ELECTRONIC SUPPORTING INFORMATION

Amine-mediated intramolecular aryl–aryl coupling in pyrazolyl-containing iodolium salts

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Materials and instrumentation. All solvents, aldehydes, isocyanides, 2-aminopyridine, were obtained from commercial sources and used as received. The iodonium salts **1a**(OTf)–**2a**$(OTf)_2$ were synthesized according to published procedures.[1, 2] All syntheses were conducted in air. Chromatographic separation was carried out using Macherey-Nagel silica gel 60 M (0.063–0.2 mm). Analytical TLC was performed on unmodified Merck ready-to-use plates (TLC silica gel 60 F254) with UV detection. Melting points were measured on a Stuart SMP30 apparatus in capillaries and are not corrected. Electrospray ionization mass-spectra were obtained on a Bruker maXis spectrometer equipped with an electrospray ionization (ESI) source. The instrument was operated in positive ion mode using an *m*/*z* range 50–1200. The nebulizer gas flow was 1.0 bar and the drying gas flow 4.0 L min^{-1}. For $HRESI^+$, the studied compounds were dissolved in MeOH. ^1H- and $^{13}C\{^1H\}$ NMR spectra were measured on a Bruker Avance 400 spectrometer in $CDCl_3$, $(CD_3)_2CO$, CD_3CN and $(CD_3)_2SO$ at 298 K; the residual solvent signal was used as the internal standard. The NMR monitoring kinetic experiments were carried out by measuring the ^1H NMR spectra every 5 min (four scans; repetition time = 4 s) following the initial equilibration period of 5 min on a Bruker Avance III 500 spectrometer in CD_3CN at 50 °C; the residual solvent signal was used as the internal standard.

Single-crystal XRD study. Single-crystal X-ray diffraction experiment was carried out on Agilent Technologies «SuperNova» diffractometers with monochromated CuKα radiation. Crystals were kept at 100(2) K during data collection. Structure have been solved by the Superflip,[3] and the ShelXT[4] structure solution programs using Charge Flipping and Intrinsic Phasing and refined by means of the ShelXL[5] program incorporated in the OLEX2[6] program package. The crystal data and details of structure refinements for **2a**$(OTf)_2$ are shown in Table S1. The structure can be obtained free of charge via the Cambridge Crystallographic Database (CCDC 2354600; https://www.ccdc.cam.ac.uk/structures/).

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

The imine (86 mg, 0.439 mmol), cyclohexyl isocyanide (13.6 μL, 0.110 mmol) and 1,4-dimethoxybenzene as the internal standard (15 mg, 0.110 mmol) were added to the CD_3CN solution of **1a**(OTf)–**3**(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_3CN (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.

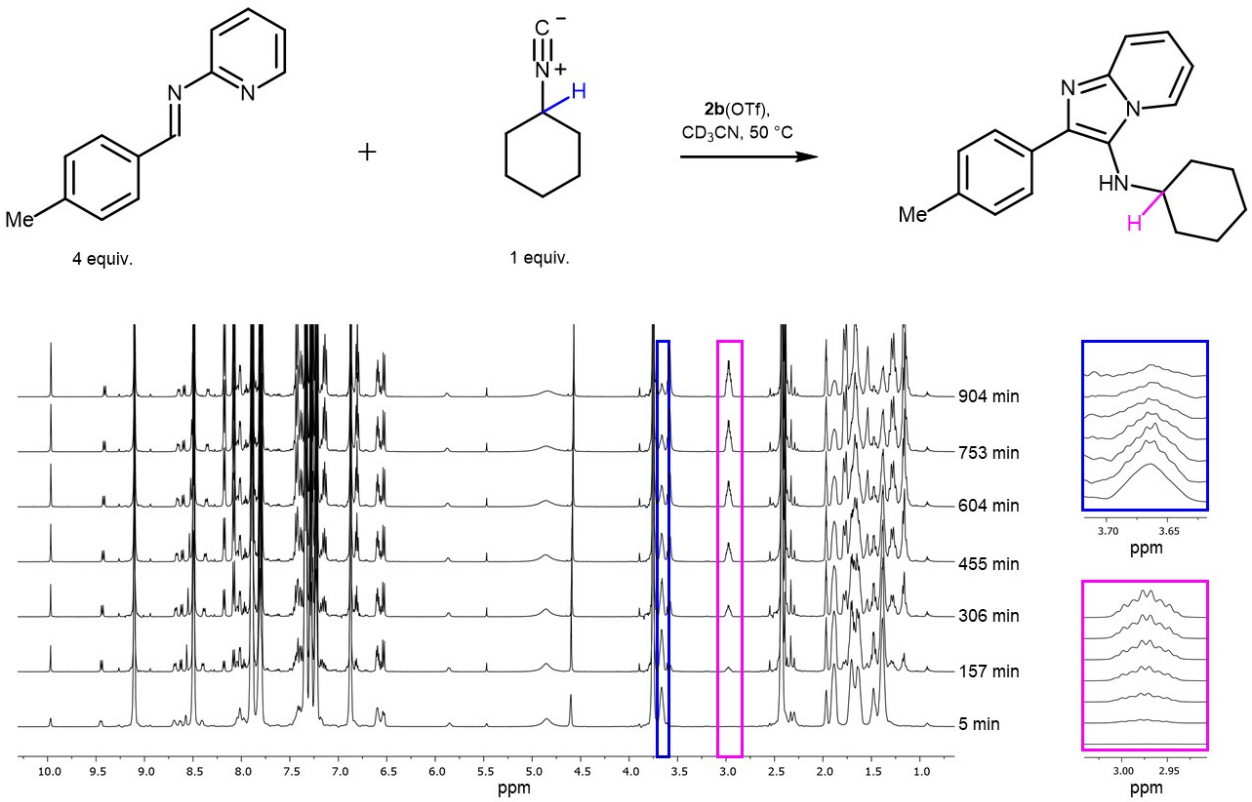


Figure S1. ^{1}H NMR spectra of the monitoring second step of reaction with **2b**(OTf) at the different time intervals.

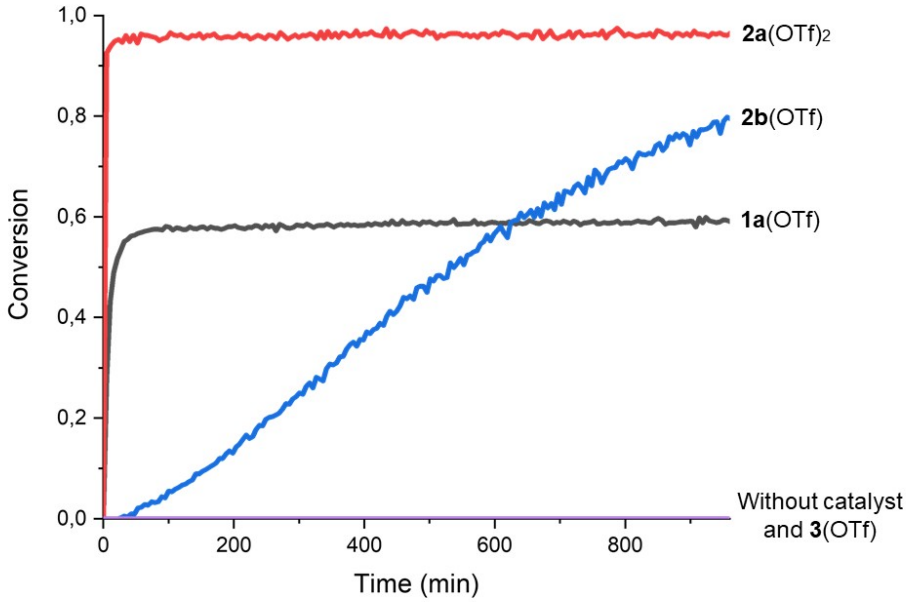


Figure S2. ^{1}H NMR monitoring of the progress of the second step of the model Groebke–Blackburn–Bienaymé reaction.

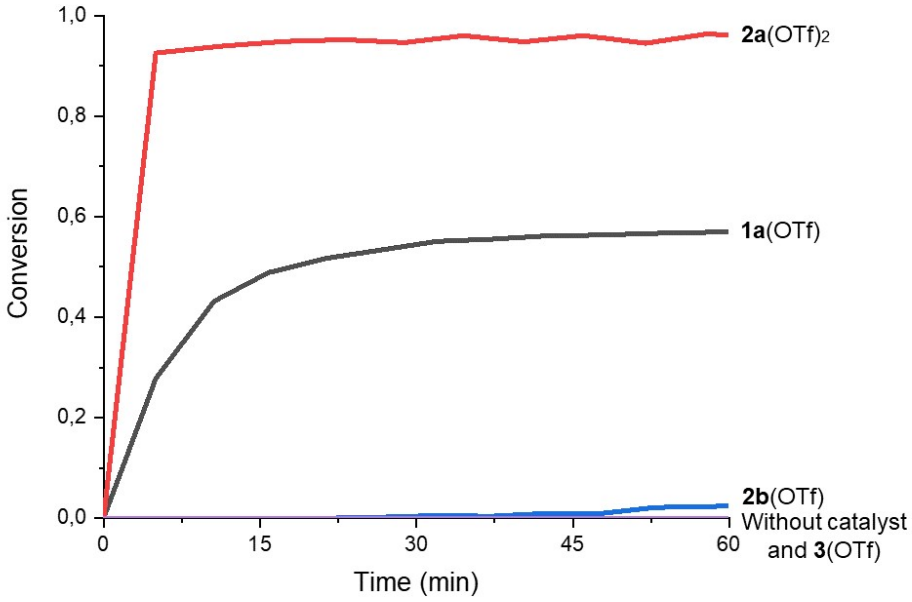
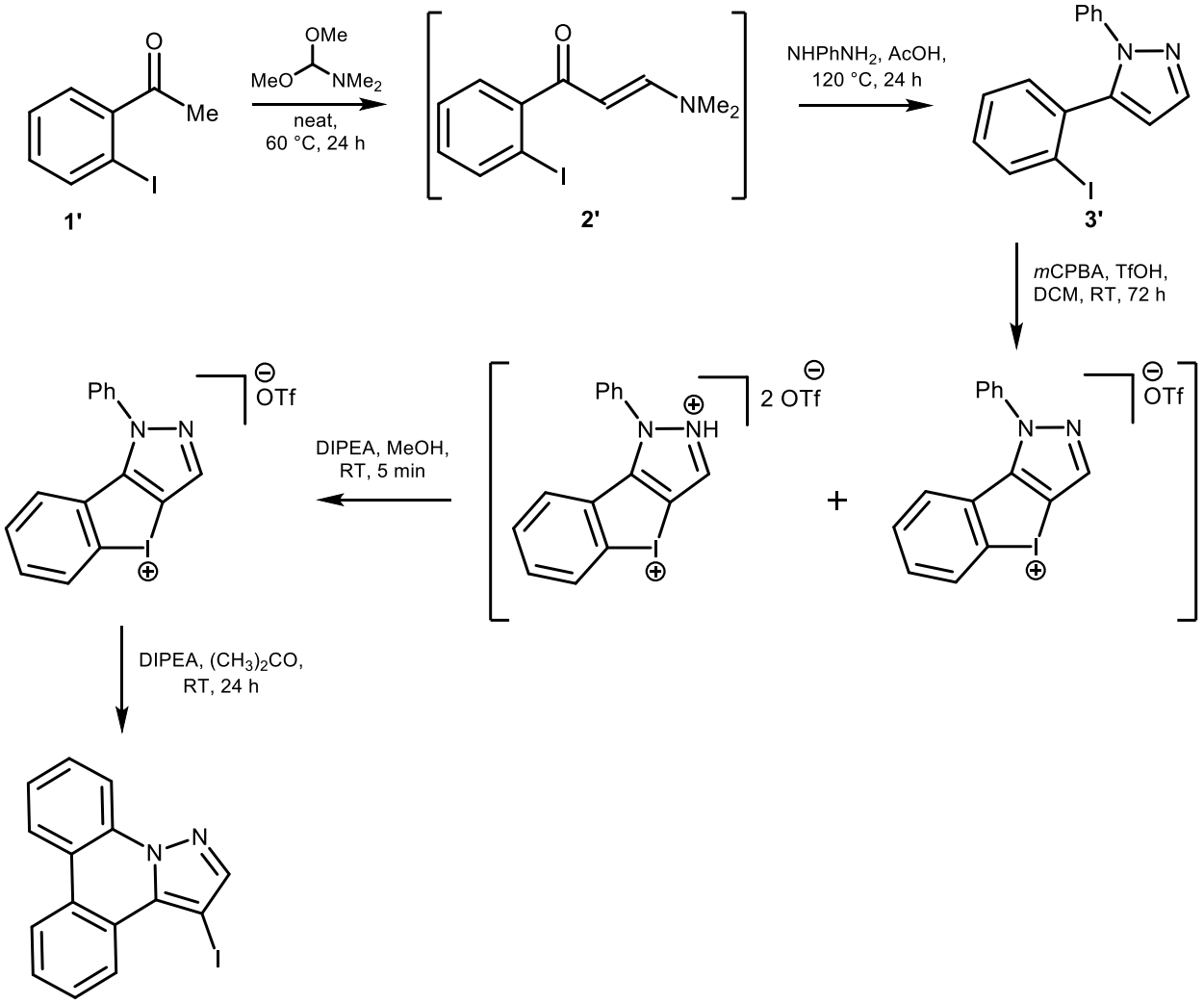


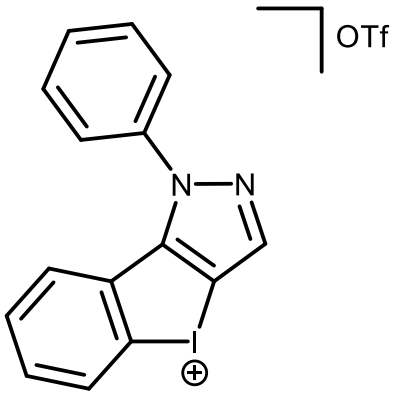
Figure S3. ^{1}H NMR monitoring of the progress of the second step of the model Groebke–Blackburn–Bienaymé reaction within the first 60 minutes.

Synthesis and characterization of 1a(OTf) **and 1b**

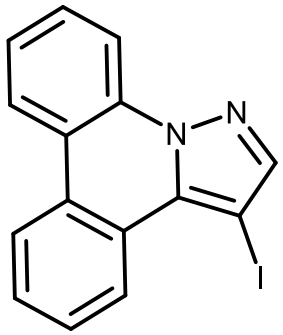


Corresponded compound was synthesized according to a previously published procedure,[1, 2] with some modifications. 2-Iodoacetophenone (1.00 g; 4.066 mmol) was dissolved in dimethylformamide-dimethylacetal (0.968 g; 8.132 mmol) and stirred at 60 °C for 24 h. After that solution was evaporated *in vacuo* 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. Compound **1a**(OTf) (0.090 g; 0.1822 mmol), obtained according to the procedure described above, was dissolved in the solution of diisopropylethylamine (0.0235 g; 0.1822 mmol) in 2 mL of acetone and stirred at RT for 24 h. After that the solvent was evaporated *in vacuo* at 50 °C, and the corresponding compound was isolated *via* column chromatography (eluent: hexane/EtOAc 95:5).

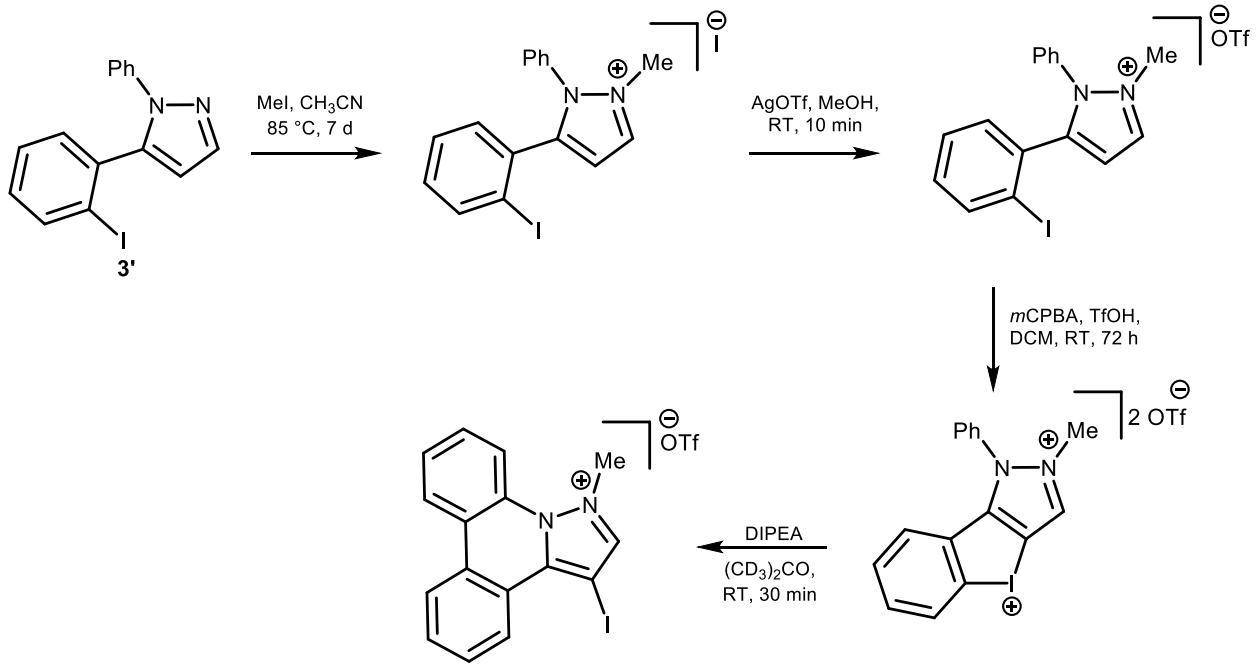


1a(OTf). Overall yield: 28% (560 mg). M.p.: 220–224 °C (decomp.). ^{1}H NMR (400.13 MHz, DMSO-d_6) δ = 8.32 (d, $^{3}J_{HH}$ = 7.9 Hz, 1H, Ar), 8.19 (s, 1H, Ar), 7.71–7.60 (m, 7H, Ar), 7.24 (dd, $^{3}J_{HH}$ = 7.5 Hz, $^{4}J_{HH}$ = 1.8 Hz, 1H, Ar). ^{13}C{^{1}H} NMR (101.61 MHz, DMSO-d_6) δ = 148.4, 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). HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{15}H_{10}N_2I$ 344.9889; Found 344.9883.

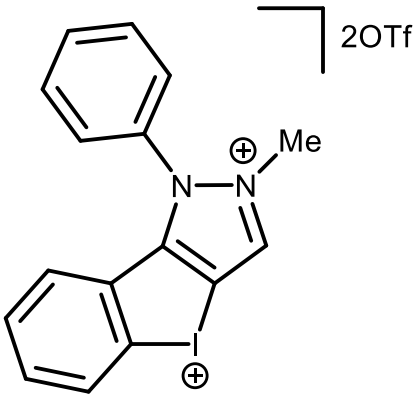


1b. Yield: 47% (42 mg). M.p.: 136–140 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ = 9.30–9.27 (m, 1H, Ar), 8.60 (d, $^{3}J_{HH}$ = 8.9 Hz, 1H, Ar), 8.46–8.40 (m, 2H, Ar), 8.03 (s, 1H, Ar), 7.71–7.65 (m, 3H, Ar), 7.54 (t, $^{3}J_{HH}$ = 8.2 Hz, 1H, Ar). ^{13}C{^{1}H} NMR (101.61 MHz, $CDCl_3$) δ = 147.7, 133.8, 133.7, 129.4, 128.8, 127.7, 127.4, 125.5, 124.0, 123.3, 122.8, 121.3, and 116.2 (Ar); 50.6 (*C*–I). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{10}N_2I$ 344.9884; Found 344.9882.

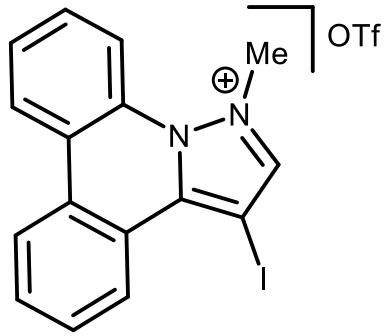
Synthesis and characterization of 2a$(OTf)_2$–2b(OTf)



Compound **3'** (0.158 g; 0.4561 mmol), obtained according to the procedure described above, was dissolved in the solution of methyl iodide (0.648 g; 4.561 mmol) in 2 mL of acetonitrile and stirred at 85 °C for 7 days. After that solution was evaporated *in vacuo* at 60 °C. The solution of silver triflate (0.132 g, 0.512 mmol) in 1 mL of methanol were added to a stirred solution of the residue in 1 mL methanol and stirred for 10 min at RT. The precipitate which formed was filtered, dried *in vacuo* at 50 °C and dissolved in the solution of triflic acid (0.114 mL, 3 equiv.) and *m*-CPBA (0.145 g, 0.647 mmol, 1.5 equiv.) in 3 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, filtered off, washed with Et_2O (2 mL), and dried at 50 °C *in vacuo*. Compound **2a**$(OTf)_2$ (0.041 g; 0.0623 mmol), obtained according to the procedure described above, was dissolved in the solution of diisopropylethylamine (0.008 g; 0.0623 mmol) in 1 mL of acetone and stirred at RT for 30 min. After that the solvent was evaporated in vacuo at 50 °C, and the residue was crystallized using ethyl acetate, filtered off, washed with EtOAc (1 mL), and dried at 50 °C *in vacuo*.

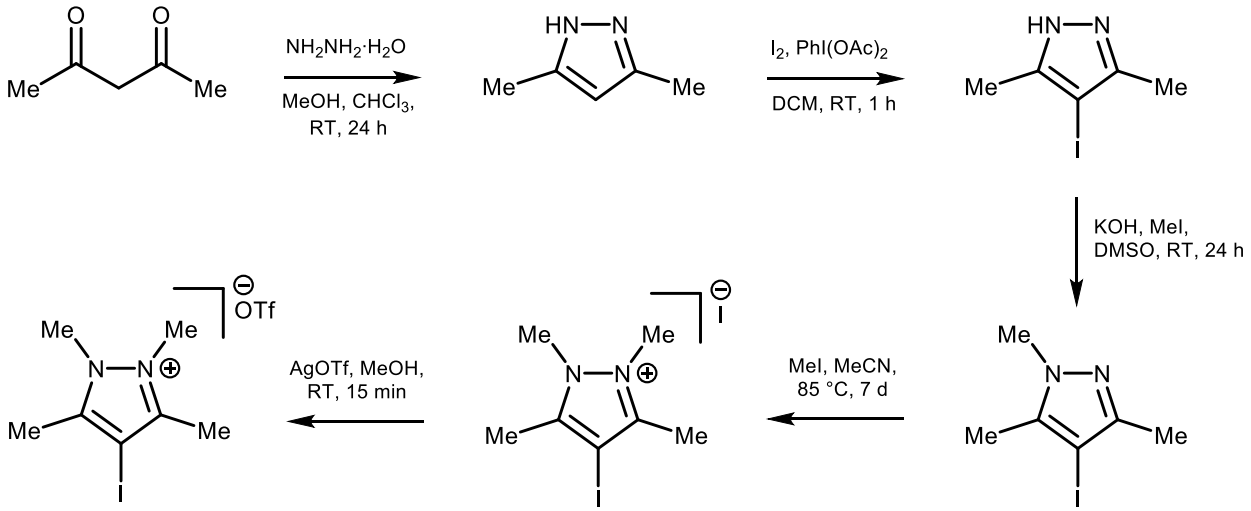


2a$(OTf)_2$. Yield: 76% (229 mg). M.p.: 250–252 °C. ^{1}H NMR (400.13 MHz, $(CD_3)_2CO$) δ = 9.25 (s, 1H, Ar), 8.56 (d, $^3J_{HH}$ = 8.5 Hz, 1H, Ar), 8.17–8.14 (m, 2H, Ar), 8.12–8.08 (m, 1H, Ar), 8.04–8.00 (m, 2H, Ar), 7.96–7.91 (m, 1H, Ar), 7.82–7.78 (m, 1H, Ar), 7.13 (dd, $^3J_{HH}$ = 7.9 Hz, $^4J_{HH}$ = 1.4 Hz, 1H, Ar), 4.39 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (101.61 MHz, $(CD_3)_2CO$) δ = 153.0, 139.3, 134.5, 131.8, 131.7, 131.0, 129.0, 128.0, 127.5, 127.3 and 93.0 (Ar); 68.4 (*C*–I); 38.8 (*C*H_3). HRMS (ESI) m/z: $[M]^{2+}$ Calcd for $C_{16}H_{13}N_2I$ 180.0056; Found 180.0062.



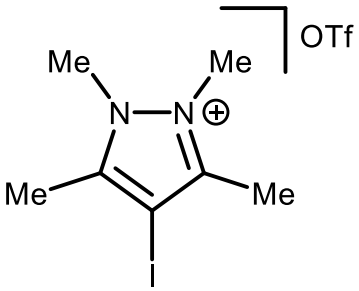
2b(OTf). Yield: 56% (22.7 mg). M.p.: 253–257 °C (decomp.). ^{1}H NMR (400.13 MHz, $(CD_3)_2CO$) δ = 9.69 (d, $^3J_{HH}$ = 9.0 Hz, 1H, Ar), 9.29 (s, 1H, Ar), 9.05–9.03 (m, 1H, Ar), 8.98 (d, $^3J_{HH}$ = 8.2 Hz, 1H, Ar), 8.93–8.91 (m, 1H, Ar), 8.16–8.12 (m, 1H, Ar), 8.09–7.99 (m, 3H, Ar), 4.39 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (101.61 MHz, $(CD_3)_2CO$) δ = 149.1, 139.1, 133.0, 130.4, 130.2, 129.9, 129.1, 129.0, 125.7, 125.1, 124.4, 123.8, 121.9 and 118.3 (Ar); 56.3 (*C*–I); 44.9 (*C*H_3). HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{16}H_{12}N_2I$ 359.040; Found 359.0040.

Synthesis and characterization of 3(OTf)



Corresponded compound was synthesized according to a previously published procedure.[7] A solution of hydrazine hydrate (1293 μL, 22.5 mmol) in MeOH (10 mL) was added to a stirred solution of one of the desired 1,3-diketones (15 mmol) in $CHCl_3$ (10 mL). The resulting solution was stirred overnight at RT. The solvent was evaporated *in vacuo* at 50 °C, and the residue was crystallized using hexane (5 mL). The precipitate was filtered off, washed with hexane (10 mL), dried at 50 °C for 2 h in air, and used without additional purification. A solution of the corresponding pyrazole (7 mmol) in CH_2Cl_2 (5 mL) was added to a stirred solution of I_2 (1067 mg, 4.2 mmol) and $PhI(OAc)_2$ (1352 mg, 4.2 mmol) in CH_2Cl_2 (5 mL). The resulting solution was stirred for 1 h at RT. The solvent was evaporated *in vacuo* at 50 °C, and the corresponding 4-iodopyrazole was isolated v*ia* column chromatography (eluent: EtOAc : hexane = 1 : 1, v/v). A solution of the 4-iodopyrazole (2.5 mmol) in DMSO (2 mL) was added to a stirred solution of KOH (280 mg, 5 mmol) and MeI (233 μL, 3.75 mmol) in DMSO (2 mL). The resulting solution was stirred overnight at RT, and then H_2O (100 mL) was added to the reaction mixture. The product was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (50 mL), and the organic layer was dried over Na_2SO_4 and filtered from the inorganics. The solvent was evaporated *in vacuo* at 50 °C, and the corresponding 1-methyl-4-iodopyrazole was used without additional purification. A solution of MeI (224 μL, 3.6 mmol) in CH_3CN (1 mL) was added to a stirred solution of the corresponding 1-methyl-3-iodopyrazole (1.2 mmol) in CH_3CN (4 mL). The resulting solution was stirred for 7 d at 85 °C, and the generated precipitate was filtered off, washed with CH_3CN (2 × 3 mL) and Et_2O (1 × 5 mL), and dried at 50 °C for 2 h in air to give the corresponding 1,2-dimethyl-4-iodopyrazolium iodide, which was used without further purification. A solution of AgOTf (136 mg, 0.53 mmol) in MeOH (2 mL) was added to a stirred

solution of the corresponding 1,2-dimethyl-4-iodo-pyrazolium iodide (0.53 mmol) in MeOH (3 mL). The suspension was stirred for 15 min at RT, and the precipitate formed was filtered off, washed with MeOH (15 mL), and the combined organic layers were evaporated *in vacuo* at 40 °C. The residue was recrystallized from EtOAc (5 mL) to give **3**(OTf). Yields on the last synthetic step are reported below.



3(OTf): Yield: 83% (176 mg). M.p.: 159–161 °C. ^{1}H-NMR (400.13 MHz, CD_3CN, ppm): δ = 3.93 (s, 6H, N–CH_3), 2.46 (s, 6H, C–CH_3). $^{13}C\{^{1}H\}$-NMR (101.61 MHz, CD_3CN, ppm): δ = 148.05 (*C*–CH_3), 121.01 (q, $^{1}J_{CF}$ = 320.7 Hz, *C*F_3), 65.56 (*C*–I), 35.06 (N–*C*H_3), 12.95 (C–*C*H3). HRMS (ESI-TOF): *m/z* calcd for $C_7H_{12}N_2I^+$: 251.0040; found: 251.0042.

Spectra of **1a**(OTf)–**3**(OTf)

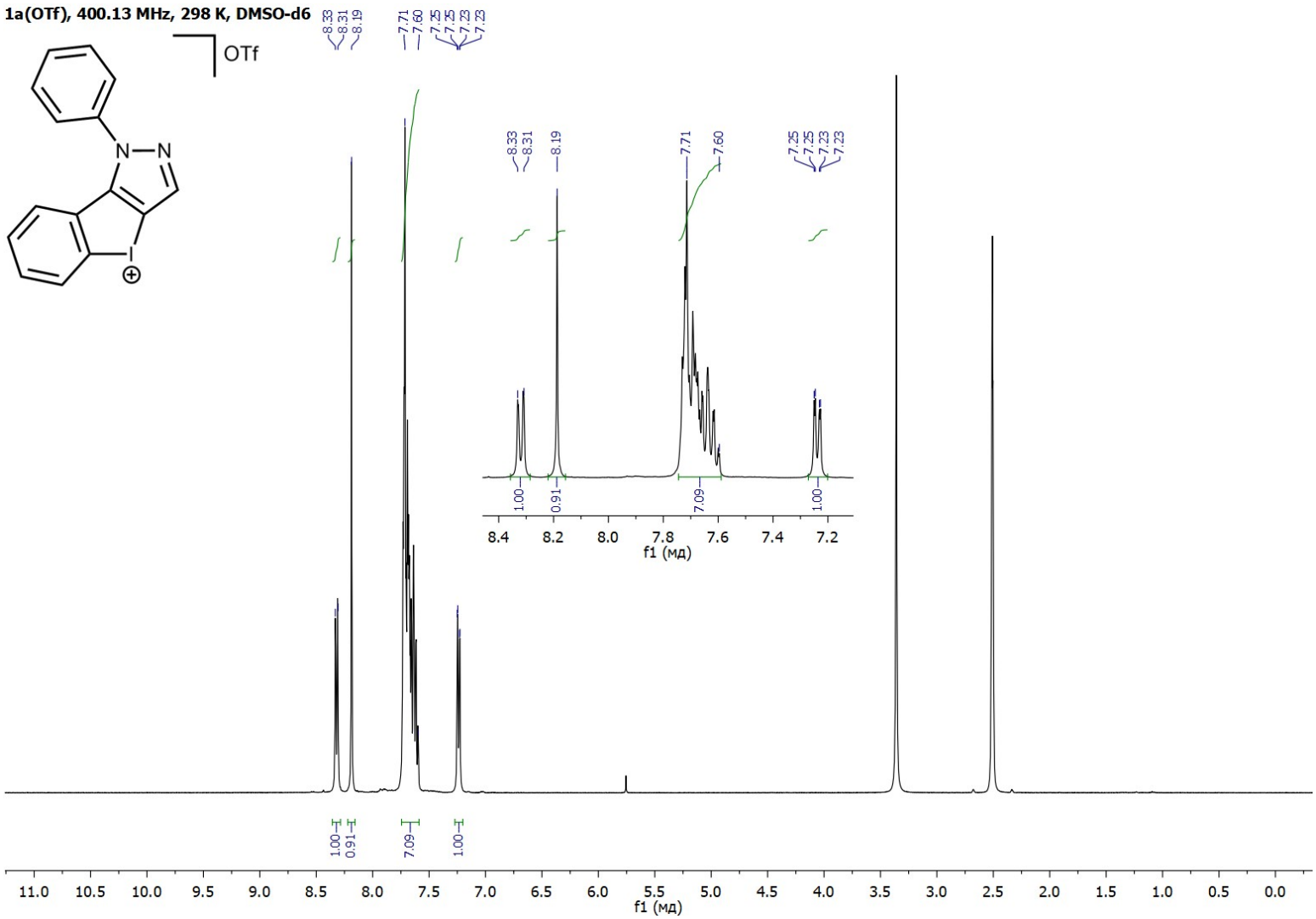


Figure S4. ^{1}H NMR spectrum of **1a**(OTf).

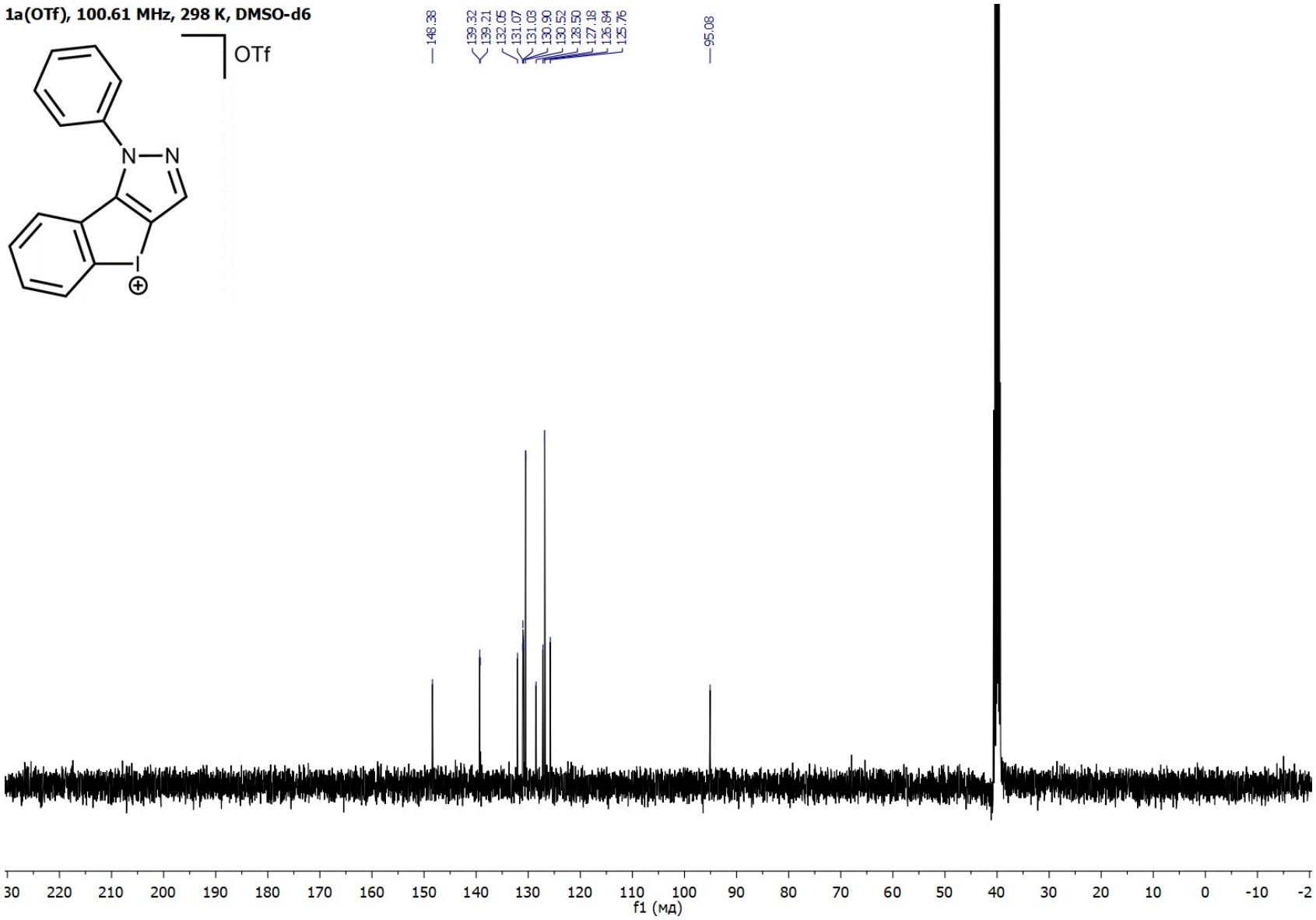


Figure S5. ^{13}C NMR spectrum of **1a**(OTf).

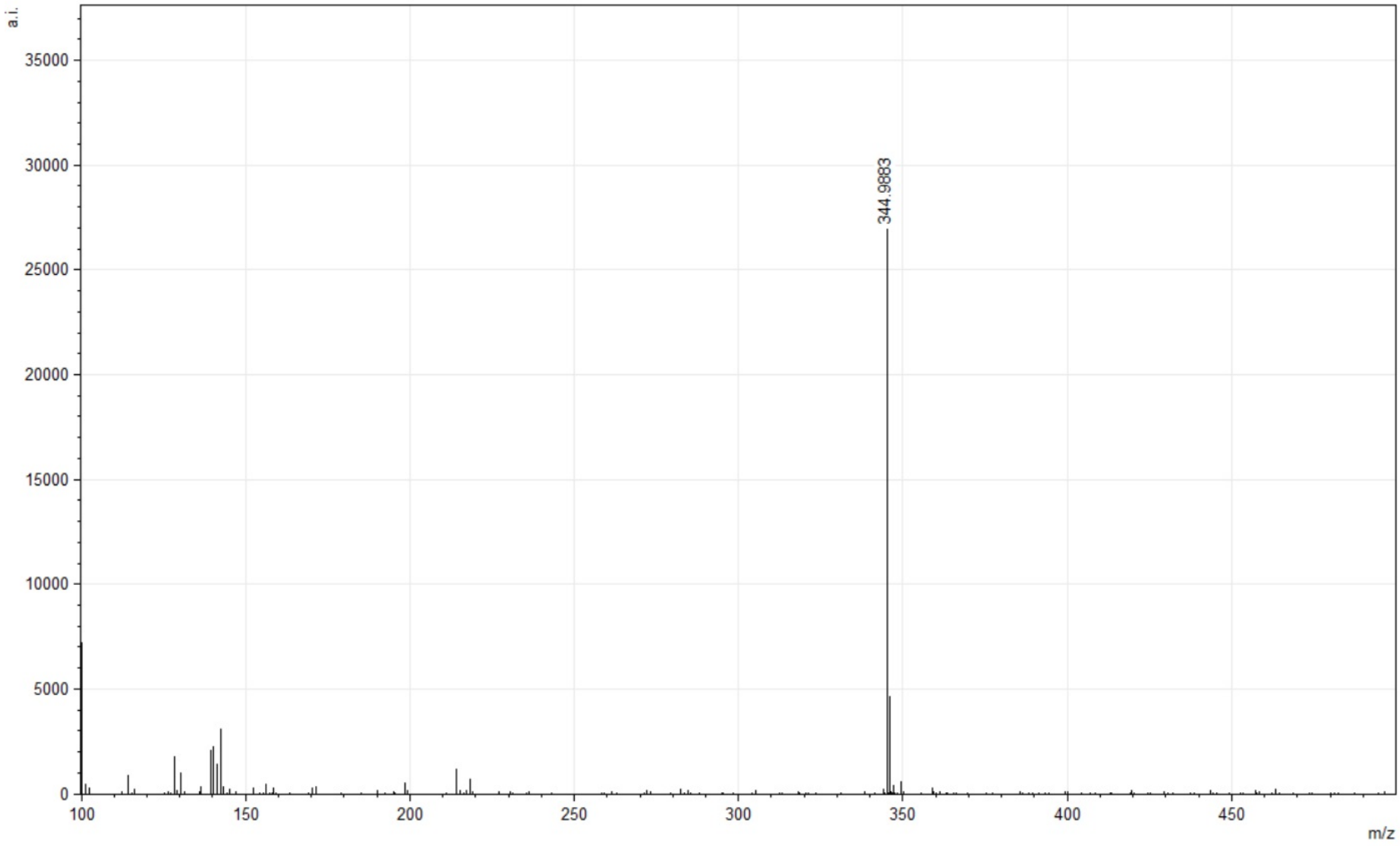


Figure S6. HRESI^{+}-MS of **1a**(OTf).

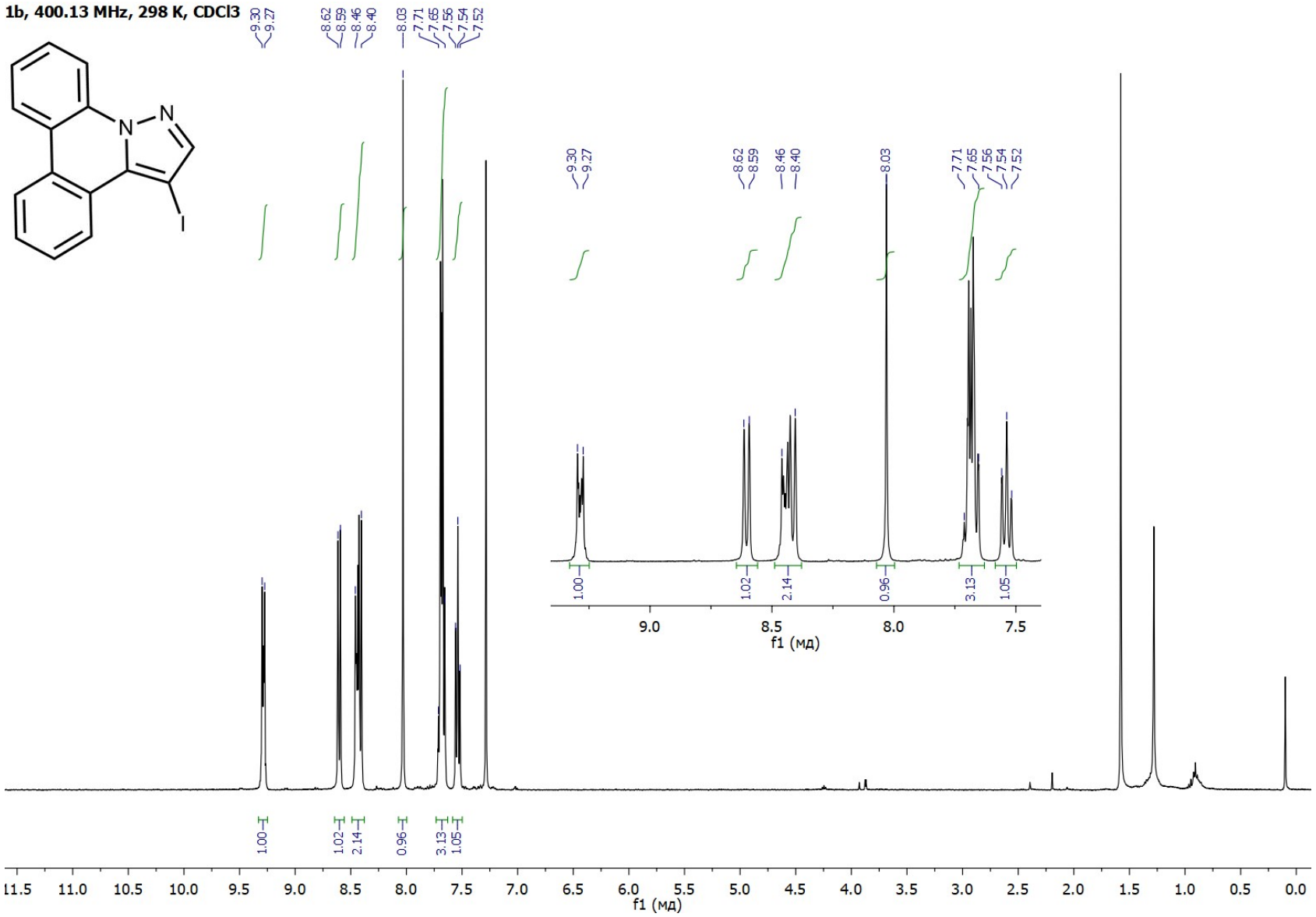


Figure S7. ^{1}H NMR spectrum of **1b**.

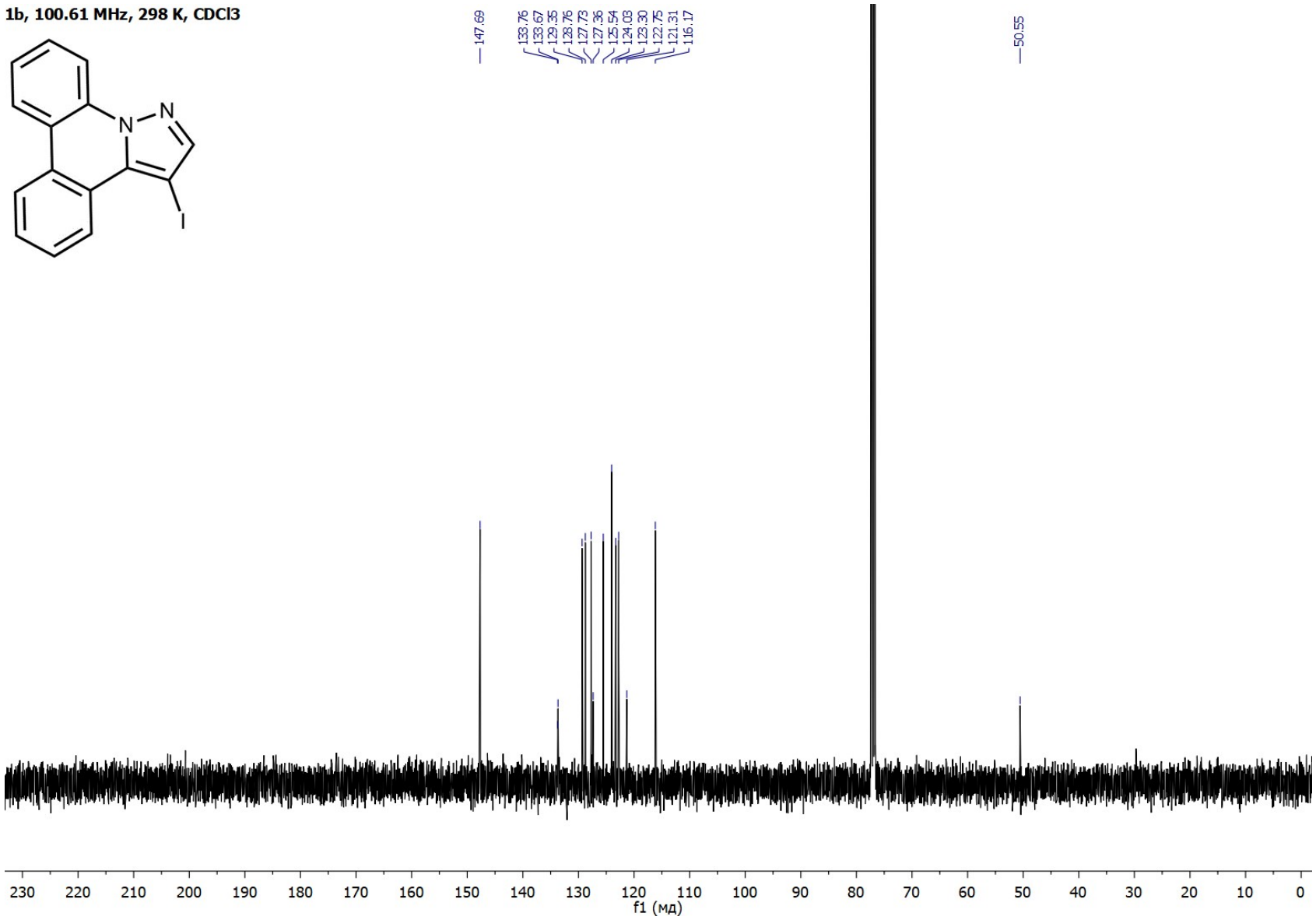


Figure S8. ^{13}C NMR spectrum of **1b**.

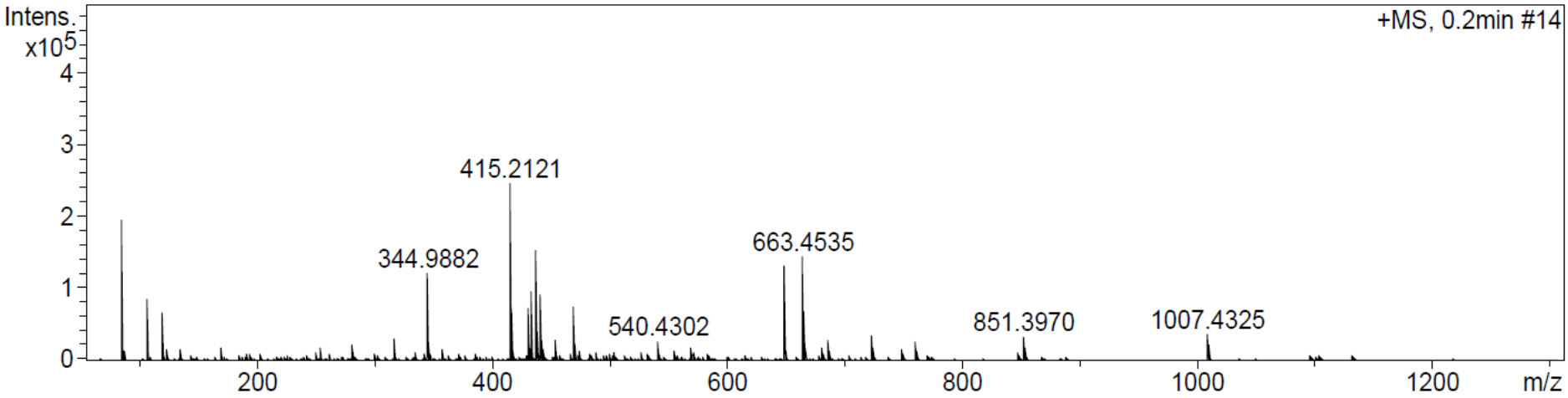


Figure S9. HRESI$^+$-MS of **1b**.

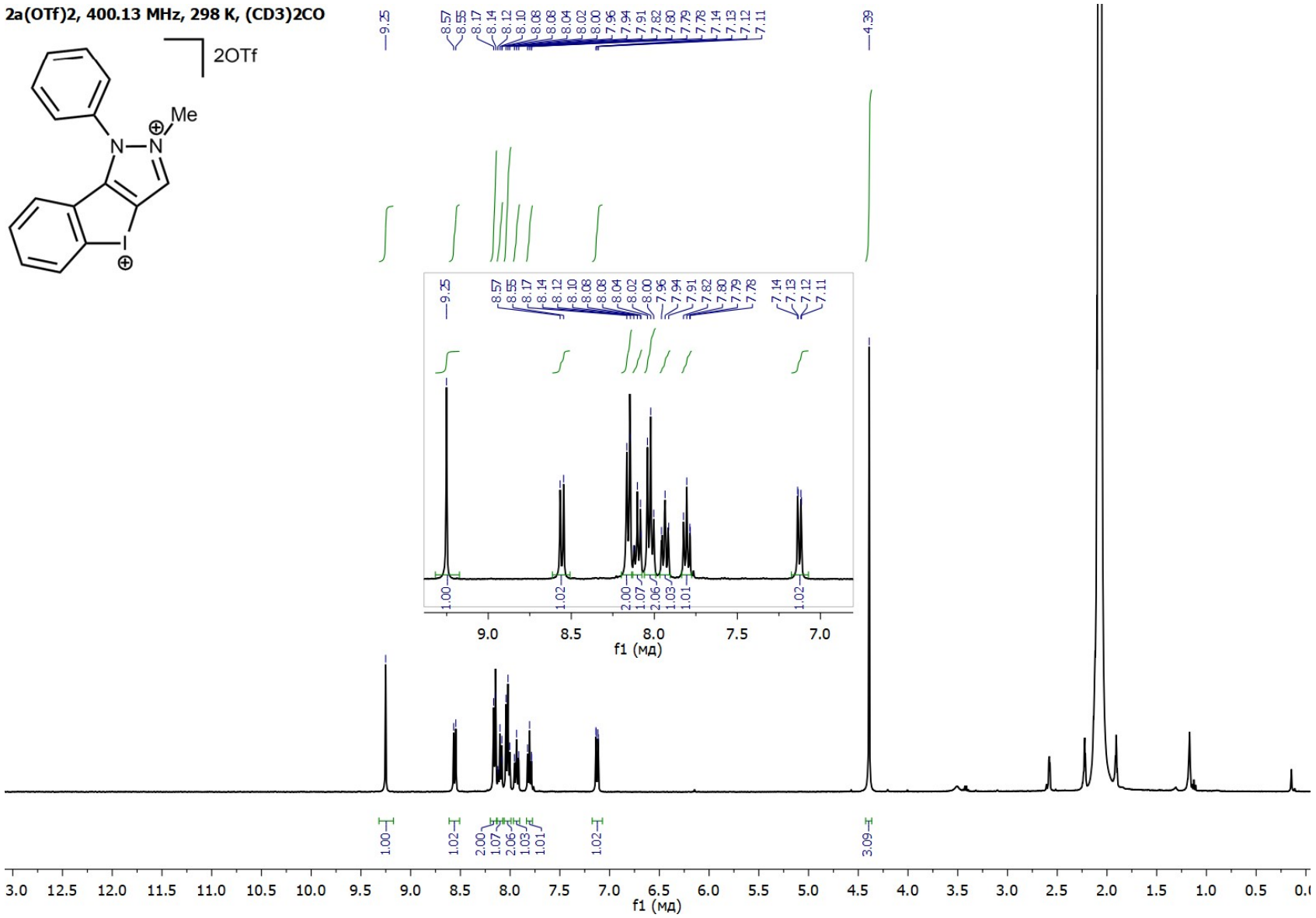


Figure S10. ^{1}H NMR spectrum of **2a**$(OTf)_2$.

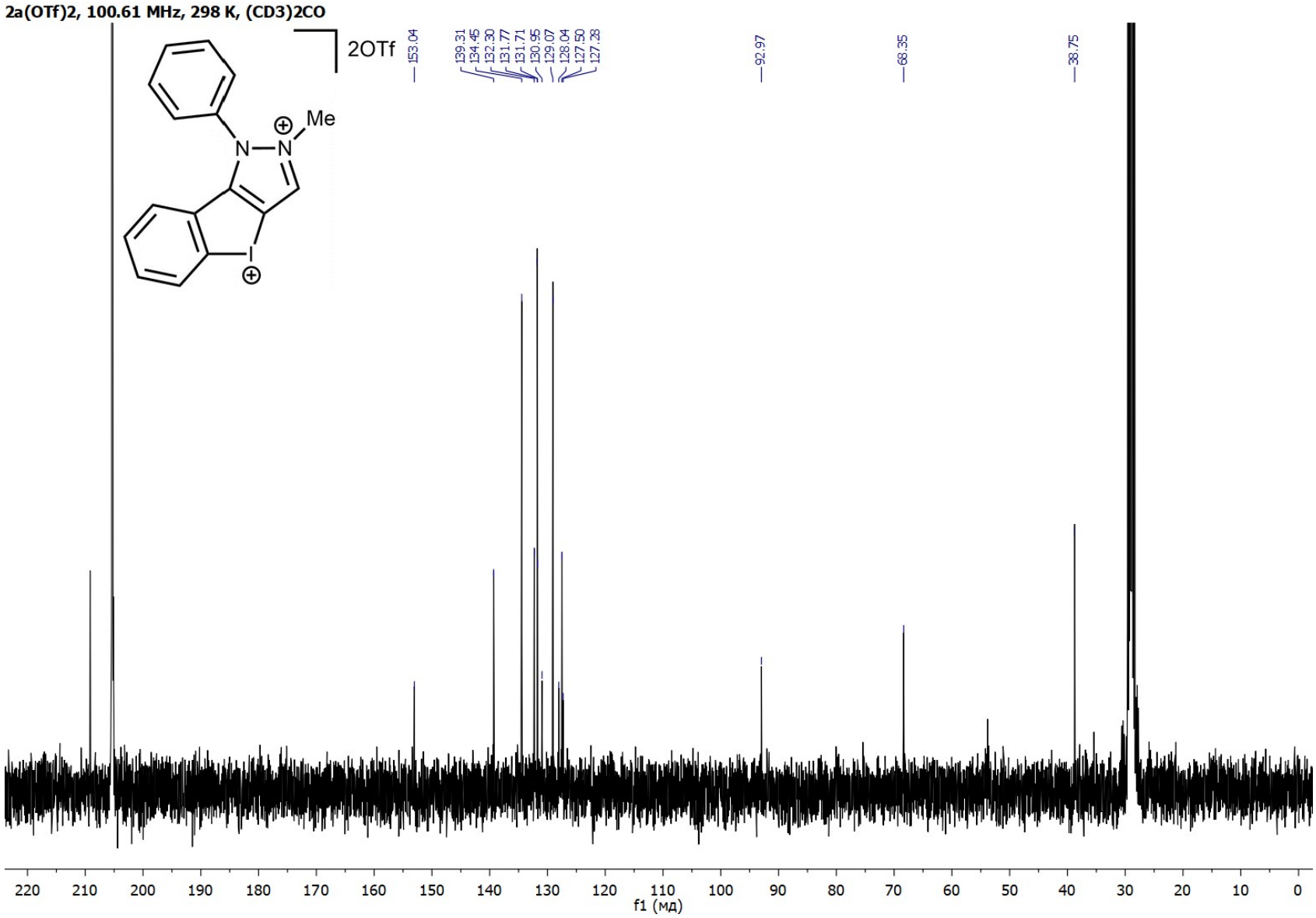


Figure S11. ^{13}C NMR spectrum of **2a**$(OTf)_2$.

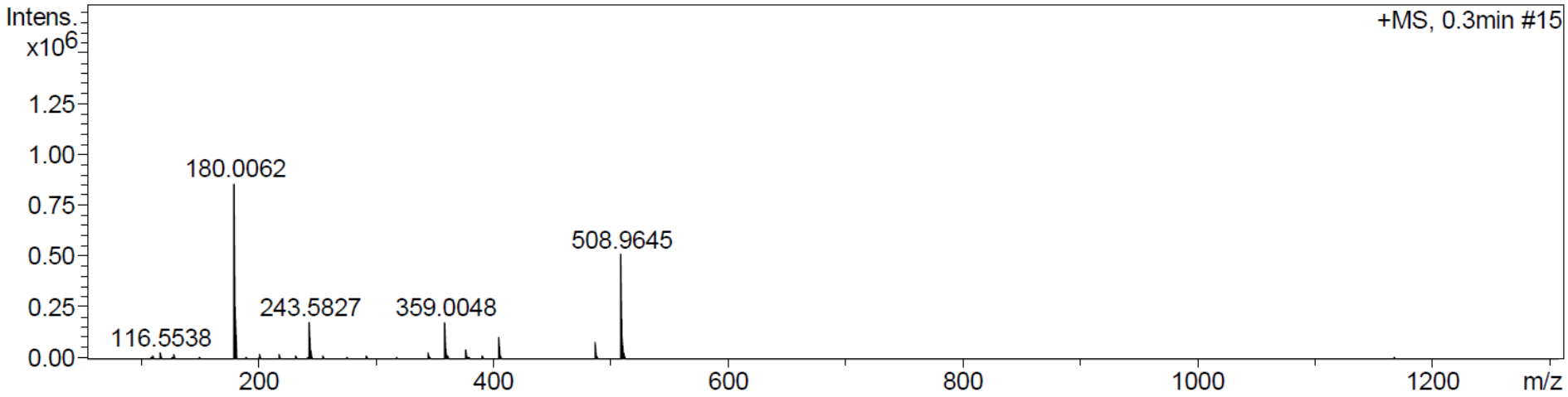


Figure S12. HRESI^{+}-MS of **2a**$(OTf)_2$.

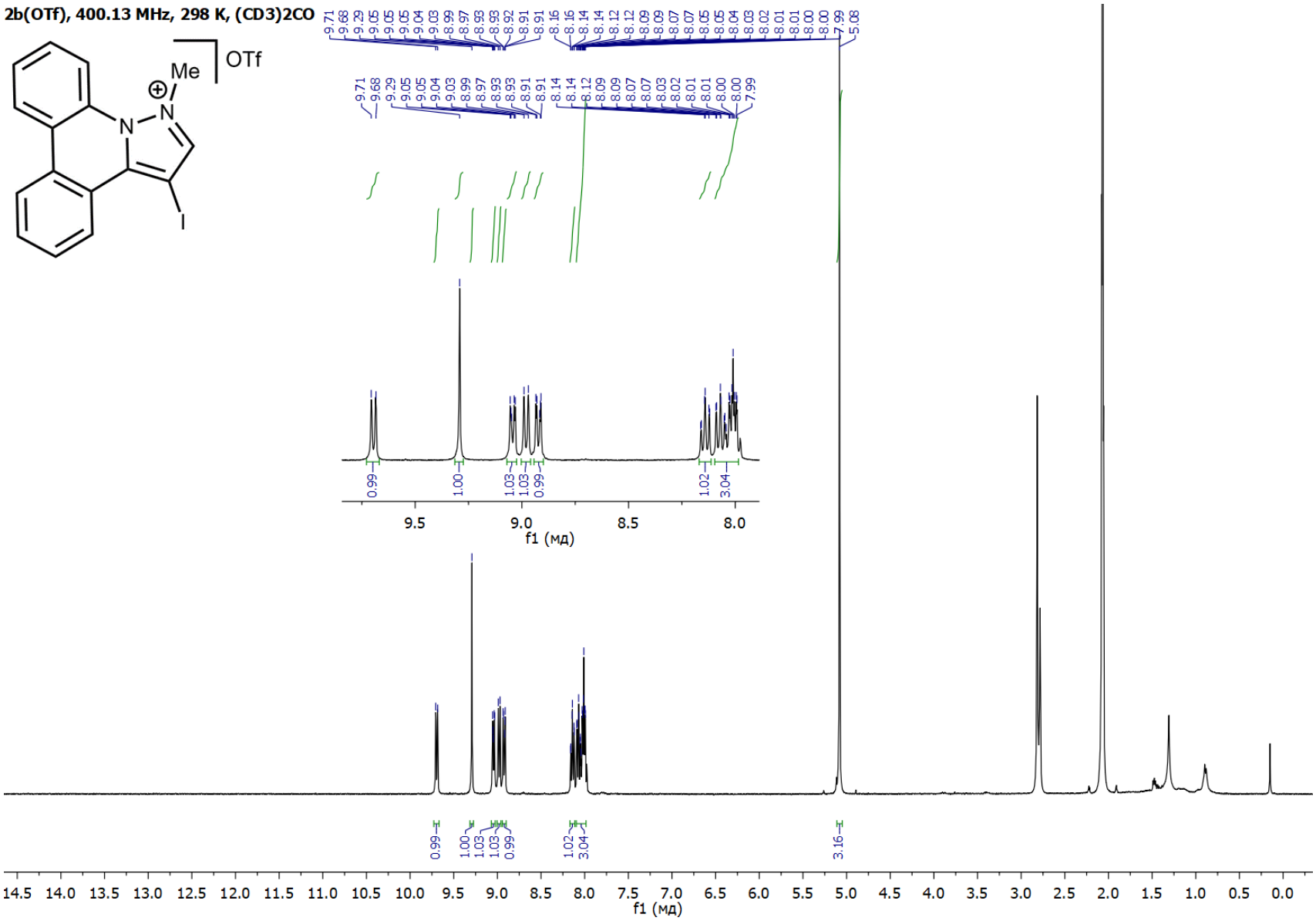


Figure S13. ^{1}H NMR spectrum of **2b**(OTf).

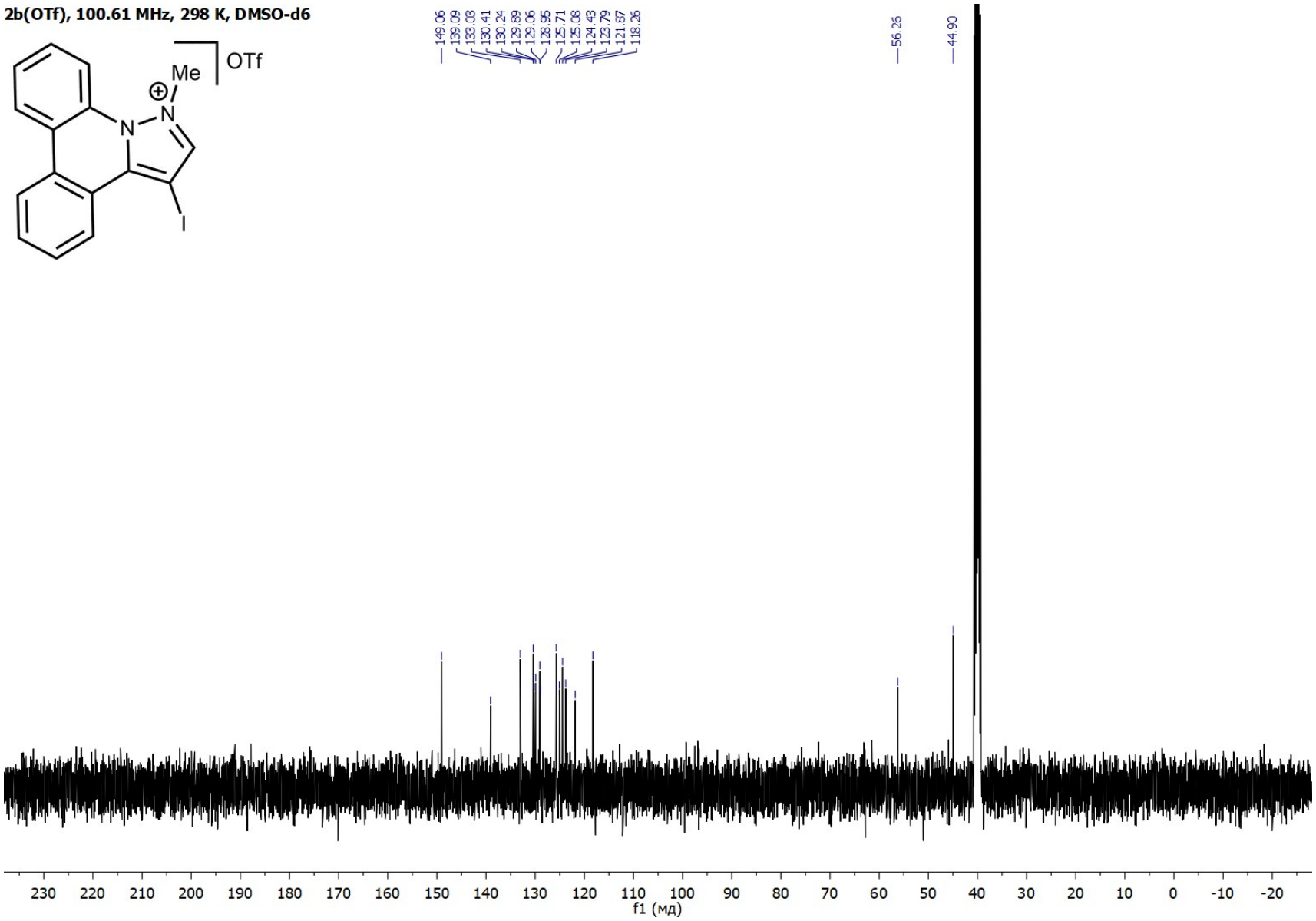


Figure S14. ^{13}C NMR spectrum of **2b**(OTf).

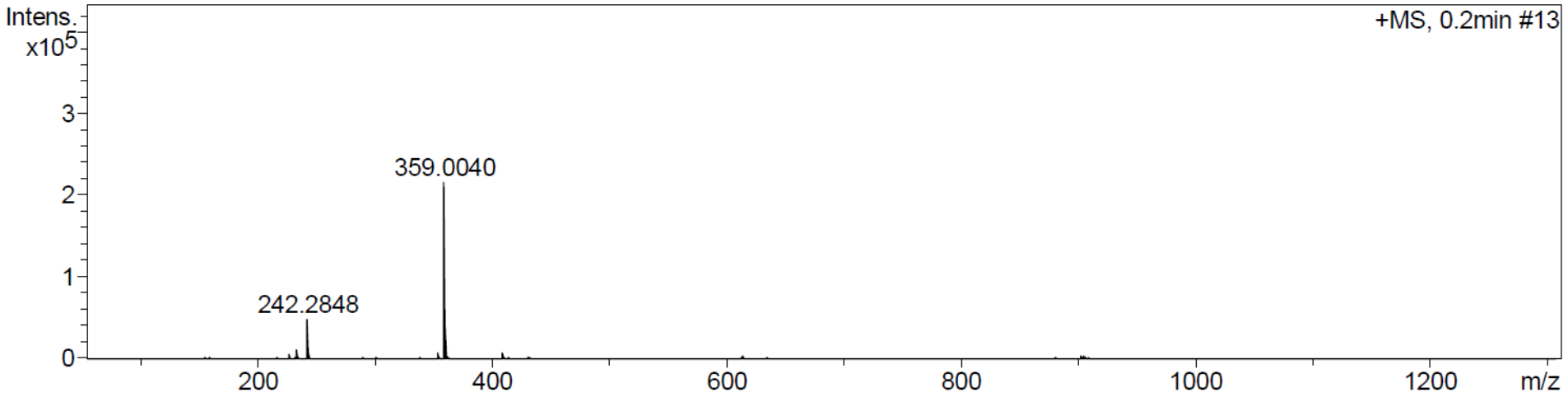


Figure S15. HRESI$^+$-MS of **2b**(OTf).

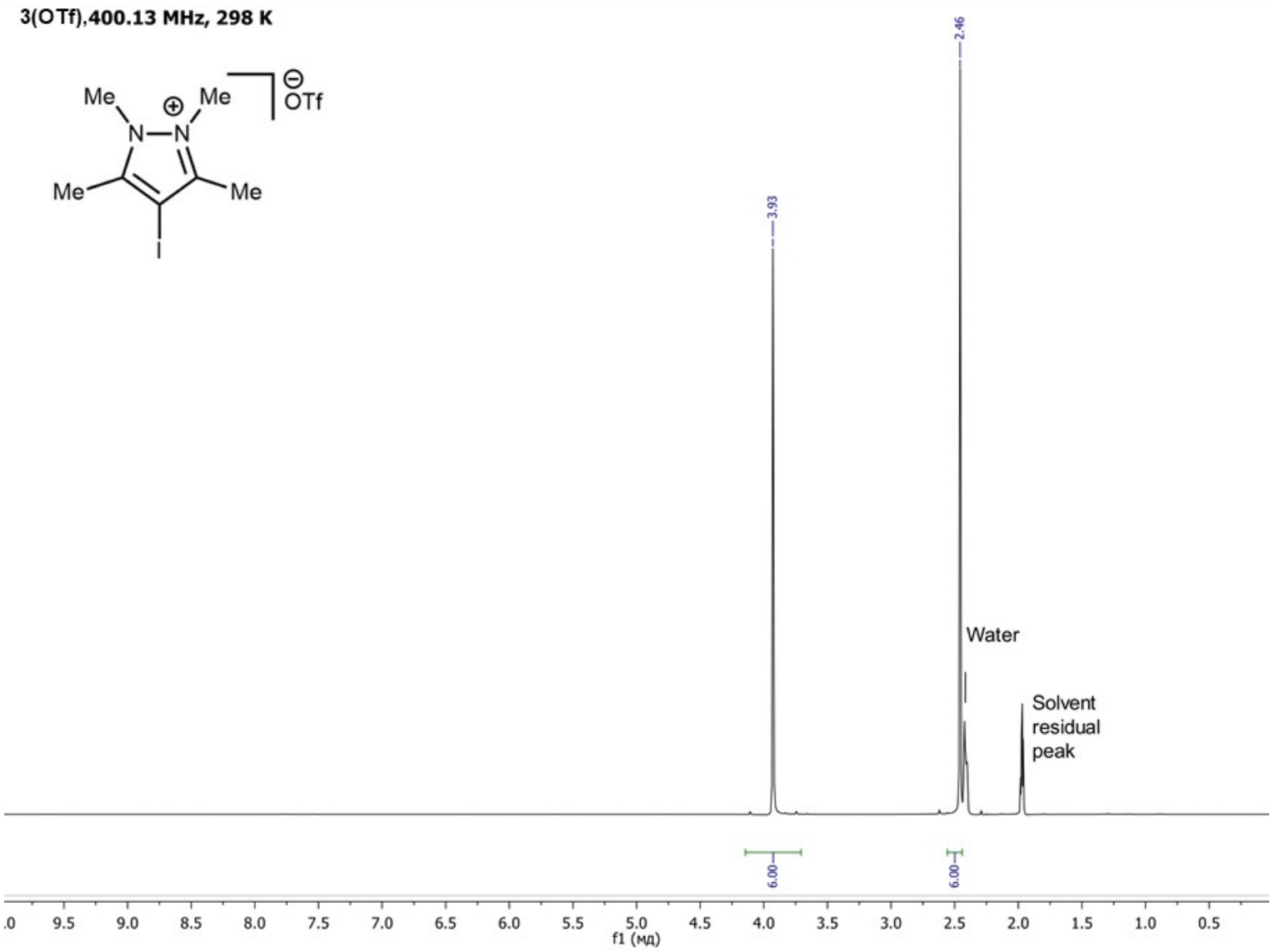


Figure S16. ^{1}H NMR spectrum of **3**(OTf).

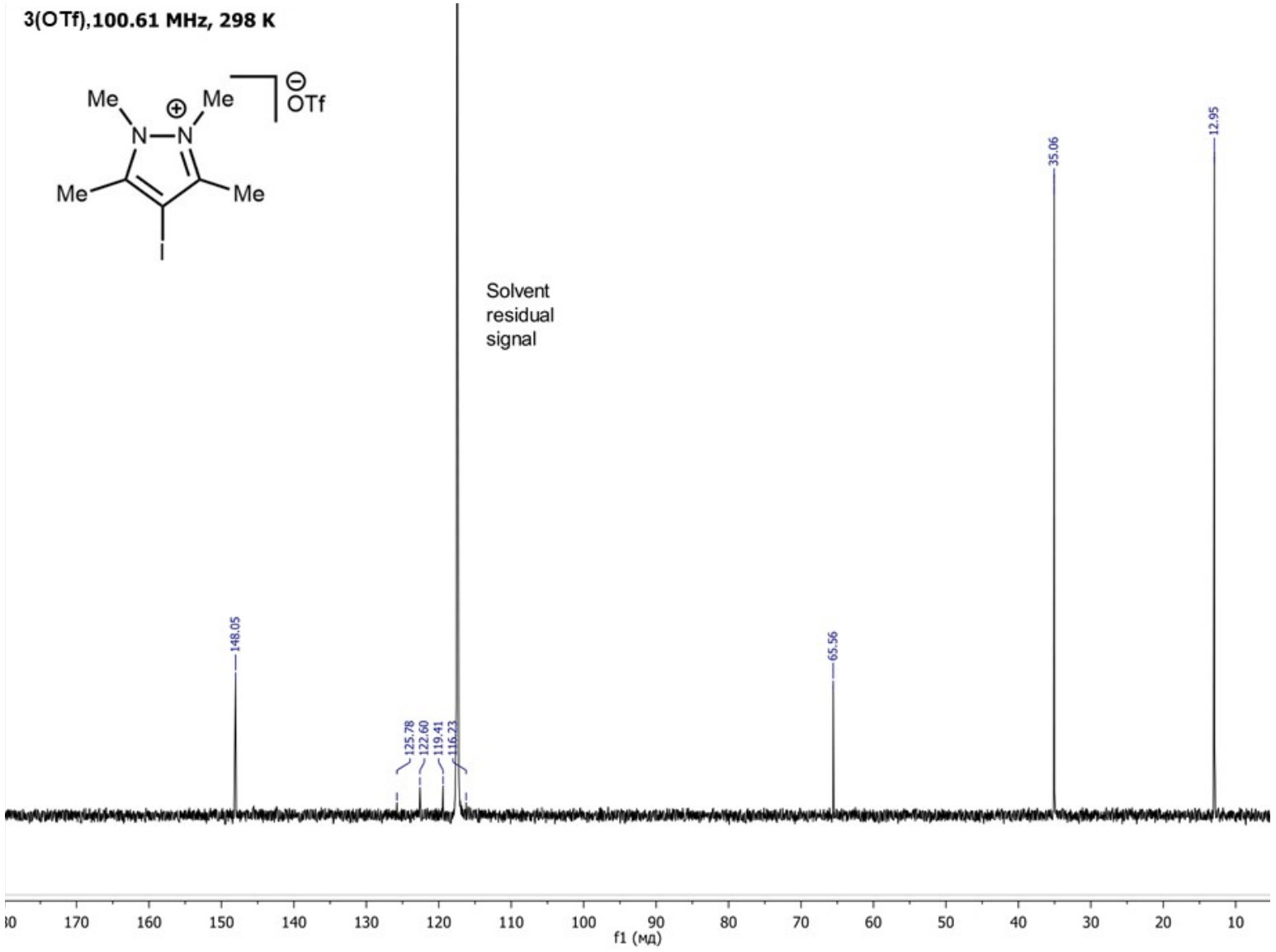


Figure S17. ^{13}C NMR spectrum of **3**(OTf).

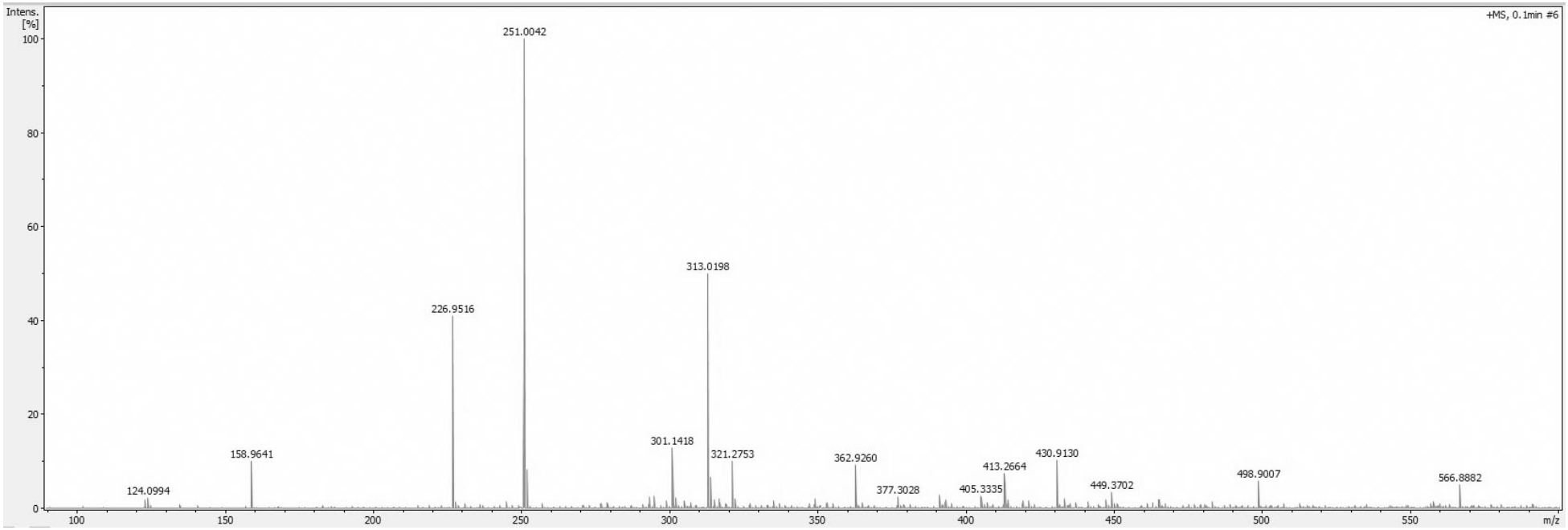


Figure S18. HRESI^{+}-MS of **3**(OTf).

^{1}H NMR monitoring of the reaction of **1a**(OTf) with bases

Diisopropylethylamine (760 mM, 10 µL, 0.0076 mmol) and TEMPO (76 mM, 10 µL, 0.00076 mmol) as the free radical scavenger were added to the $(CD_3)_2CO$ solution of **1a**(OTf) (12.7 mM, 600 µL, 0.0076 mmol) and placed in an NMR tube. For the reaction without free radical scavenger, the same quantity of the amine was added to the $(CD_3)_2CO$ solution of **1a**(OTf) and placed in an NMR tube. For the reaction with inorganic bases, the same quantity of **1a**(OTf) was dissolved in 580 µL $(CD_3)_2CO$, added to the D_2O solution of NaOH and K_2CO_3 (1.25 mM, 20 µL, 0.025 mmol) and placed in an NMR tube. The NMR tube was sealed, and the obtained homogeneous solution was maintained at RT for 24 h in an NMR spectrometer. The reaction was monitored by measuring the time-dependent integral density of the pyrazole proton group signals in **1a**(OTf) and in the product of the reaction. For all reactions, the conversion coincides with the yield of the main product, and for the reaction with K_2CO_3, a by-product is formed along with the main product.

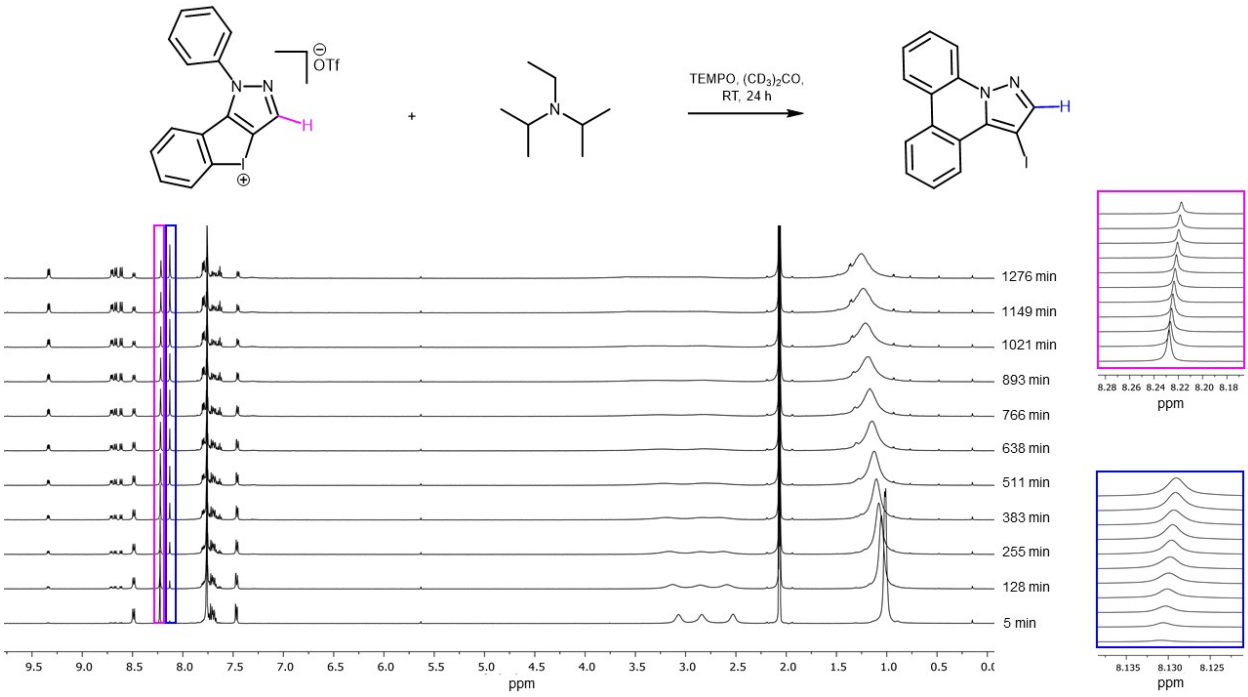


Figure S19. ^{1}H NMR spectra of the monitoring reaction **1a**(OTf) with DIPEA in the presence of TEMPO at the different time intervals.

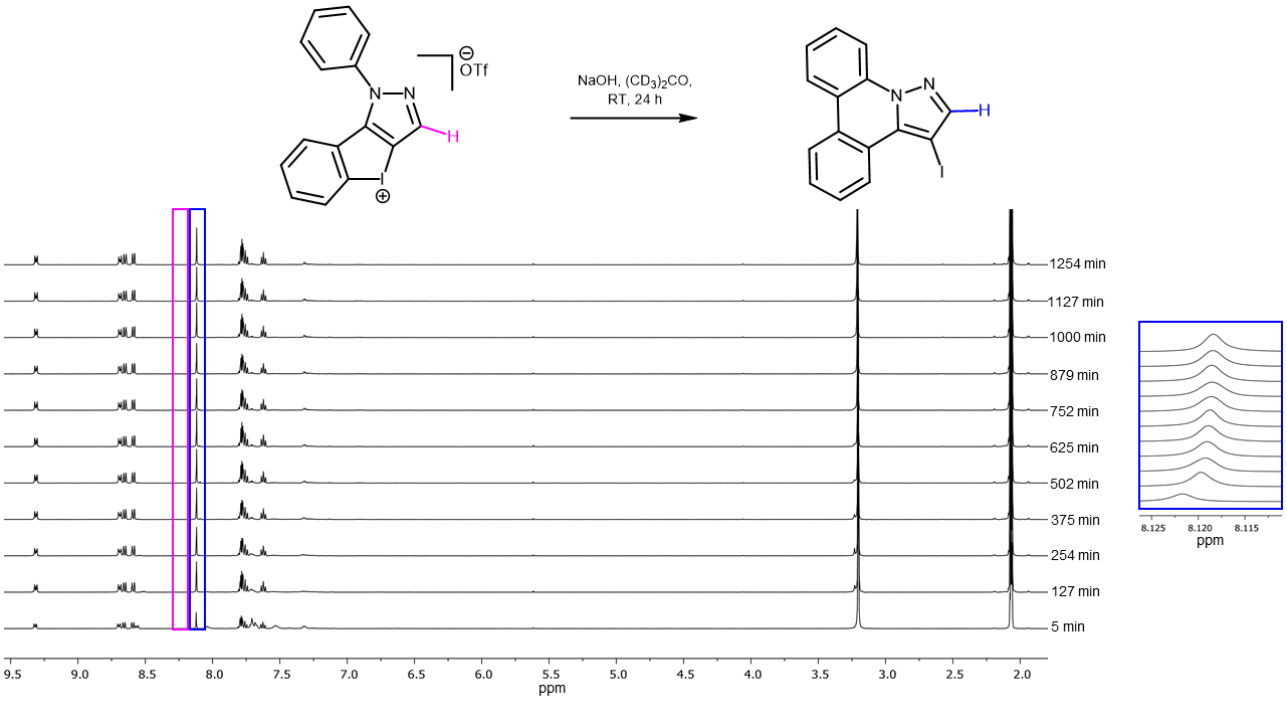


Figure S20. ^{1}H NMR spectra of the monitoring reaction **1a**(OTf) with NaOH at the different time intervals.

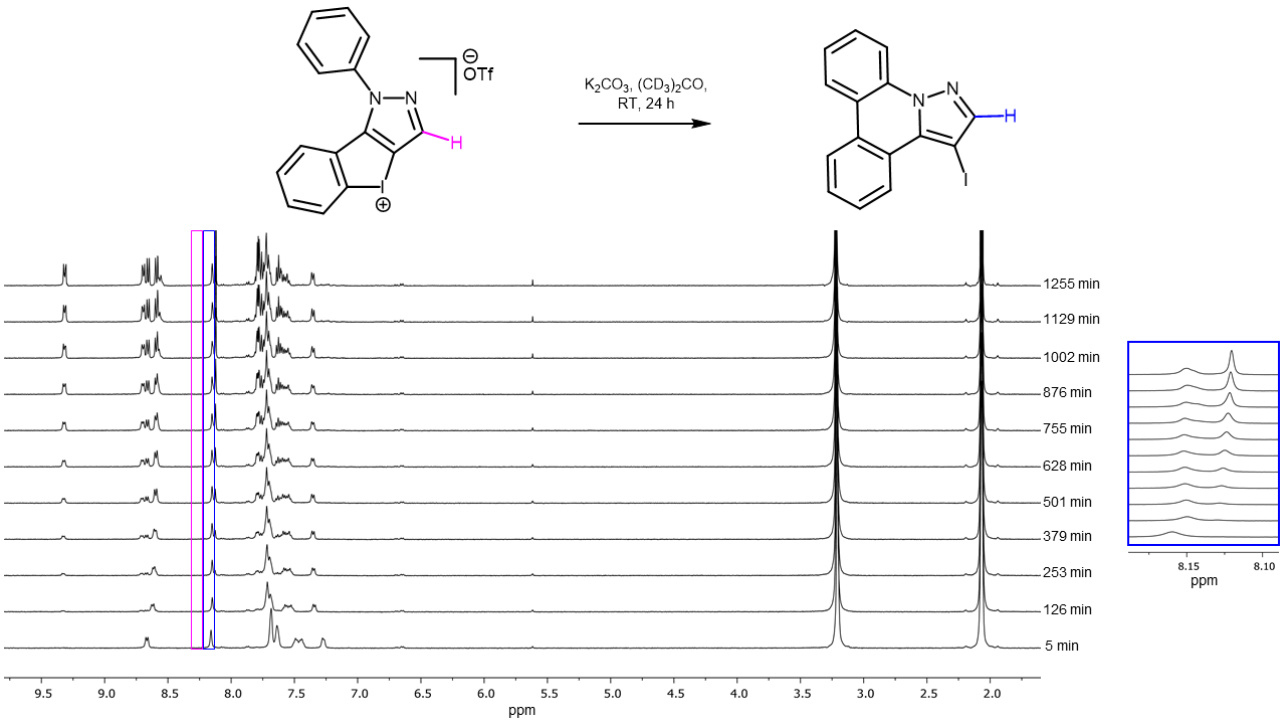


Figure S21. ^{1}H NMR spectra of the monitoring reaction **1a**(OTf) with K_2CO_3 at the different time intervals.

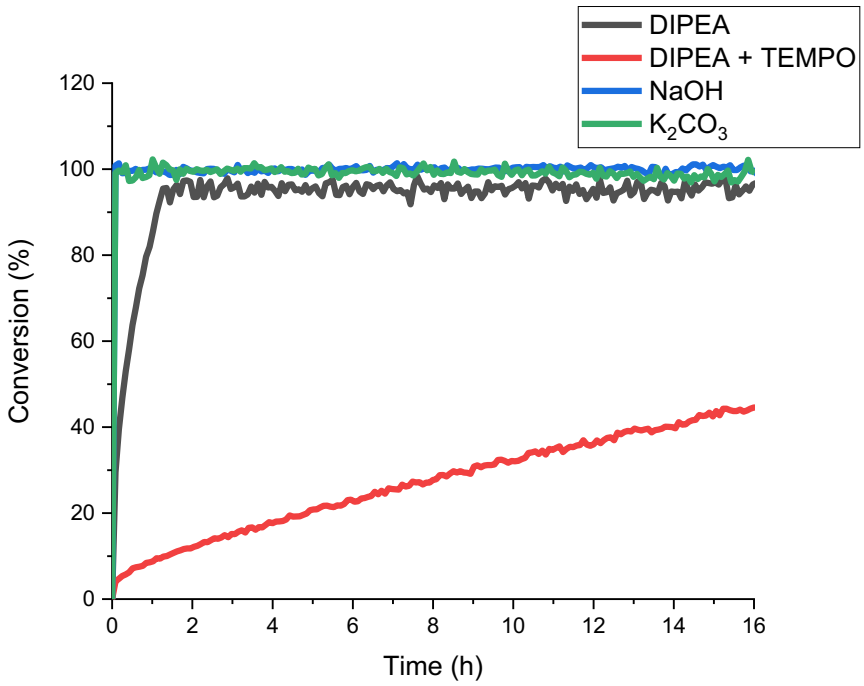


Figure S22. ^{1}H NMR monitoring of the reaction of **1a**(OTf) with different bases.

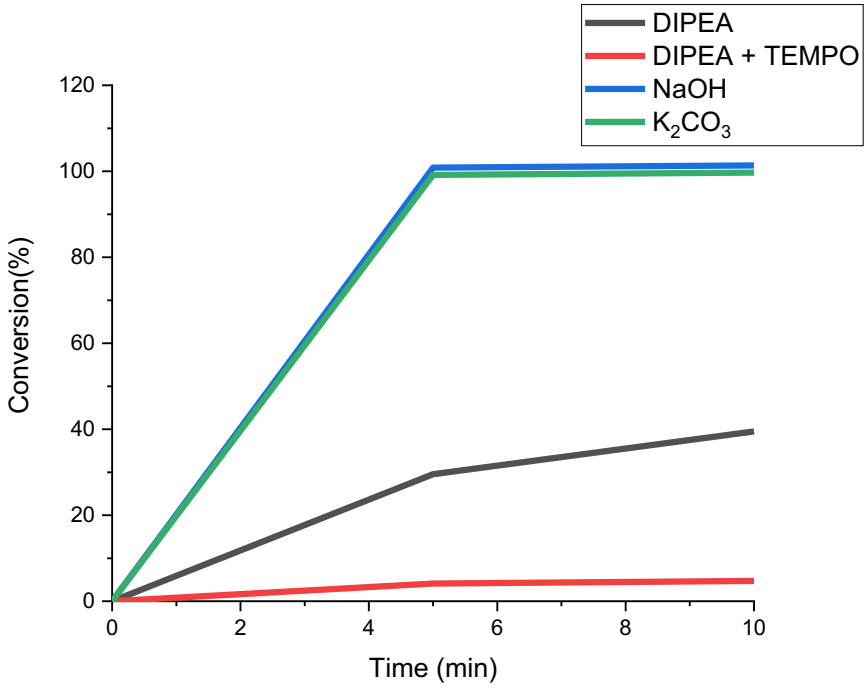


Figure S23. ^{1}H NMR monitoring of the reaction of **1a**(OTf) with different bases within the first 10 minutes.

Table S1. Crystal data for **2a**$(OTf)_2$.

Identification code	**2a**$(OTf)_2$
Empirical formula	$C_{18}H_{13}F_6IN_2O_6S_2$
Formula weight	658.32
Temperature/K	100(2)
Crystal system	triclinic
Space group	P-1
a/Å	9.9399(5)
b/Å	10.6305(5)
c/Å	11.8378(4)
α/°	64.339(4)
β/°	84.268(3)
γ/°	83.514(4)
Volume/Å^3	1118.45(9)
Z	2
ρ_{calc} g/cm^3	1.955
μ/mm^{-1}	13.845
F(000)	644
Crystal size/mm^3	0.08 × 0.05 × 0.03
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.3 to 124.982
Index ranges	-11 ≤ h ≤ 11, -12 ≤ k ≤ 12, -13 ≤ l ≤ 12
Reflections collected	9126
Independent reflections	3519 [Rint = 0.0809, Rsigma = 0.0667]
Data/restraints/parameters	3519/0/311
Goodness-of-fit on F^2	1.216
Final R indexes [I⩾2σ (I)]	R1 = 0.0850, wR2 = 0.2504
Final R indexes [all data]	R1 = 0.1002, wR2 = 0.2881
Largest diff. peak/hole / e·Å^{-3}	2.70/-2.30
CSD code	2354600

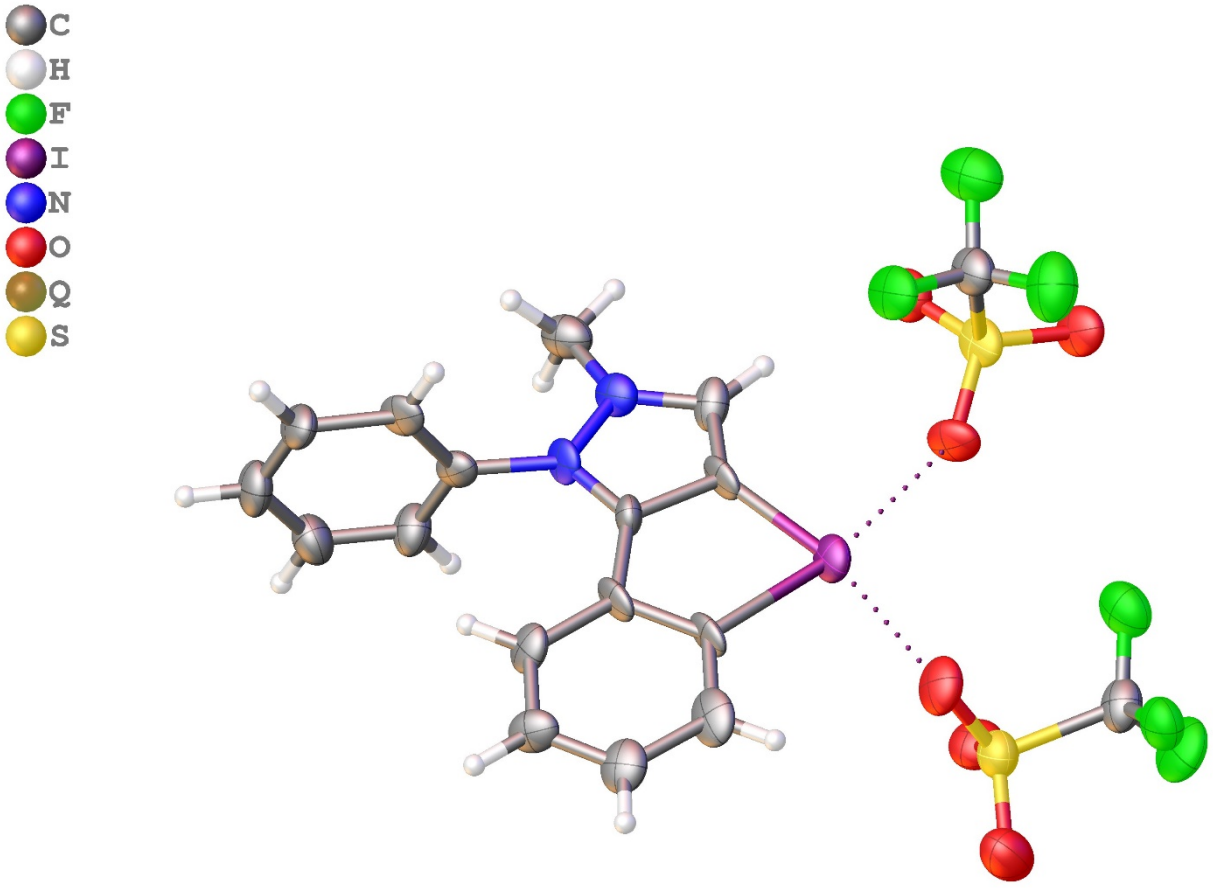


Figure S24. A thermal ellipsoid plot for **2a**$(OTf)_2$.

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