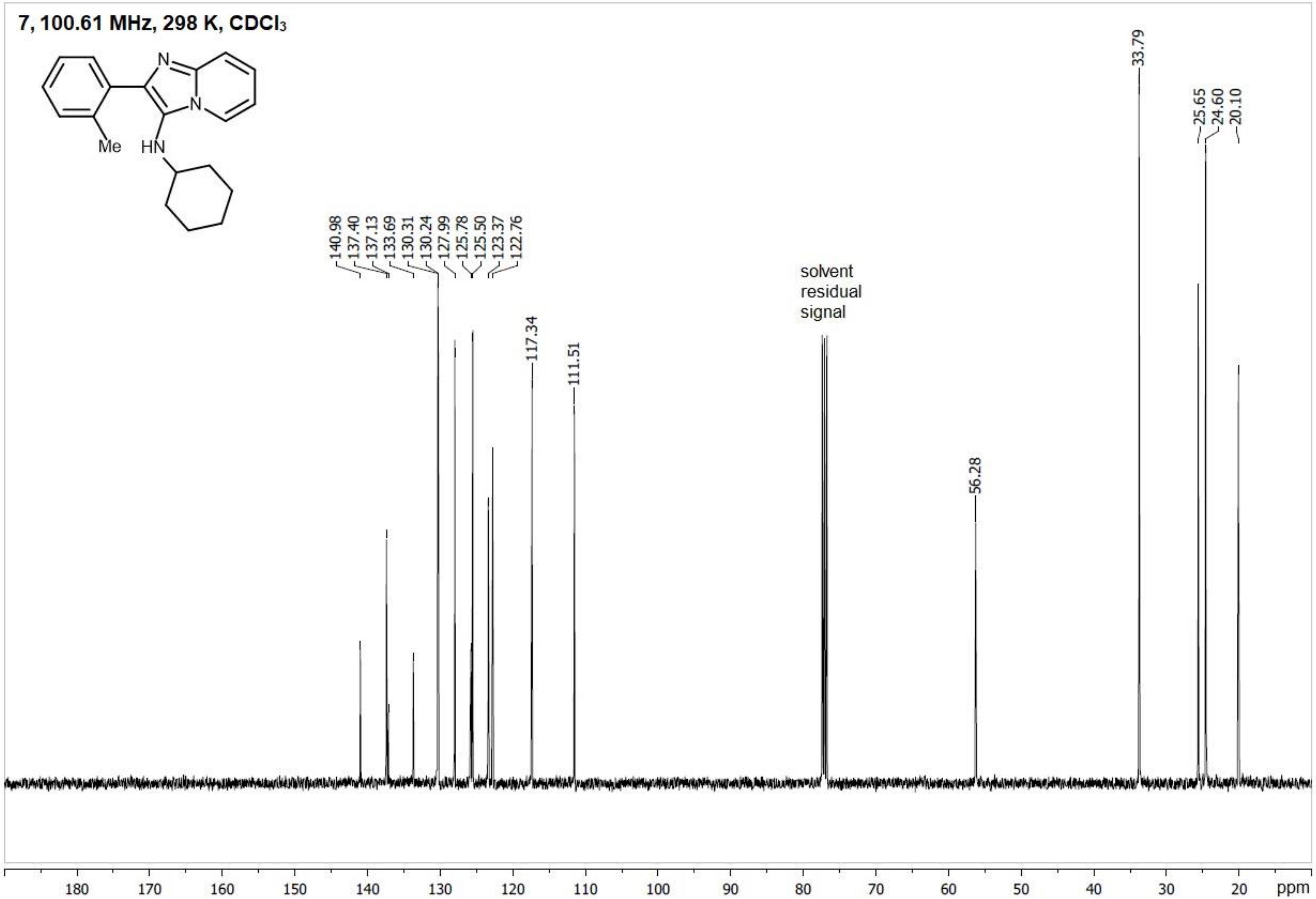


Figure S42. $^{13}C\{^{1}H\}$ NMR spectrum of **7**.

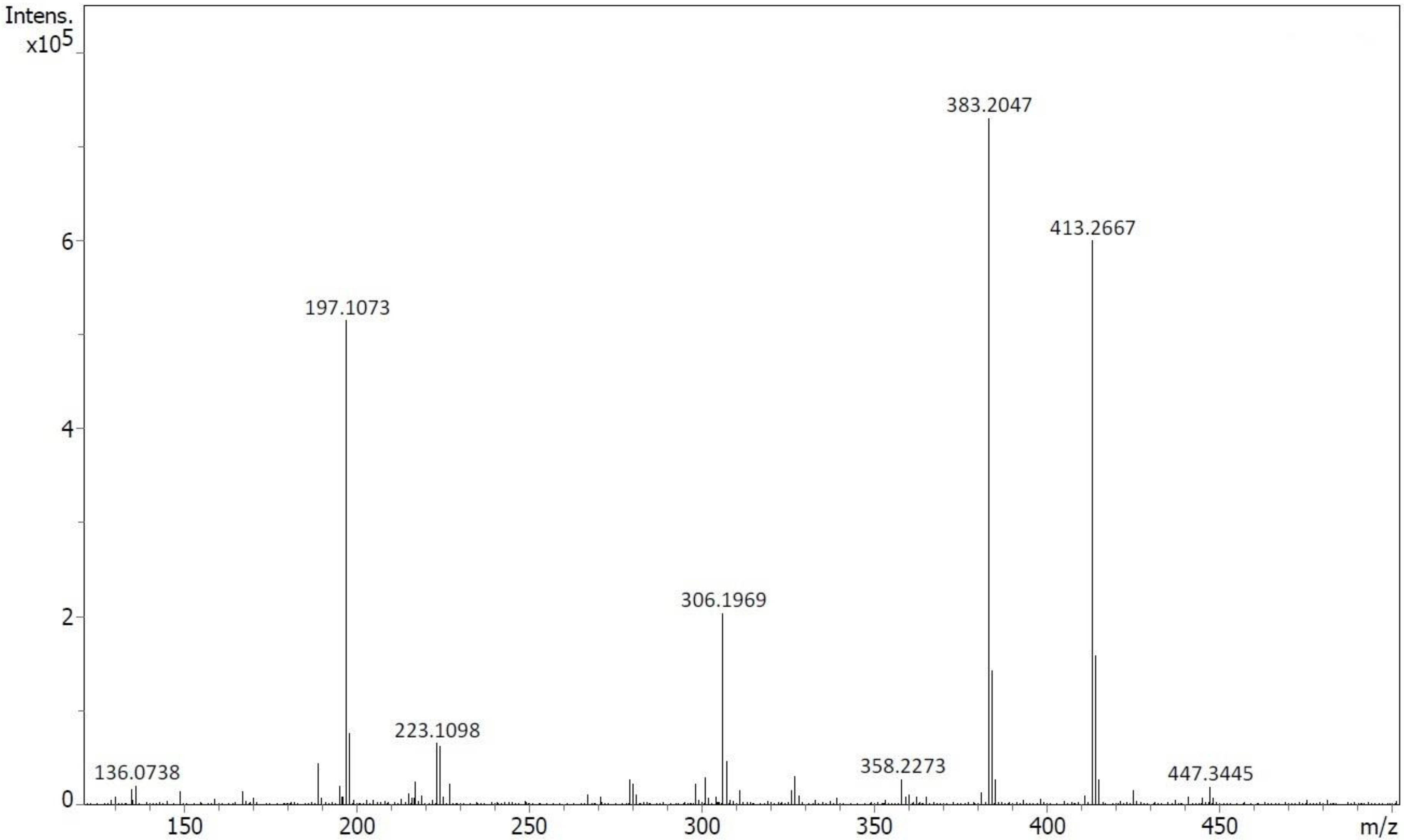


Figure S43. HRESI$^+$-MS of **7**.

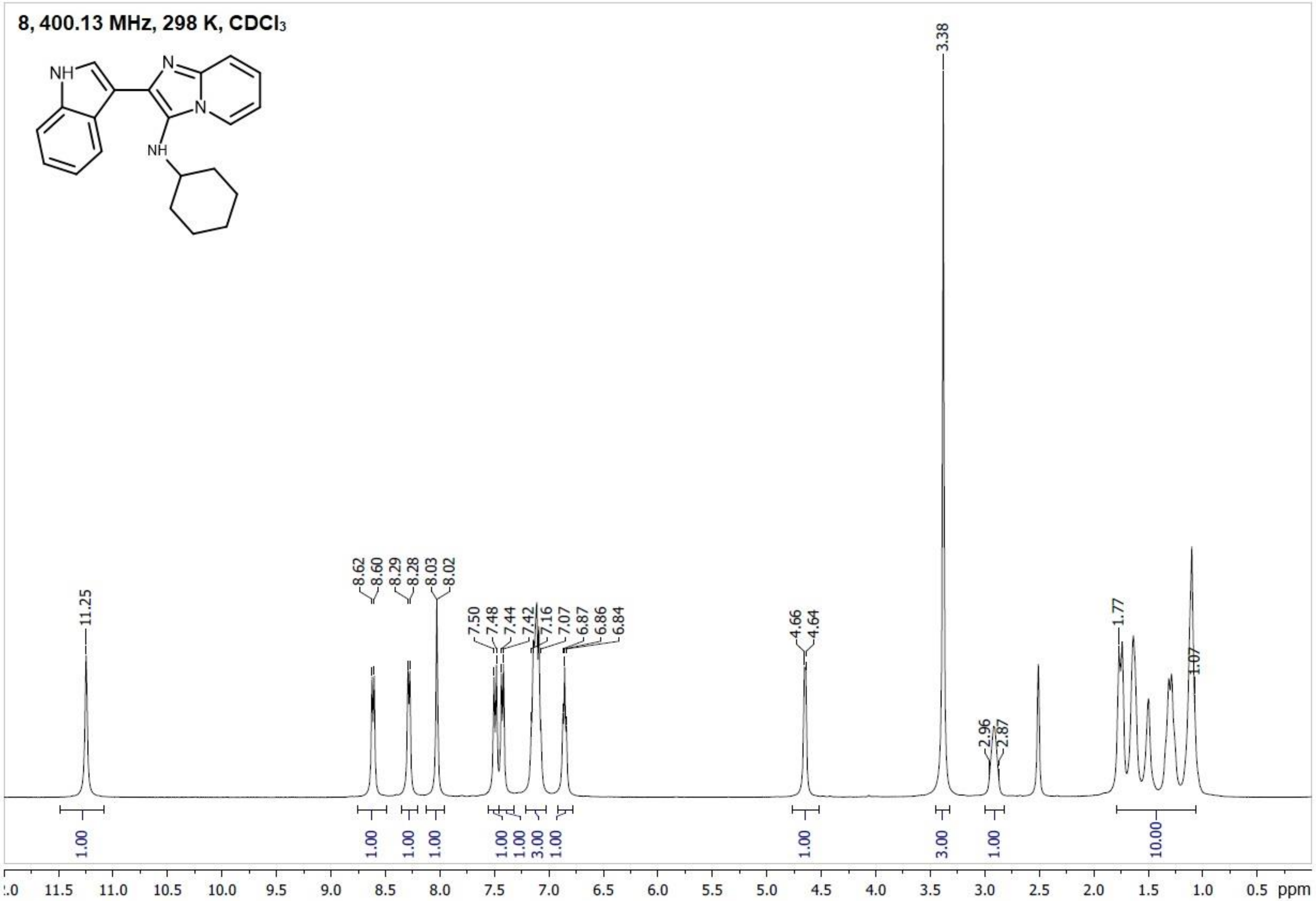


Figure S44. ¹H NMR spectrum of **8**.

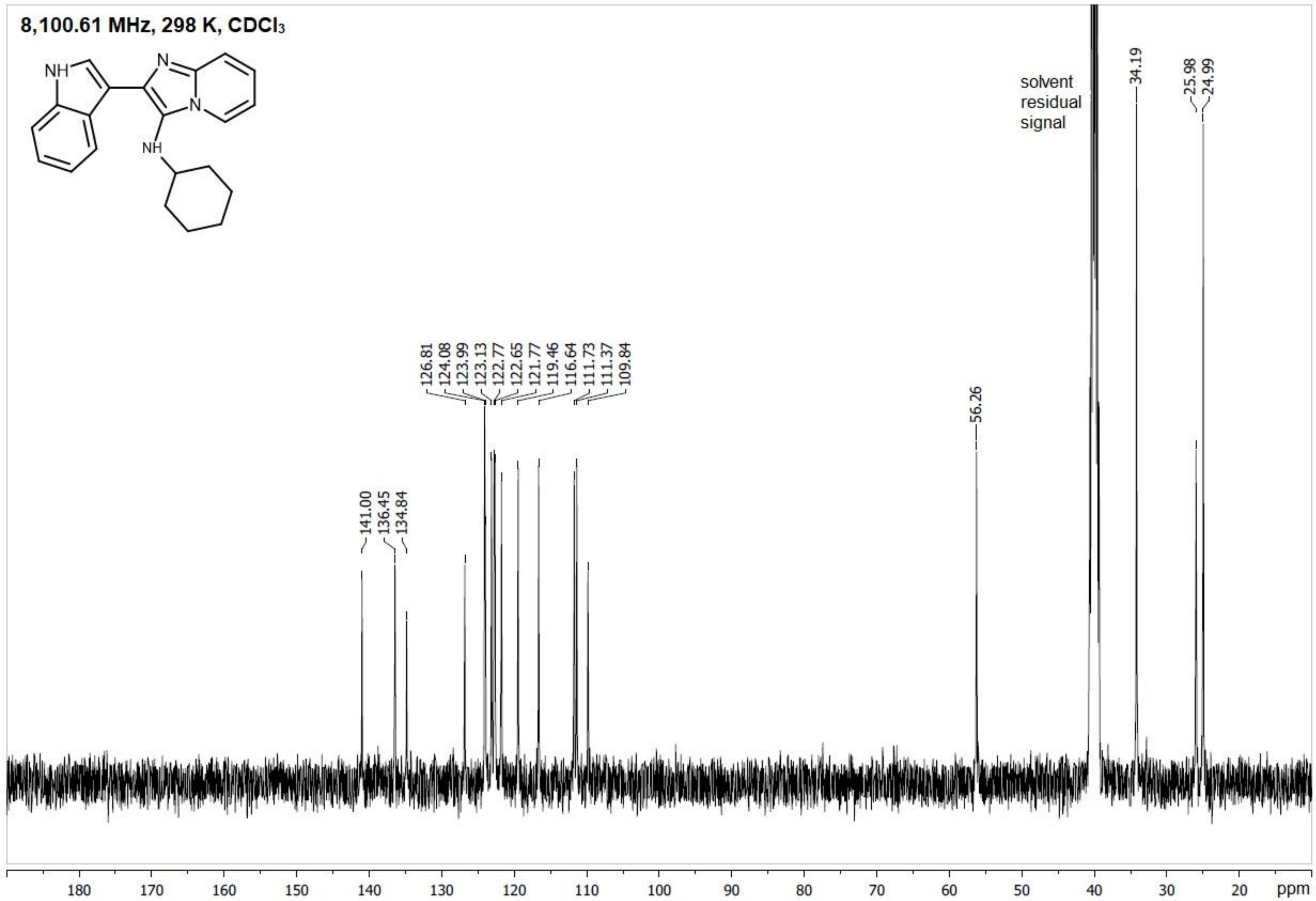


Figure S45. $^{13}C\{^{1}H\}$ NMR spectrum of **8**.

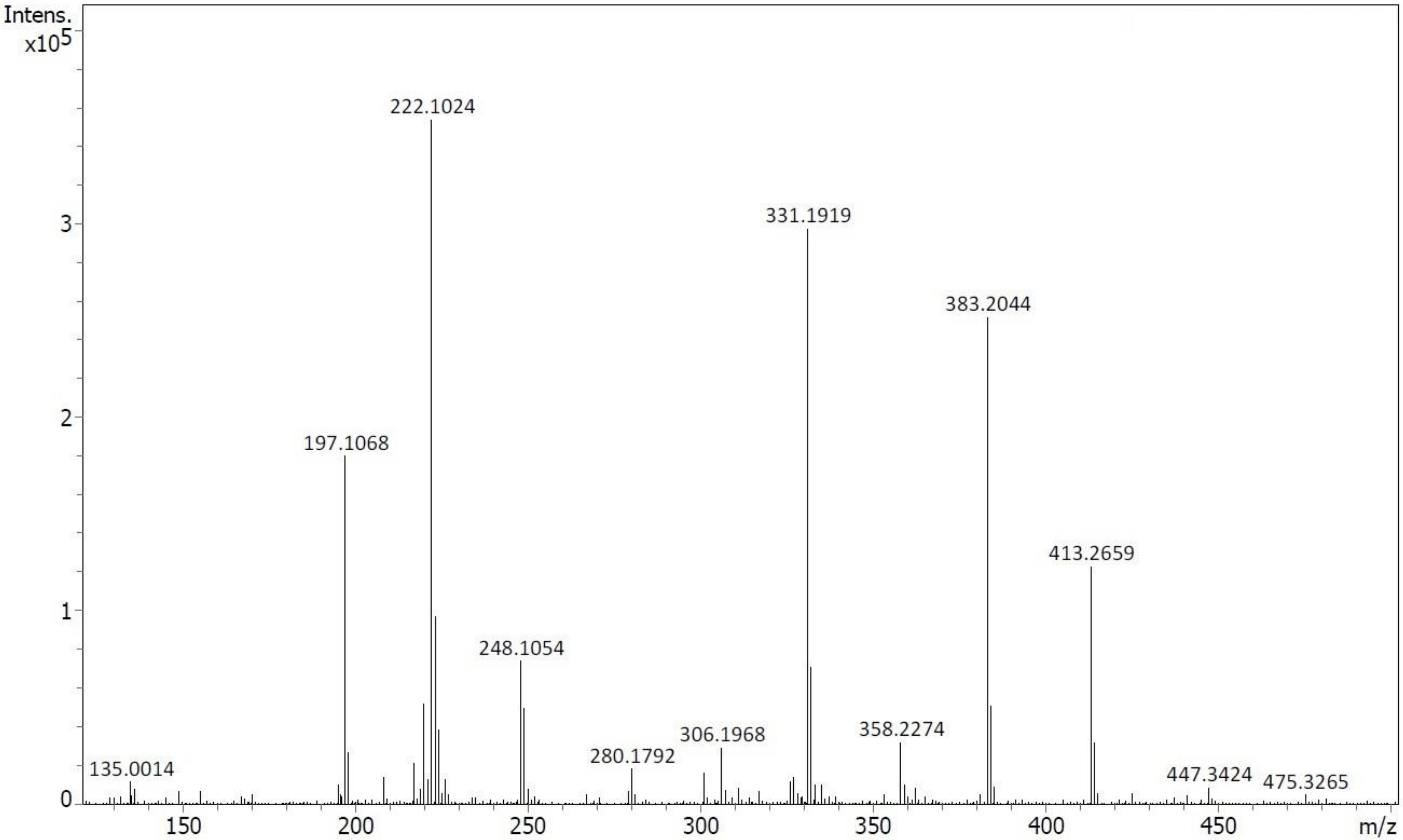


Figure S46. HRESI$^+$-MS of **8**.

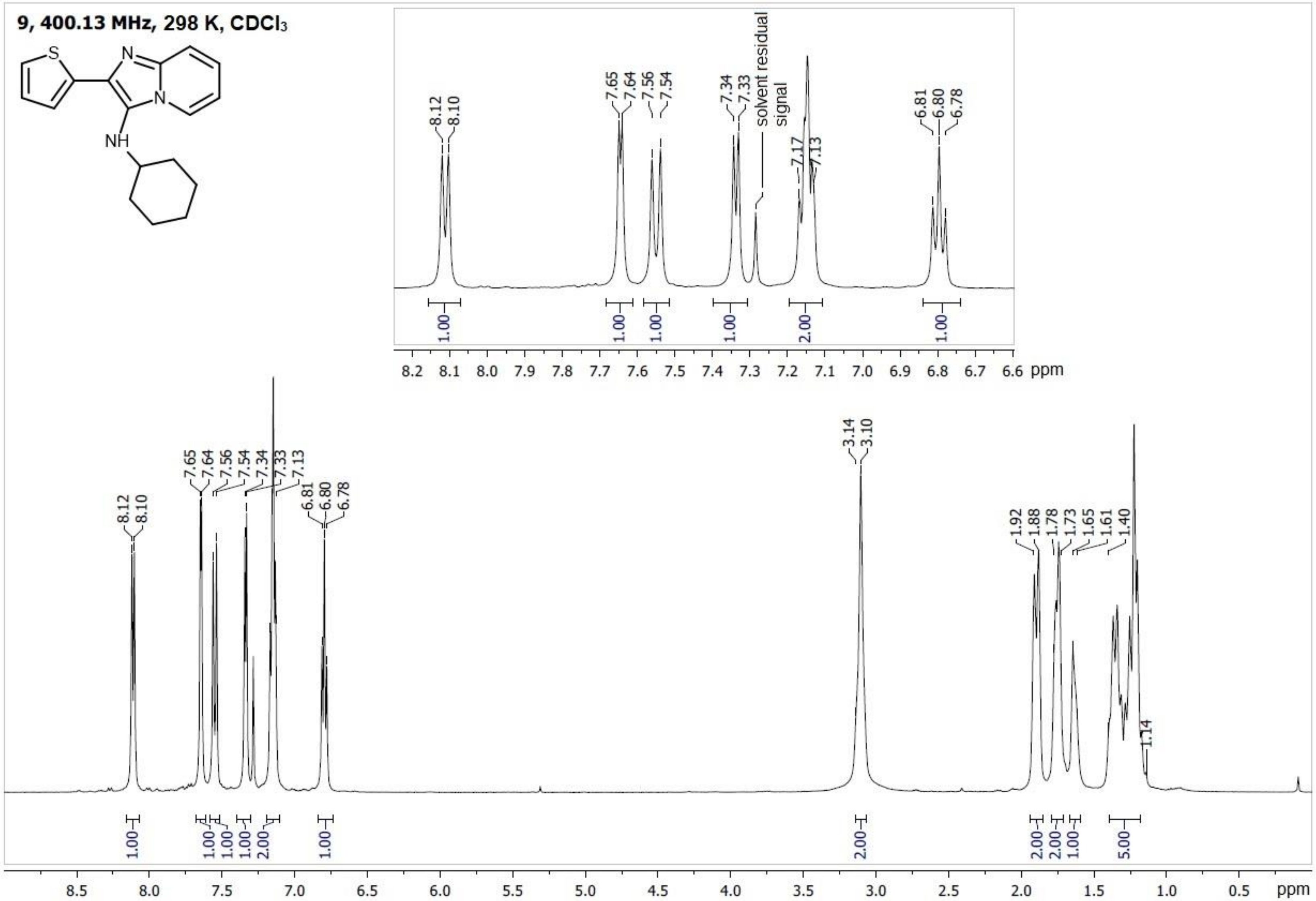


Figure S47. ^{1}H NMR spectrum of **9**.

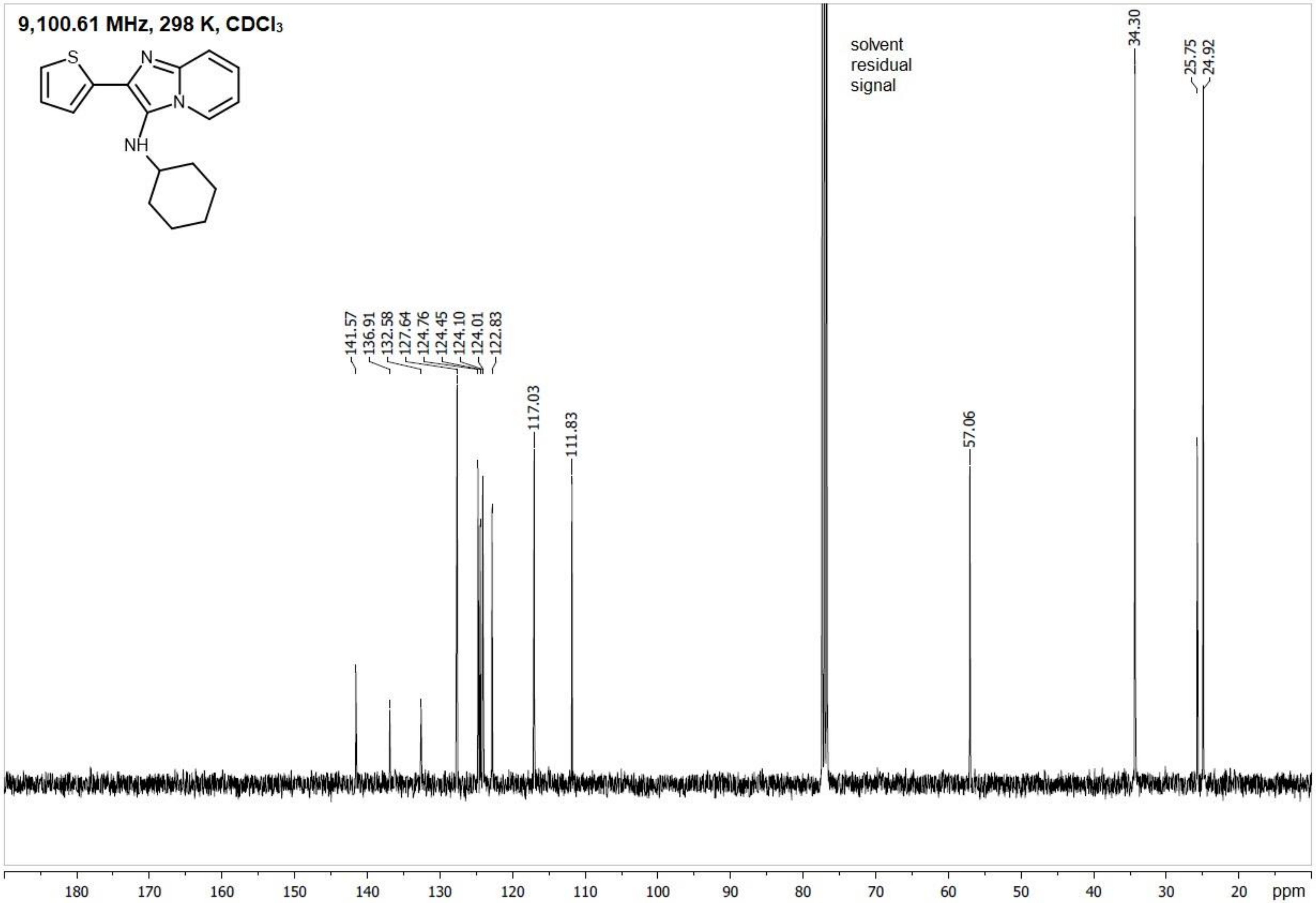


Figure S48. $^{13}C\{^{1}H\}$ NMR spectrum of **9**.

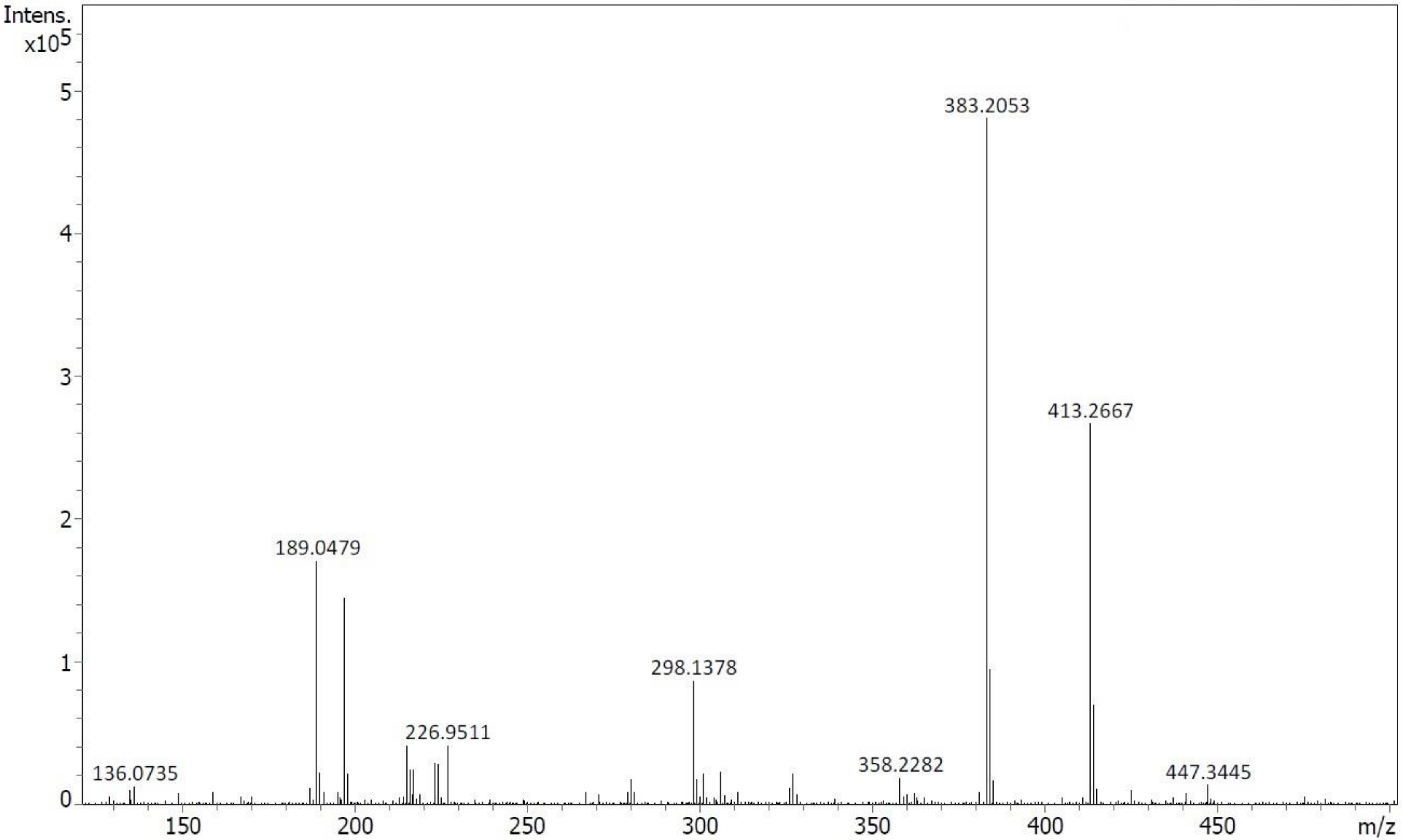


Figure S49. HRESI$^+$-MS of **9**.

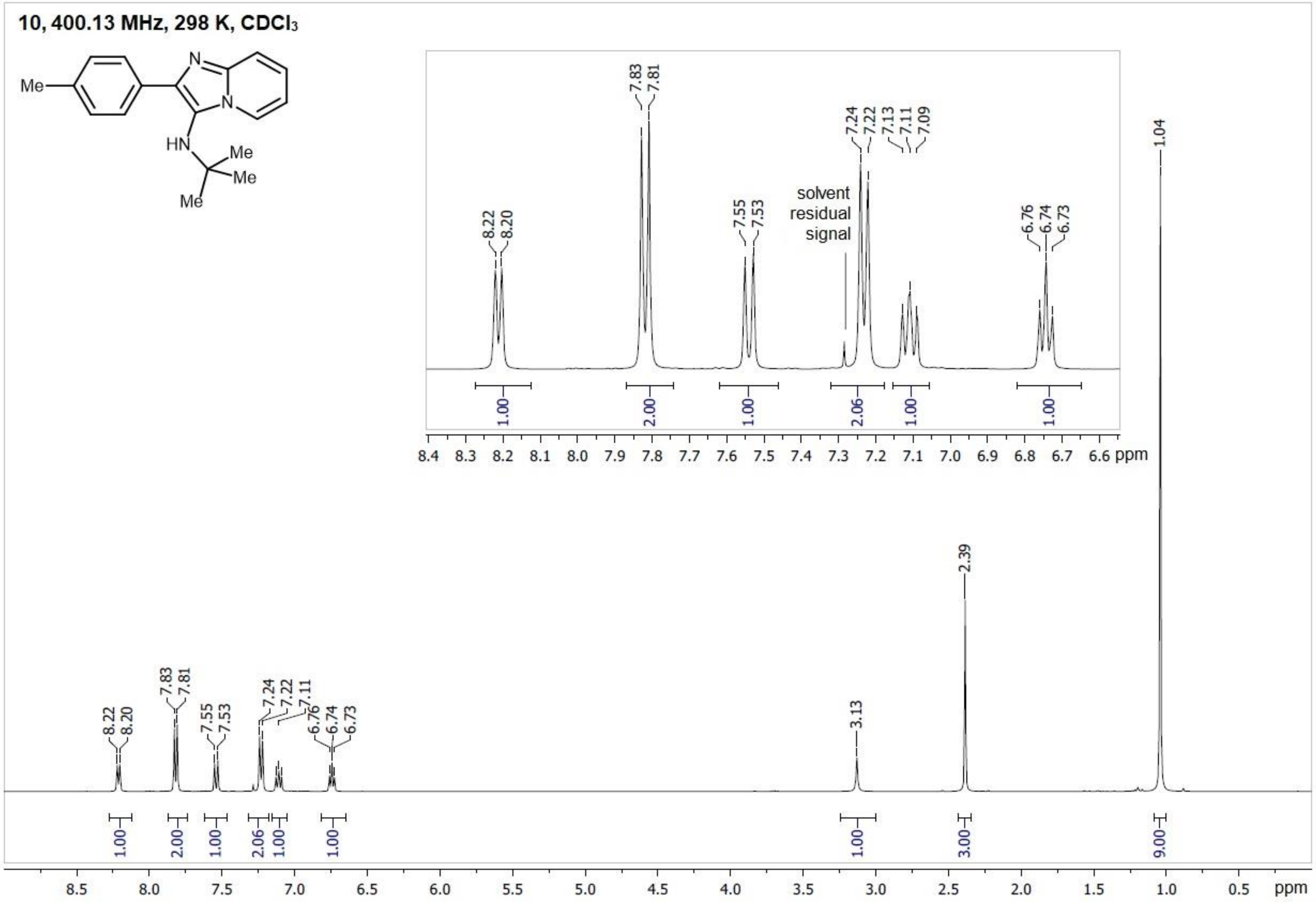


Figure S50. ^{1}H NMR spectrum of **10**.

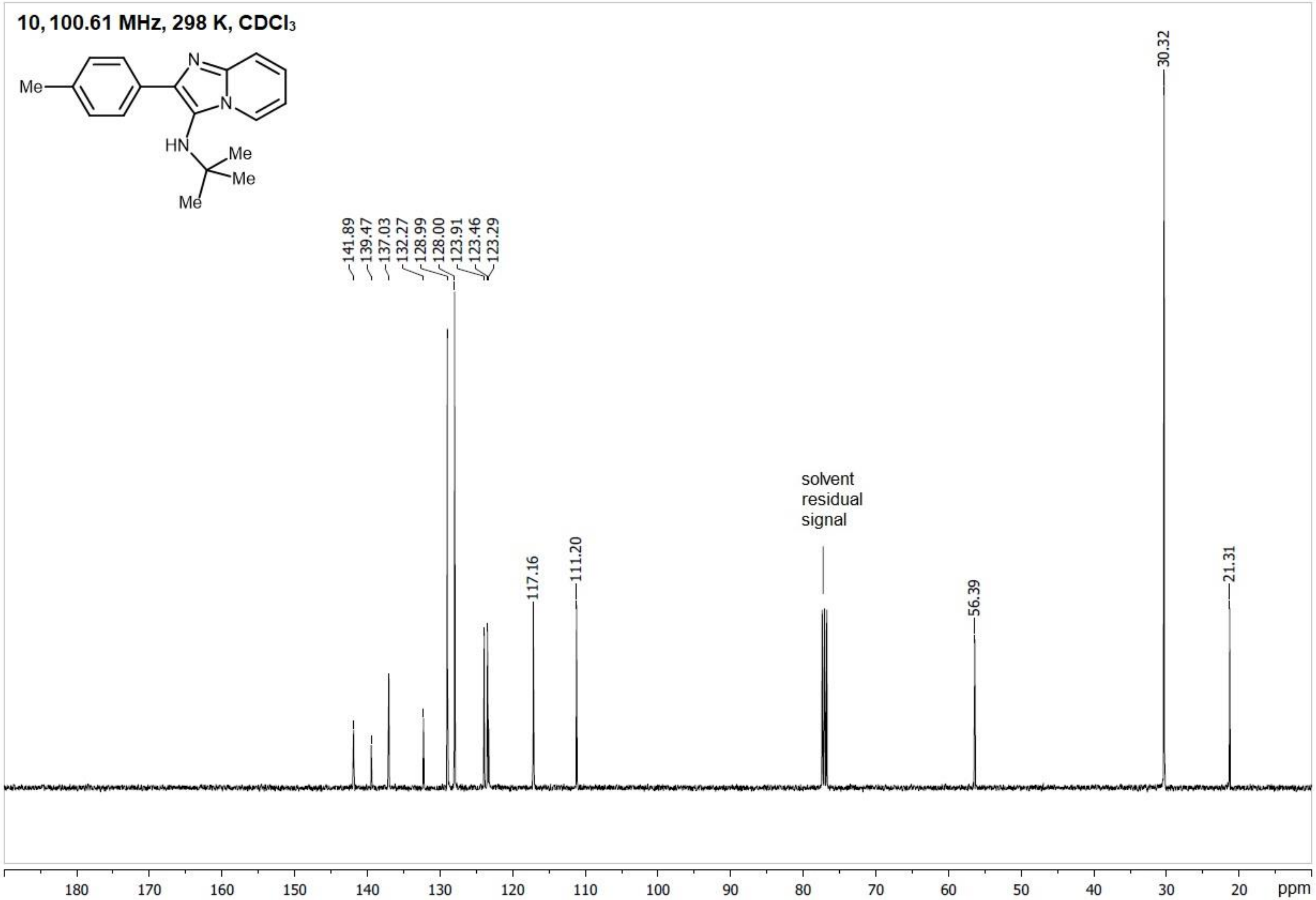


Figure S51. $^{13}C\{^{1}H\}$ NMR spectrum of **10**.

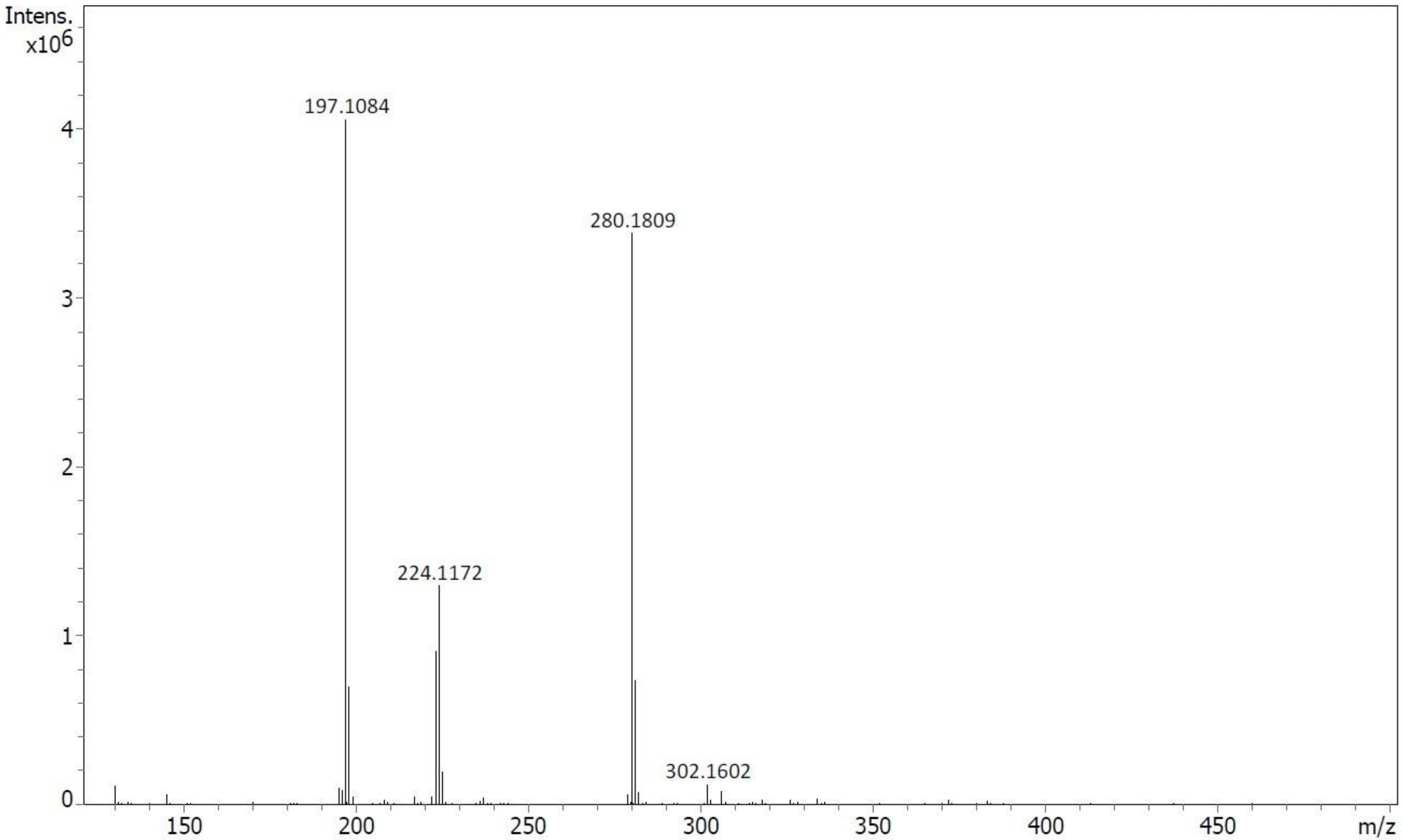


Figure S52. HRESI$^+$-MS of **10**.

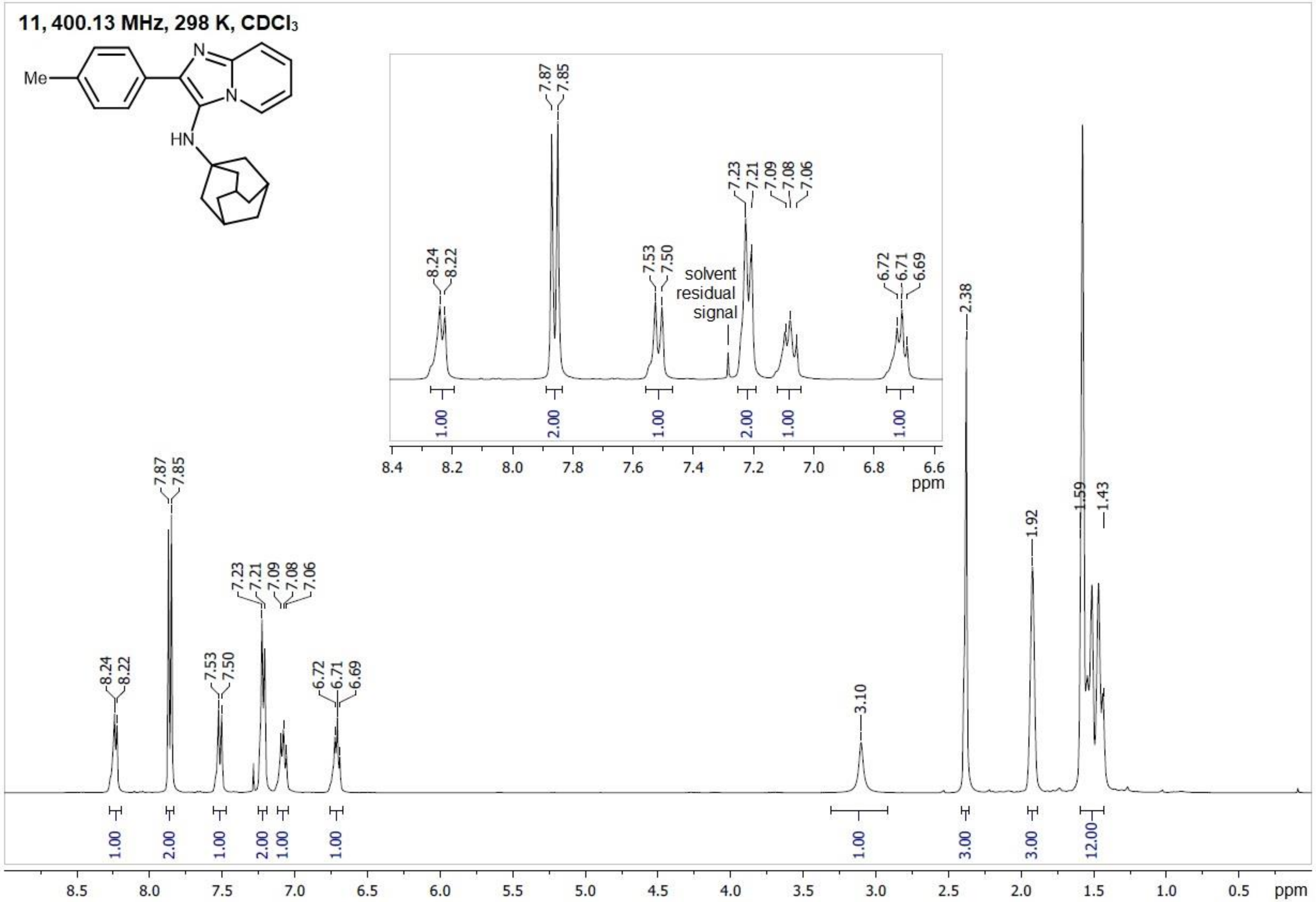


Figure S53. ^{1}H NMR spectrum of **11**.

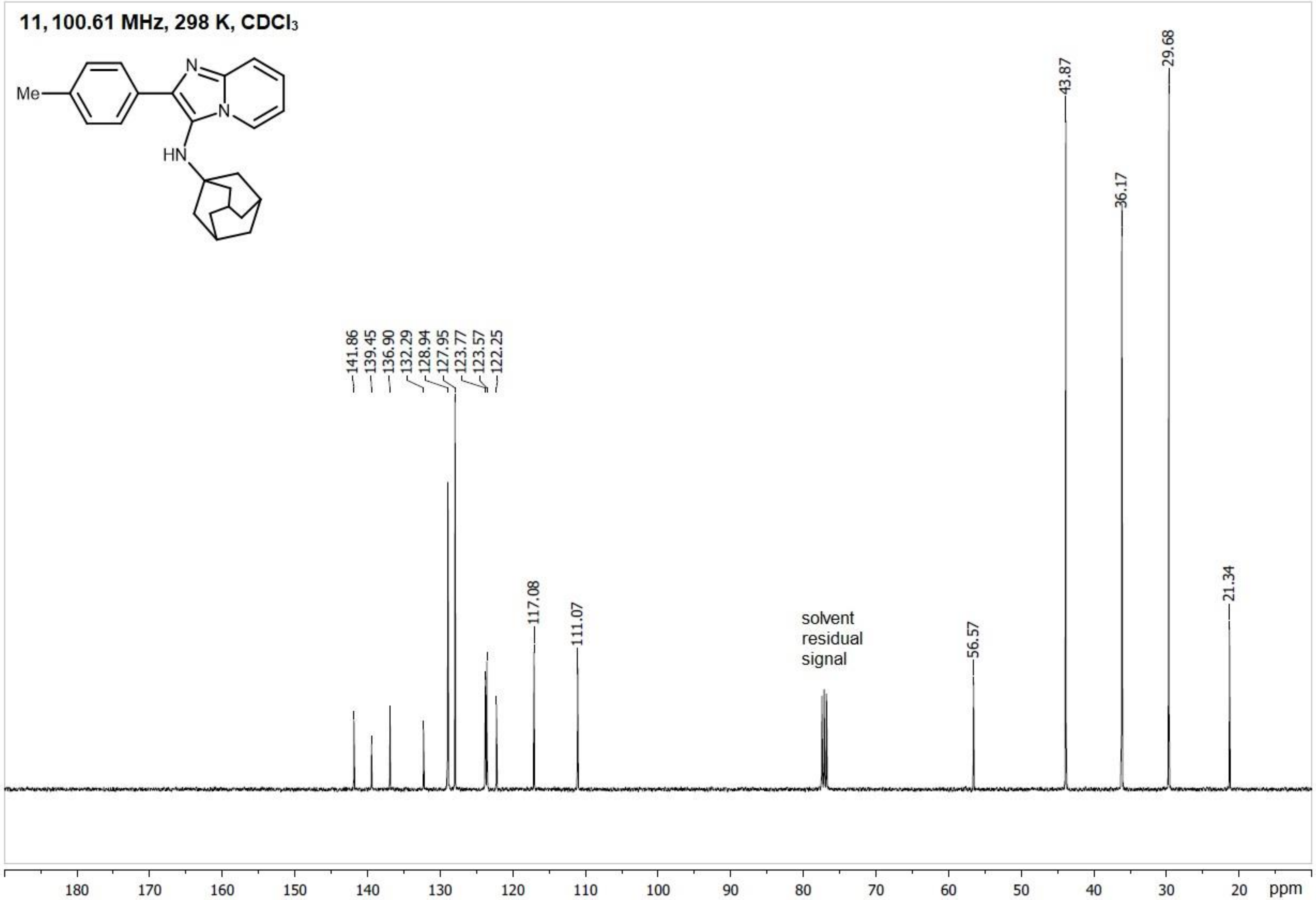


Figure S54. $^{13}C\{^{1}H\}$ NMR spectrum of **11**.

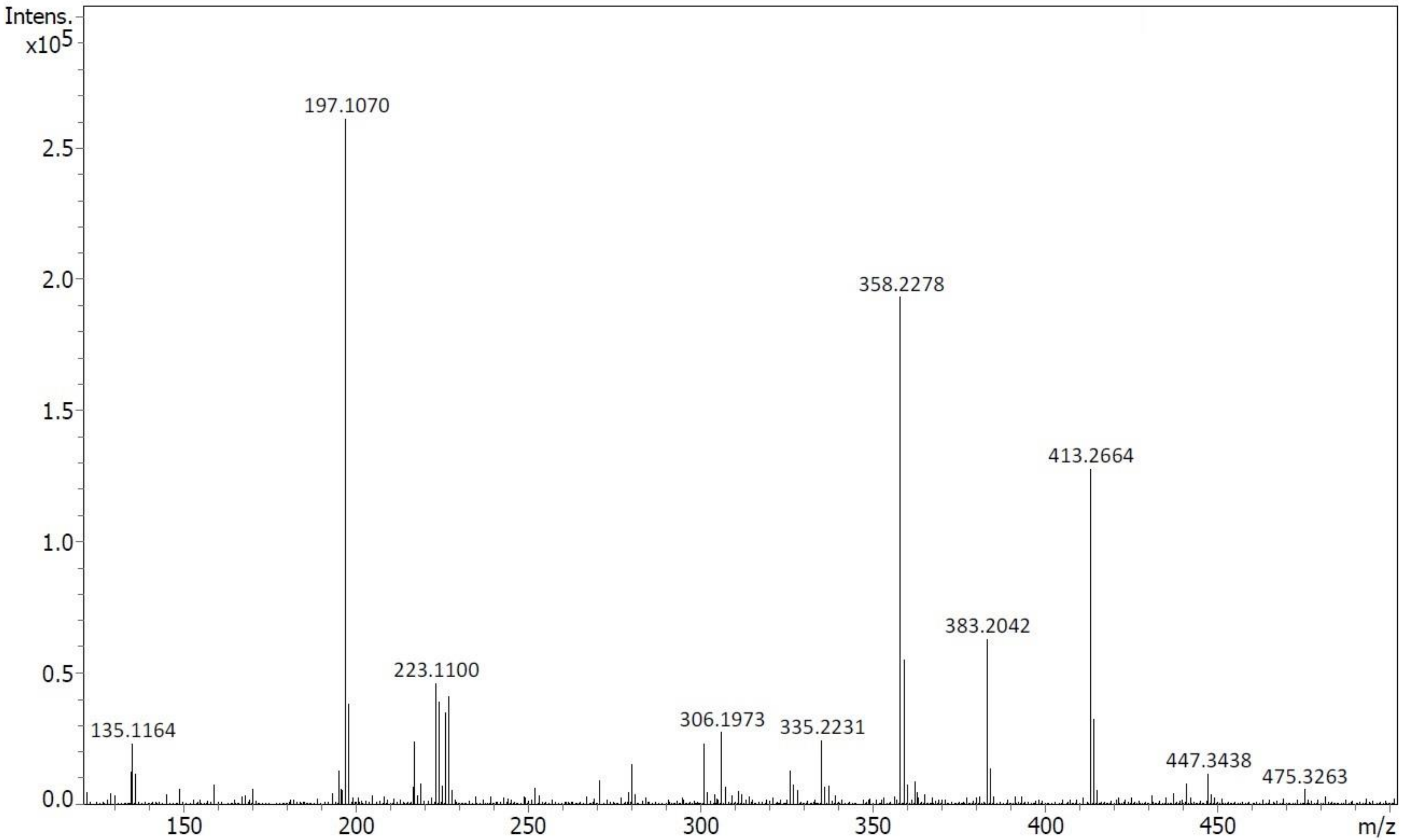


Figure S55. HRESI$^+$-MS of **11**.

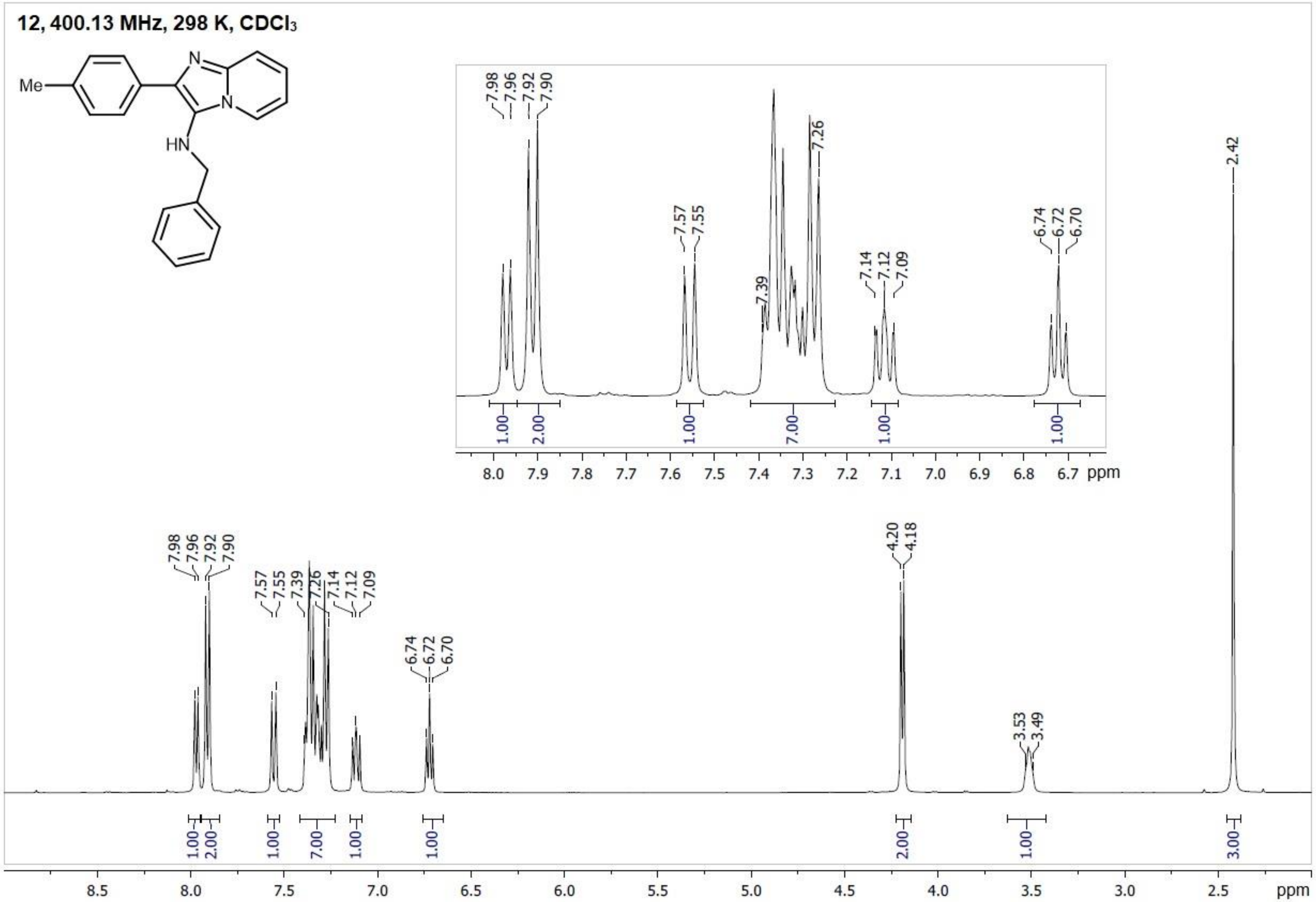


Figure S56. ^{1}H NMR spectrum of **12**.

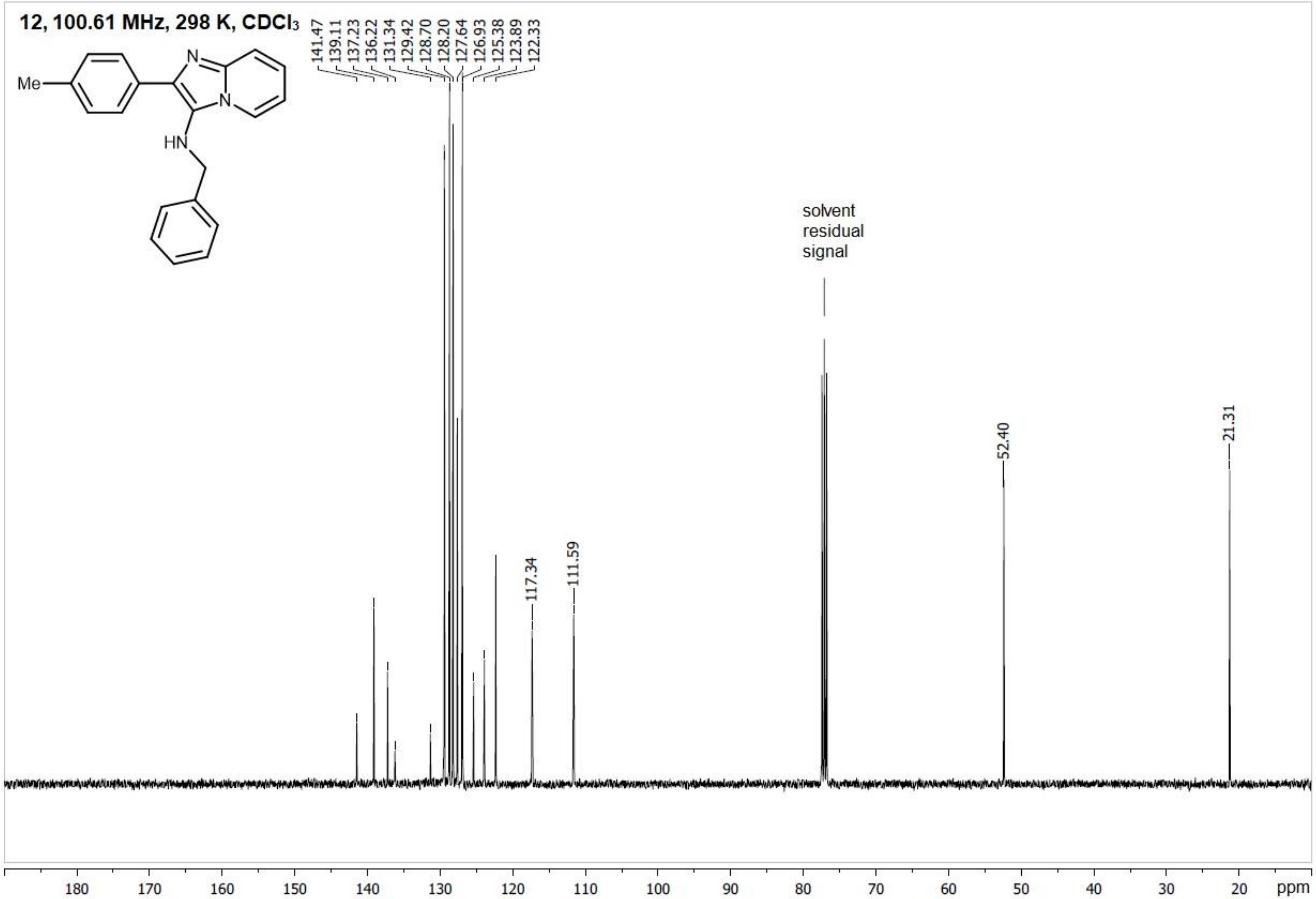


Figure S57. $^{13}C\{^{1}H\}$ NMR spectrum of **12**.

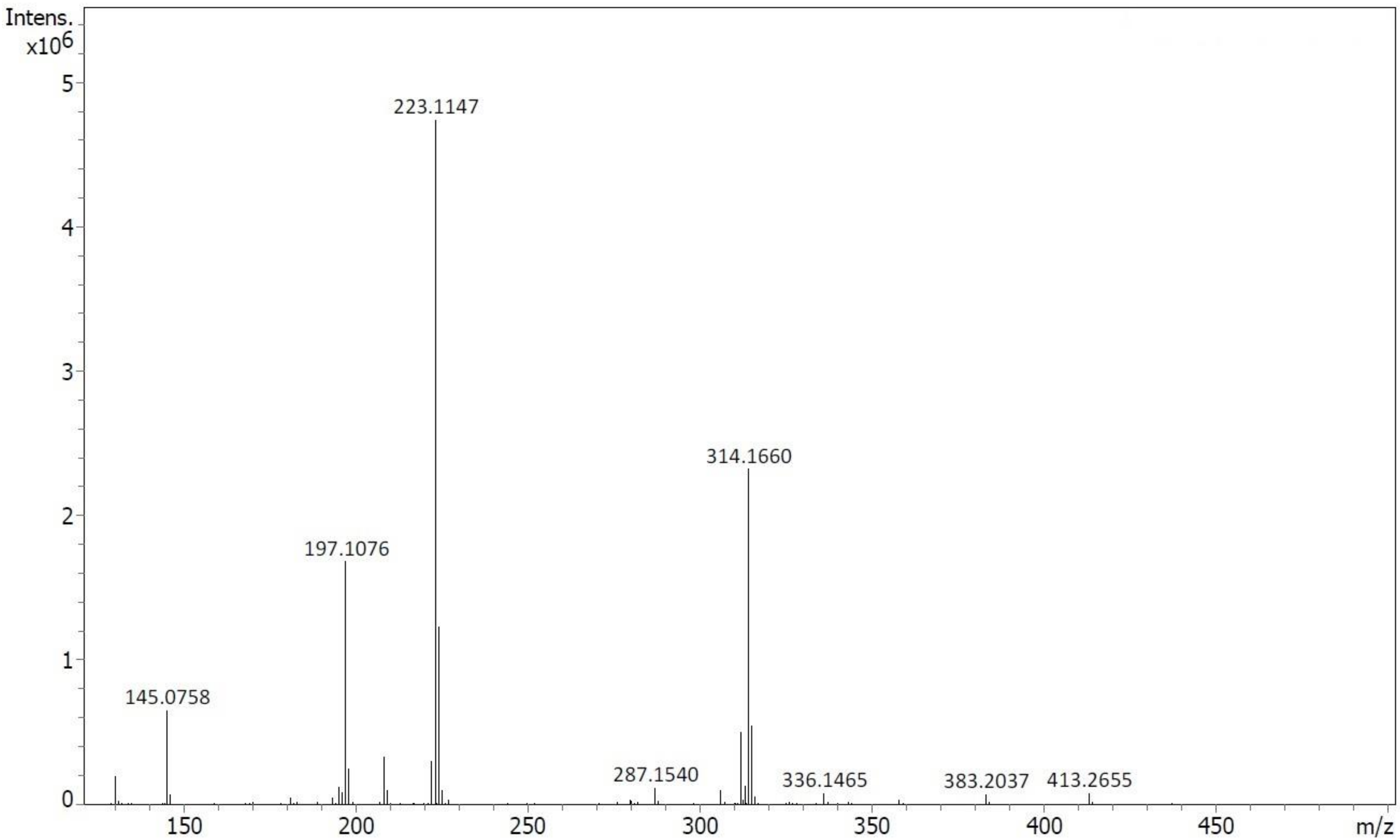


Figure S58. HRESI$^+$-MS of **12**.

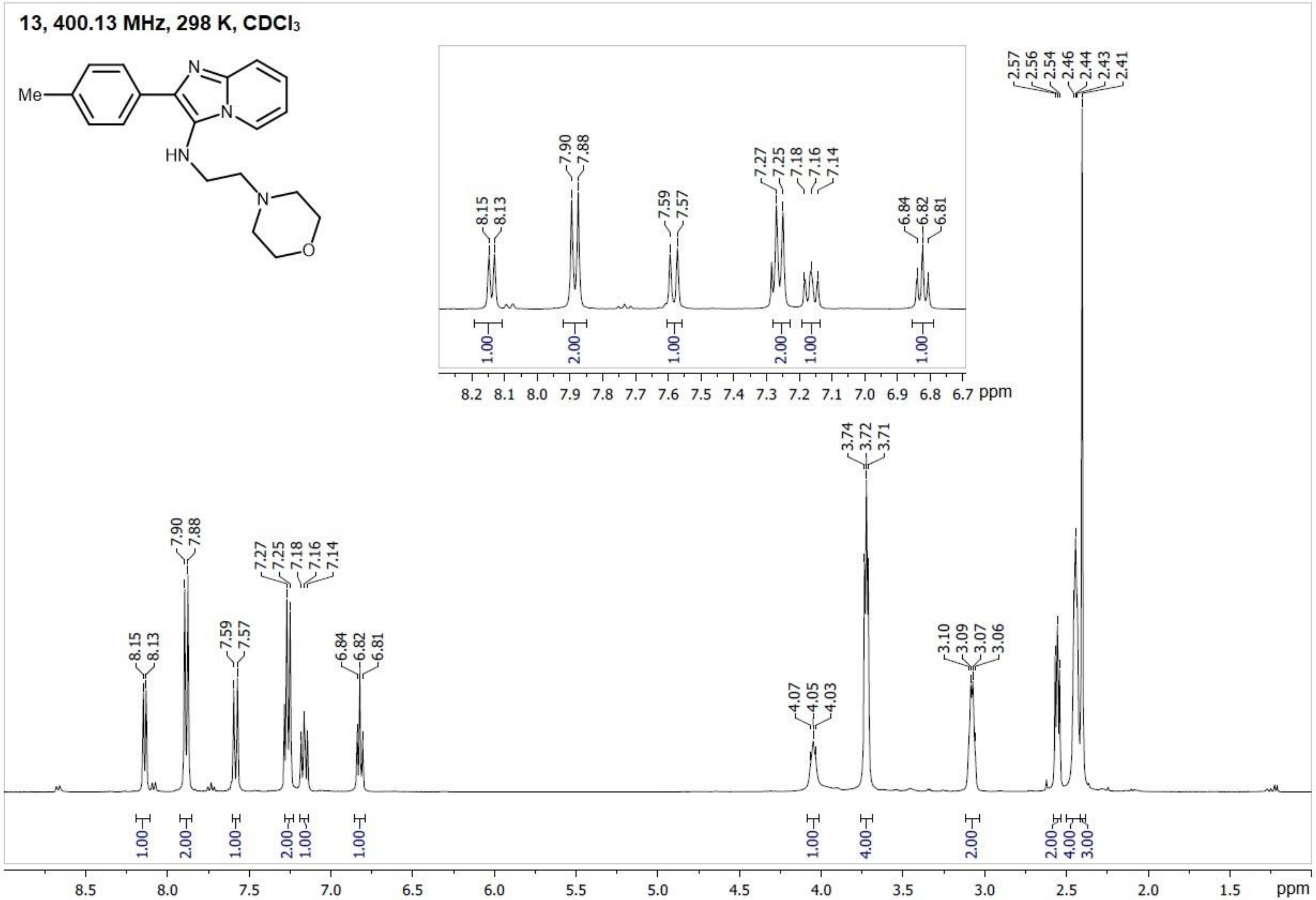


Figure S59. [1]H NMR spectrum of **13**.

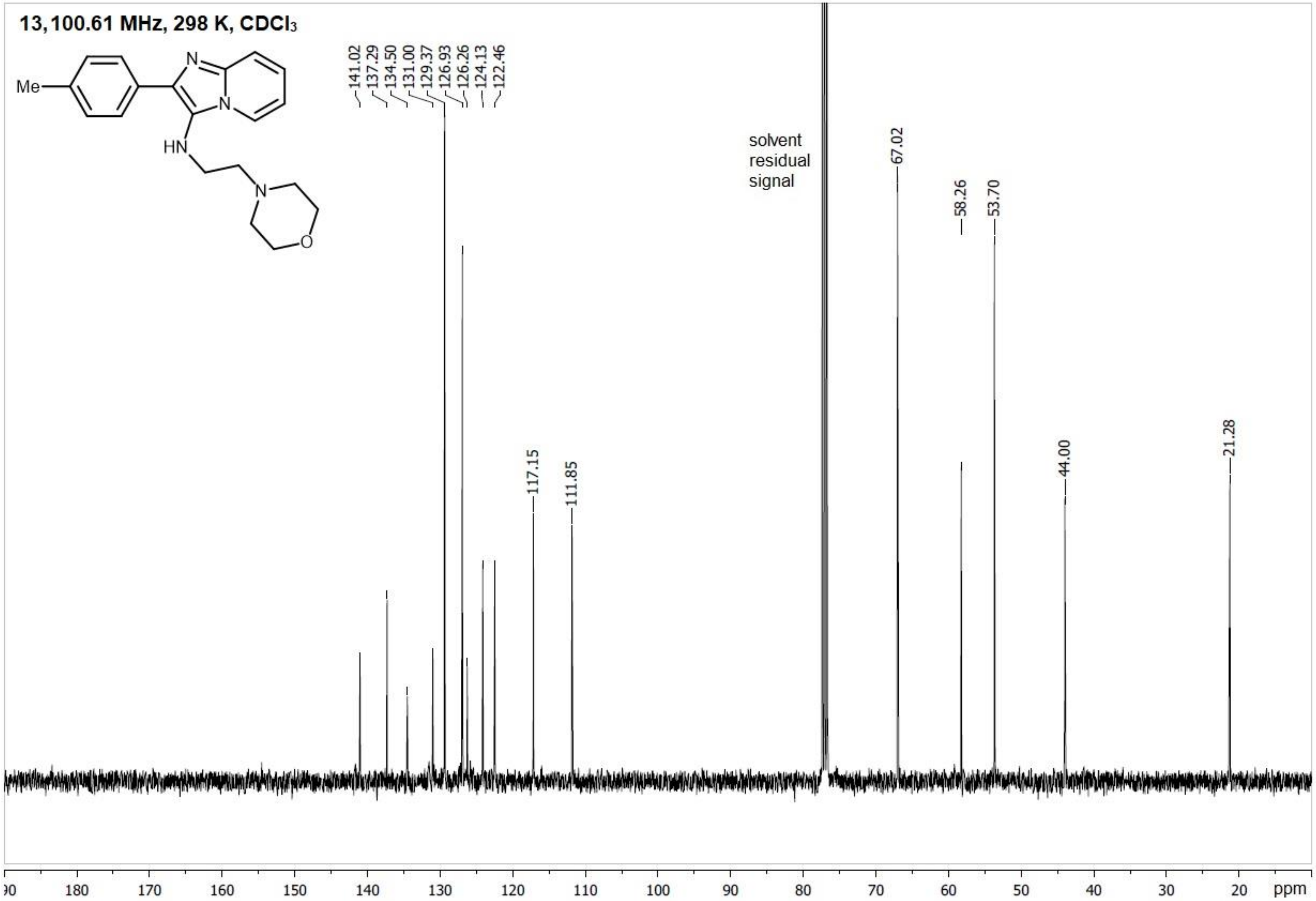


Figure S60. $^{13}C\{^{1}H\}$ NMR spectrum of **13**.

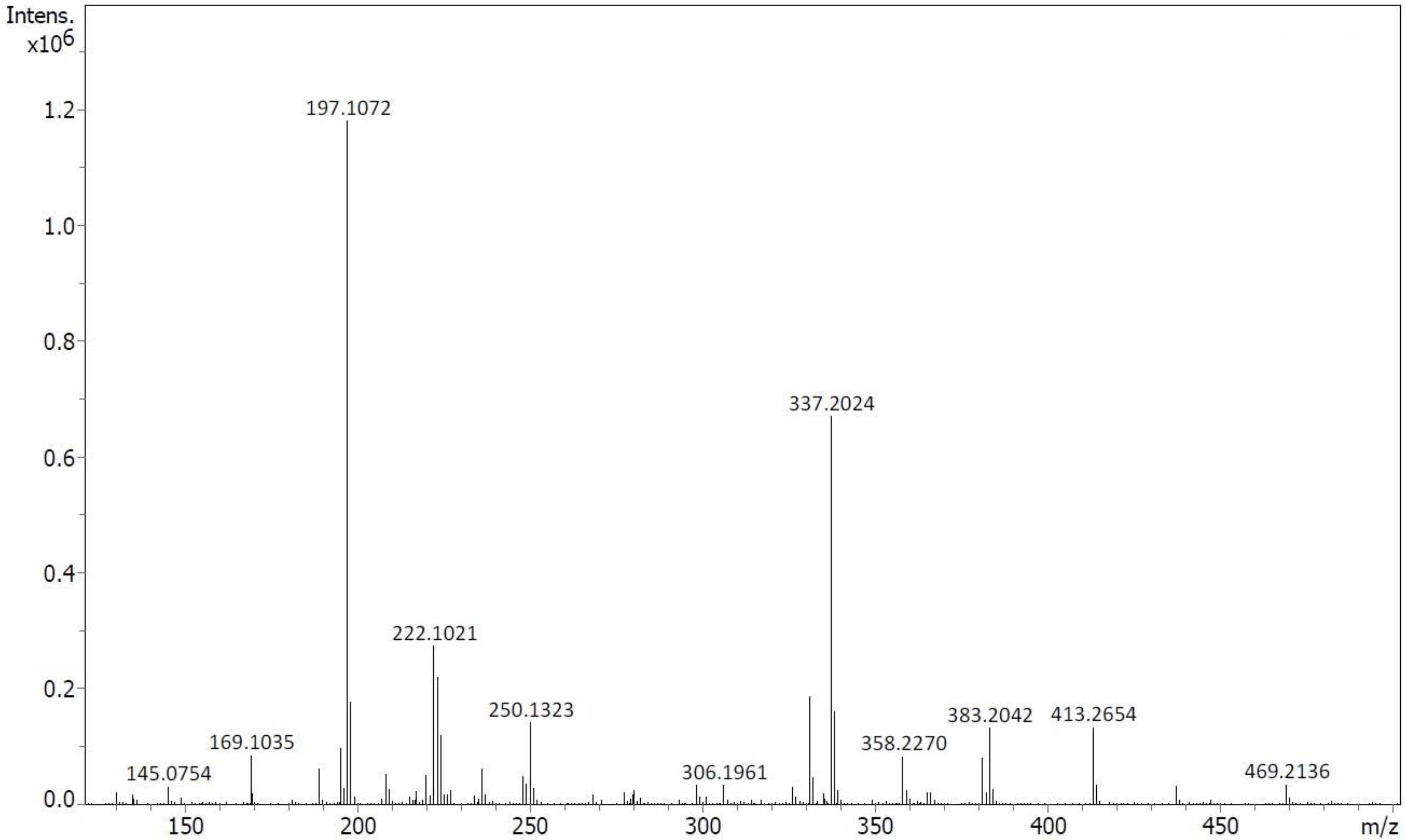


Figure S61. HRESI$^+$-MS of **13**.

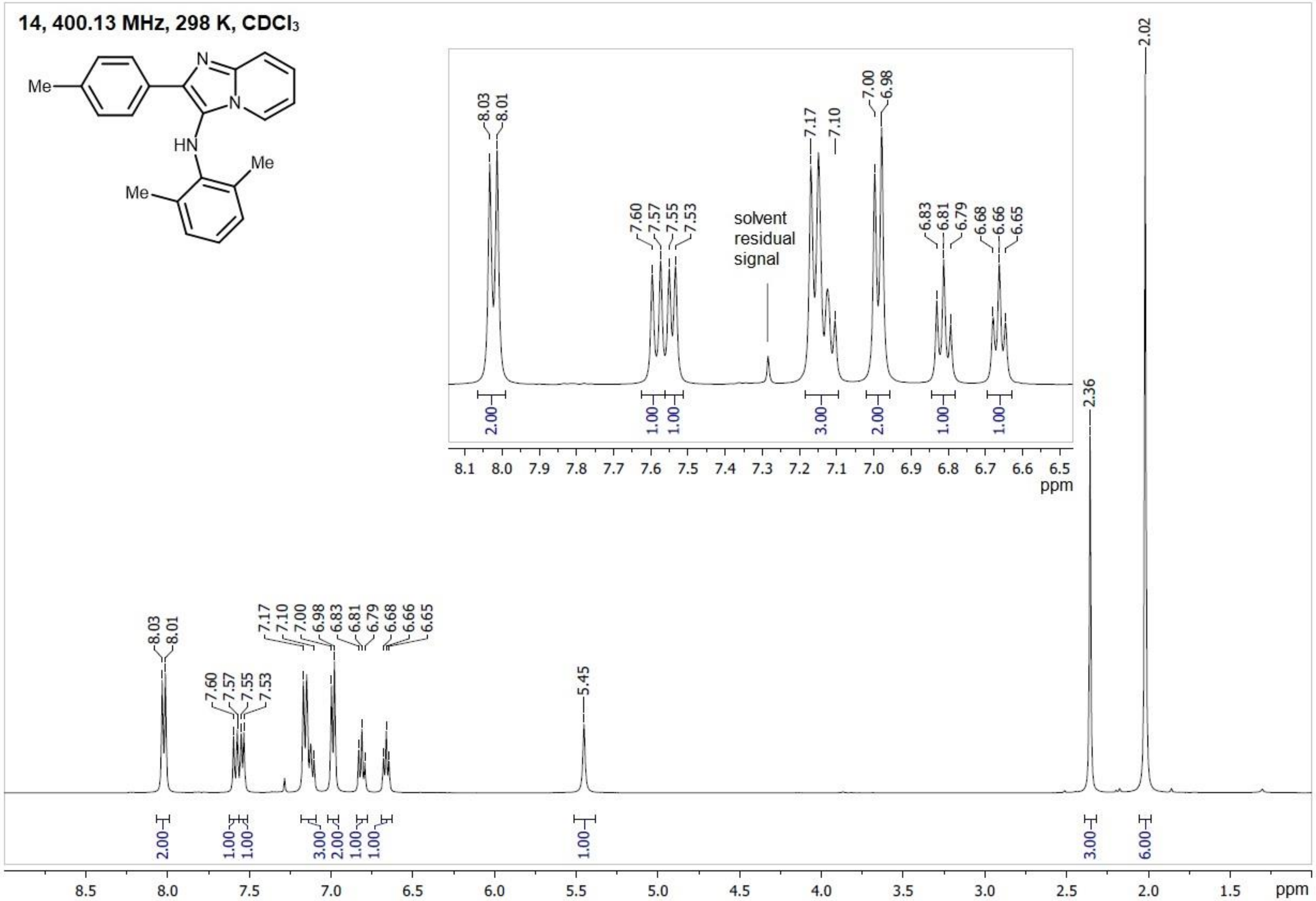


Figure S62. ^{1}H NMR spectrum of **14**.

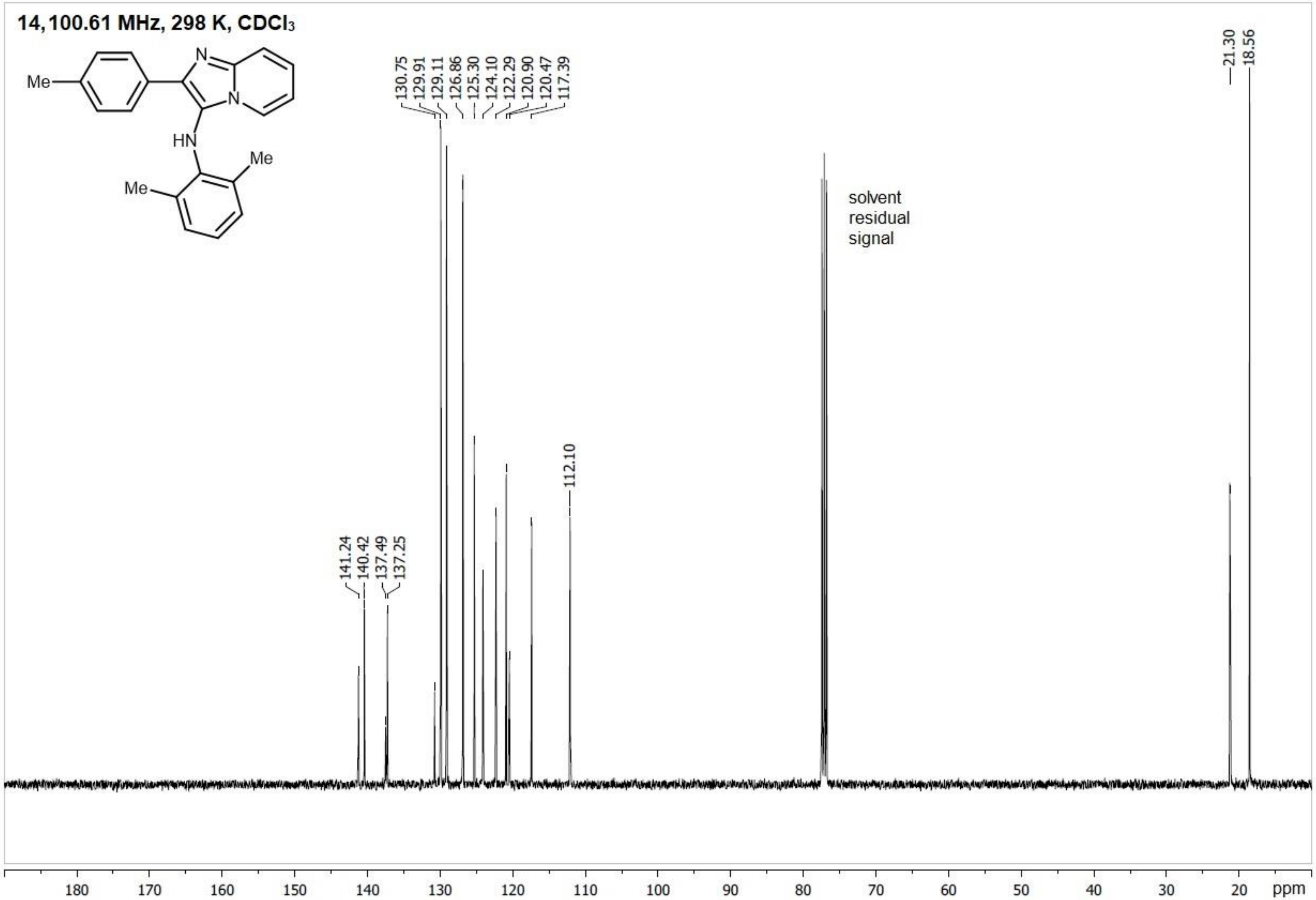


Figure S63. $^{13}C\{^{1}H\}$ NMR spectrum of **14**.

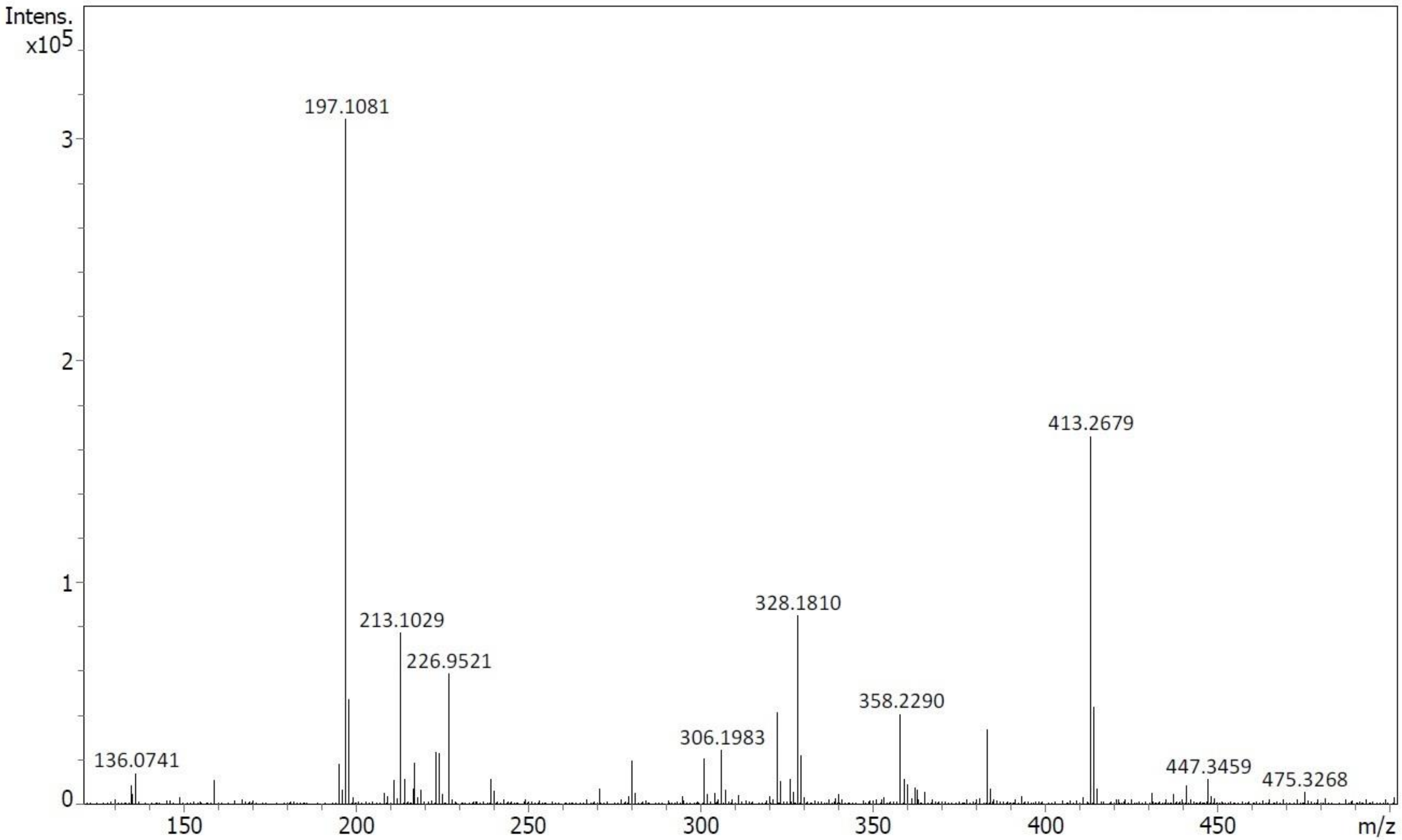


Figure S64. HRESI$^+$-MS of **14**.

Table S1. Crystal data for **Cat3**^{OTf} and **Cat4**^{OTf}.

Identification code	**Cat3**^{OTf}	**Cat4**^{OTf}
Empirical formula	$C_{16}H_{11}F_3IN_2O_3S$	$C_{15}H_9F_3IN_3O_3S$
Formula weight	494.22	495.21
Temperature/K	100(2)	
Crystal system	monoclinic	
Space group	$P2_1/c$	$P2_1/c$
a/Å	5.68910(10)	12.4433(2)
b/Å	30.3093(6)	12.38770(10)
c/Å	9.9602(3)	11.9729(2)
α/°	90	90
β/°	105.586(3)	116.297(2)
γ/°	90	90
Volume/Å^3	1654.31(7)	1654.55(5)
Z	4	4
ρ_{calc} g/cm^3	1.988	1.988
μ/mm^{-1}	16.893	16.911
F(000)	964.0	960.0
Crystal size/mm^3	0.12 × 0.07 × 0.03	0.14 × 0.08 × 0.06
Radiation	Cu Kα (λ = 1.54184)	
2Θ range for data collection/°	5.832 to 134.95	7.926 to 136.266
Index ranges	$-6 \le h \le 6$, $-36 \le k \le 34$, $-11 \le l \le 11$	$-13 \le h \le 14$, $-14 \le k \le 14$, $-14 \le l \le 14$
Reflections collected	16046	15508
Independent reflections	2962 [R_{int} = 0.1072, R_{sigma} = 0.0537]	3012 [R_{int} = 0.0376, R_{sigma} = 0.0253]
Data/restraints/parameters	2962/0/235	3012/0/236
Goodness-of-fit on F^2	1.052	1.030
Final R indexes [I⩾2σ (I)]	R_1 = 0.0417, wR_2 = 0.1067	R_1 = 0.0209, wR_2 = 0.0520
Final R indexes [all data]	R_1 = 0.0424, wR_2 = 0.1077	R_1 = 0.0218, wR_2 = 0.0525
Largest diff. peak/hole / e·Å^{-3}	1.10/–1.60	0.61/–0.56
CSD code	2212225	2212224

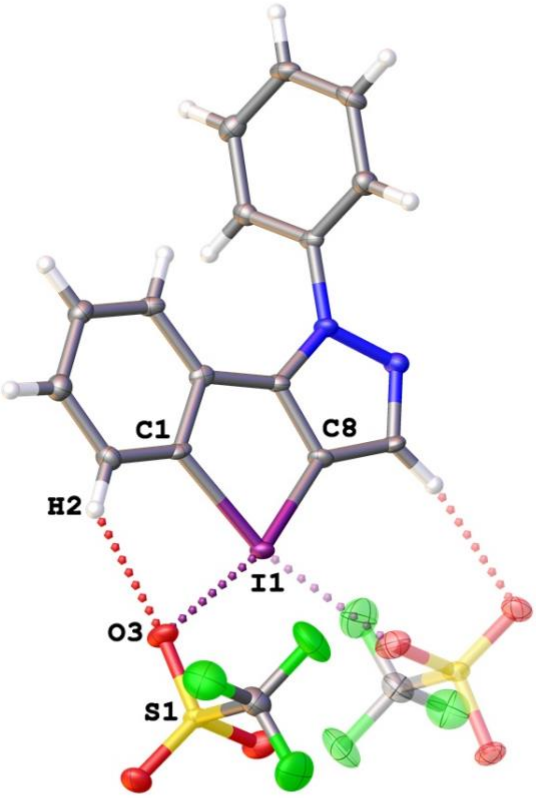


Figure S65. A thermal ellipsoid plot for **Cat3**^{OTf}.

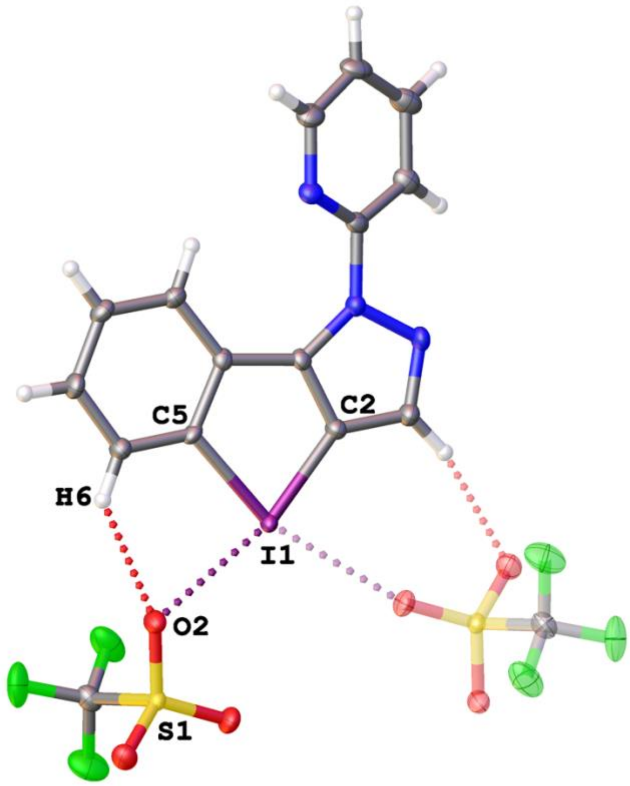


Figure S66. A thermal ellipsoid plot for **Cat4**^{OTf}.

Table S2. Calculated total electronic energies (E, in Hartree), enthalpies (H, in Hartree), Gibbs free energies (G, in Hartree), and entropies (S, cal/mol•K) for optimized equilibrium model structures.

Model structure	E	H	G	S
A	-727.539741069	-727.245460	-727.309705	135.215
B	-1055.46225191	-1054.987923	-1055.068834	170.293
C	-1055.47011881	-1054.994620	-1055.078358	176.241
Cat1	-473.054769811	-472.882786	-472.930383	100.176
Cat1_twoMeOH	-704.405640220	-704.115688	-704.185012	145.904
Cat2	-737.259074338	-736.999217	-737.059468	126.809
Cat2_twoMeOH	-968.612520912	-968.235804	-968.317627	172.210
Cat3	-697.964529114	-697.736021	-697.793254	120.457
Cat3_twoMeOH	-929.317870854	-928.971669	-929.049430	163.662
Cat4	-714.002393732	-713.785701	-713.842506	119.555
Cat4_twoMeOH	-945.355867129	-945.021578	-945.099111	163.183
CNCy	-327.945075733	-327.765443	-327.804941	83.132
D_Cat1	-1200.60425168	-1200.134965	-1200.227369	194.481
D_Cat2_a	-1464.81050513	-1464.255020	-1464.361158	223.388
D_Cat2_b	-1464.81026900	-1464.253944	-1464.359420	221.991
D_Cat3_a	-1425.51659930	-1424.990957	-1425.091964	212.588
D_Cat3_b	-1425.51642229	-1424.991688	-1425.094988	217.413
D_Cat4_a	-1441.55457544	-1441.041057	-1441.143084	214.735
D_Cat4_b	-1441.55680883	-1441.043667	-1441.145953	215.279
E_Cat1	-1528.53196695	-1527.882862	-1527.992725	231.228
E_Cat2_a	-1792.74223254	-1792.005874	-1792.127685	256.373
E_Cat2_b	-1792.74412295	-1792.007792	-1792.127169	251.249
E_Cat3_a	-1753.44897129	-1752.743217	-1752.859154	244.010
E_Cat3_b	-1753.44622106	-1752.740309	-1752.857513	246.678
E_Cat4_a	-1769.48472020	-1768.790899	-1768.907085	244.535
E_Cat4_b	-1769.48645264	-1768.792848	-1768.909528	245.574
F_Cat1	-1528.54358251	-1527.892583	-1528.003797	234.071
F_Cat2_a	-1792.75092310	-1792.013428	-1792.137467	261.062
F_Cat2_b	-1792.74993081	-1792.012200	-1792.137168	263.018
F_Cat3_a	-1753.45784978	-1752.750627	-1752.871010	253.366
F_Cat3_b	-1753.45632777	-1752.749036	-1752.867751	249.857
F_Cat4_a	-1769.49549357	-1768.800760	-1768.922870	257.001
F_Cat4_b	-1769.49737825	-1768.802136	-1768.920384	248.873
MeOH	-115.663537382	-115.607102	-115.633972	56.553
A_without_MeOH	-611.861433449	-611.626322	-611.680556	114.145
B_without_MeOH	-939.780058617	-939.364833	-939.436893	151.662
C_without_MeOH	-939.786769065	-939.370243	-939.444200	155.654
Cat1_MeOH	-588.730828594	-588.499401	-588.557021	121.271
Cat2_MeOH_and_sigma-hole_in_a_position	-852.935895057	-852.618519	-852.686323	142.707
Cat2_MeOH_and_sigma-hole_in_b_position	-852.935921854	-852.617834	-852.689867	151.606
Cat3_MeOH_and_sigma-hole_in_a_position	-813.641249802	-813.353876	-813.421361	142.036

Cat3_MeOH_and_sigma-hole_in_b_position	-813.641735547	-813.354427	-813.420870	139.842
Cat4_MeOH_and_sigma-hole_in_a_position	-829.679171329	-829.403586	-829.471021	141.930
Cat4_MeOH_and_sigma-hole_in_b_position	-829.679685086	-829.404309	-829.470298	138.886
CNCy	-327.945075733	-327.765443	-327.804941	83.132
D_Cat1	-1200.60425168	-1200.134965	-1200.227369	194.481
D_Cat2_a	-1464.81050513	-1464.255020	-1464.361158	223.388
D_Cat2_b	-1464.81026900	-1464.253944	-1464.359420	221.991
D_Cat3_a	-1425.51659930	-1424.990957	-1425.091964	212.588
D_Cat3_b	-1425.51642229	-1424.991688	-1425.094988	217.413
D_Cat4_a	-1441.55457544	-1441.041057	-1441.143084	214.735
D_Cat4_b	-1441.55680883	-1441.043667	-1441.145953	215.279
E_Cat1	-1528.53196695	-1527.882862	-1527.992725	231.228
E_Cat2_a	-1792.74223254	-1792.005874	-1792.127685	256.373
E_Cat2_b	-1792.74412295	-1792.007792	-1792.127169	251.249
E_Cat3_a	-1753.44897129	-1752.743217	-1752.859154	244.010
E_Cat3_b	-1753.44622106	-1752.740309	-1752.857513	246.678
E_Cat4_a	-1769.48472020	-1768.790899	-1768.907085	244.535
E_Cat4_b	-1769.48645264	-1768.792848	-1768.909528	245.574
F_Cat1	-1528.54358251	-1527.892583	-1528.003797	234.071
F_Cat2_a	-1792.75092310	-1792.013428	-1792.137467	261.062
F_Cat2_b	-1792.74993081	-1792.012200	-1792.137168	263.018
F_Cat3_a	-1753.45784978	-1752.750627	-1752.871010	253.366
F_Cat3_b	-1753.45632777	-1752.749036	-1752.867751	249.857
F_Cat4_a	-1769.49549357	-1768.800760	-1768.922870	257.001
F_Cat4_b	-1769.49737825	-1768.802136	-1768.920384	248.873

Table S3. Calculated values of total electronic energies, enthalpies, and Gibbs free energies of activation and reaction ($\Delta E^{\neq}$, $\Delta H^{\neq}$, $\Delta G^{\neq}$, ΔE, ΔH, and ΔG in kJ/mol) for model processes.

Model process	**$\Delta E^{\neq}$**	**$\Delta H^{\neq}$**	**$\Delta G^{\neq}$**	**ΔE**	**ΔH**	**ΔG**
A + CNCy → **C** (via **B**)	59.2	60.3	120.3	38.6	42.8	95.3
A + **Cat1_twoMeOH** → **D_Cat1** + 2 MeOH				36.9	31.5	-1.6
A + **Cat2_twoMeOH** → **D_Cat2_a** + 2 MeOH				38.5	31.6	-4.6
A + **Cat2_twoMeOH** → **D_Cat2_b** + 2 MeOH				39.2	34.4	-0.1
A + **Cat3_twoMeOH** → **D_Cat3_a** + 2 MeOH				36.6	31.4	-2.0
A + **Cat3_twoMeOH** → **D_Cat3_b** + 2 MeOH				37.1	29.5	-10.0
A + **Cat4_twoMeOH** → **D_Cat4_a** + 2 MeOH				36.6	30.9	-5.8
A + **Cat4_twoMeOH** → **D_Cat4_b** + 2 MeOH				30.8	24.1	-13.3
D_Cat1 + CNCy → **F_Cat1** (via **E_Cat1**)	45.6	46.1	103.9	15.1	20.5	74.9
D_Cat2_a + CNCy → **F_Cat2_a** (via **E_Cat2_a**)	35.0	38.3	100.9	12.2	18.5	75.2
D_Cat2_b + CNCy → **F_Cat2_b** (via **E_Cat2_b**)	29.5	30.4	97.6	14.2	18.9	71.4
D_Cat3_a + CNCy → **F_Cat3_a** (via **E_Cat3_a**)	33.4	34.6	99.1	10.0	15.2	68.0
D_Cat3_b + CNCy → **F_Cat3_b** (via **E_Cat3_b**)	40.1	44.2	111.4	13.6	21.3	84.5
D_Cat4_a + CNCy → **F_Cat4_a** (via **E_Cat4_a**)	39.2	41.0	107.5	10.9	15.1	66.0
D_Cat4_b + CNCy → **F_Cat4_b** (via **E_Cat4_b**)	40.5	42.7	108.6	11.8	18.3	80.1
A_without_MeOH + CNCy → **C_without_MeOH**	69.4	70.7	127.6	51.8	56.5	108.4
A_without_MeOH + **Cat1_MeOH** → **D_Cat1**				-31.5	-24.3	26.8
A_without_MeOH + **Cat2_MeOH_and_sigma-hole_in_a_position** → **D_Cat2_a**				-34.6	-26.7	15.0
A_without_MeOH + **Cat2_MeOH_and_sigma-hole_in_b_position** → **D_Cat2_b**				-33.9	-25.7	28.9
A_without_MeOH + **Cat3_MeOH_and_sigma-hole_in_a_position** → **D_Cat3_a**				-36.5	-28.2	26.1
A_without_MeOH + **Cat3_MeOH_and_sigma-hole_in_b_position** → **D_Cat3_b**				-34.8	-28.7	16.9
A_without_MeOH + **Cat4_MeOH_and_sigma-hole_in_a_position** → **D_Cat4_a**				-36.7	-29.3	22.3
A_without_MeOH + **Cat4_MeOH_and_sigma-hole_in_b_position** → **D_Cat4_b**				-41.2	-34.2	12.9
D_Cat1 + CNCy → **F_Cat1** (via **E_Cat1**)	45.6	46.1	103.9	15.1	20.5	74.9
D_Cat2_a + CNCy → **F_Cat2_a** (via **E_Cat2_a**)	35.0	38.3	100.9	12.2	18.5	75.2
D_Cat2_b + CNCy → **F_Cat2_b** (via **E_Cat2_b**)	29.5	30.4	97.6	14.2	18.9	71.4
D_Cat3_a + CNCy → **F_Cat3_a** (via **E_Cat3_a**)	33.4	34.6	99.1	10.0	15.2	68.0
D_Cat3_b + CNCy → **F_Cat3_b** (via **E_Cat3_b**)	40.1	44.2	111.4	13.6	21.3	84.5
D_Cat4_a + CNCy → **F_Cat4_a** (via **E_Cat4_a**)	39.2	41.0	107.5	10.9	15.1	66.0
D_Cat4_b + CNCy → **F_Cat4_b** (via **E_Cat4_b**)	40.5	42.7	108.6	11.8	18.3	80.1