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Micro-photo-flow reactor system for fused N-heteroaryl scaffold synthesis and late-stage functionalization of pyrazolopyridines

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1: General information.

1.1 Material and method used in experiments.

Most of the reagents and chemicals were purchased from Sigma-Aldrich and AVRA chemicals, which were used without further purification and demineralized water (18.2 mS conductivity) was used in all experiments. All work-up and purification procedures were carried out with the reagent-grade solvents. Analytical thin-layer chromatography (TLC) was performed using analytical chromatography silica gel 60 F254 precoated plates (0.25 mm). The developed chromatogram was analysed by UV lamp (254 nm). Polytetrafluoroethylene (PTFE) (id = 100-1000 μm) tubing, T-junction, and high-purity Perfluoro alkoxy alkanes (PFA) tubing were also purchased from Upchurch IDEX HEALTH & SCIENCE. The syringe pump, heating system, back pressure controller (BPR), valve, catalytic reactor, and Asia Manager PC software system were all purchased from Syrris Asia System. Photo rector, blue LED reactor, and catalytic reactor were all purchased from the Smart Chem. Synth. Pvt. Ltd. Hyderabad, India.

1.2 Measurement method.

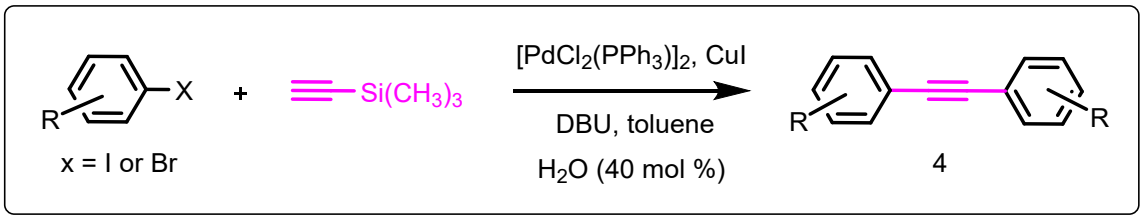
Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker 700, 600, 500, 400 or 300 MHz in $CDCl_3$, DMSO-d_6, or CD_3OD solvent. Chemical shifts for ^1H NMR were expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm). Chemical shifts for ^{13}C NMR were expressed in ppm relative to $CDCl_3$ (δ 77.0 ppm) or CD_3OD (49.00) and data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, quin = quintet, sext = sextet, m = multiplet), coupling constants (Hz), and integration. High-resolution mass spectra (HRMS) were obtained from a JMS-T100TD instrument (DART) and Thermo Fisher Scientific Exactive (APCI). Power-Sonic 405 sonication instrument was used for washing the metal surface. ATR analysis was conducted on portable FTIR spectrometer Bruker ALPHA and Datalog model DCS-PS-6401 power supply system was used to supply the constant

current. The melting point was conducted on POLMAN MP-96. Han's Yueming laser series (model CMA0604-B-A, Carbon dioxide based, laser power 60W).

2. Preparation of starting materials.

2.1 Substituted fused 2-aryl benzimidazoles: The following starting materials **3a-3r** were synthesized according to previously described methods.[1, 2]

2.2 Preparation of Substituted alkynes (4): 1,2-diphenylethyne (**4a**) oct-4-yne (**4d**) and but-2-yne-1,4-diol (**4e**) were purchased from commercial sources.



Alkynes (4b-4c) were prepared following the described procedure.[3] A 100 mL Schlenk with a magnetic stir bar was purged with dry argon, and charged with $[PdCl_2(PPh_3)]_2$ (0.3 mmol, 3 mol %), CuI (1 mmol, 10 mol %) and starting material iodide or bromide (10 mmol, 100 mol %). Then, dry toluene (50 mL, 0.2 M) was added by syringe under a dry argon flow. Argon-sparged DBU (60 mmol, 600 mol %) was then added by syringe, followed by a purge of the reaction Schlenk with argon. Trimethylsilylacetylene (5 mmol, 50 mol %) was then added by syringe, followed immediately by distilled water (4 mmol, 40 mol %). The reaction Schlenk was covered in aluminum foil and left stirring at room temperature for aryl iodide, or 80 ºC for aryl bromide substrates for 18 h. Then the reaction mixture was partitioned in diethyl ether and distilled water (50 mL each). The organic layer was washed with 10% HCl (3 X 75 mL), saturated with aqueous NaCl (1 X 75 mL), dried over Na_2SO_4, then filtered and the solvent removed in vacuo. The crude product was purified by silica gel column chromatography using a mixture of n-Hex/EtOAc as eluent

3. Fabrication and Design of micro-photo flow reactor (µ-PFR).

3.1 Fabrication of homemade micro - photo flow reactor (µ-PFR)

For the micro-photo flow reaction, we have used homemade micro-photo flow reactor. To the fabrication of photo flow reactor, we have used acrylic sheet (length 150 mm × width 150 mm × height 6 mm) and make a coil shaped double spiral grooving using a laser cutter. Then the PFA tubing (OD 1/16", ID 1.0mm, Length = 3.2m, volume = 2.5 mL) was placed in the grooving. (Fig. S1).

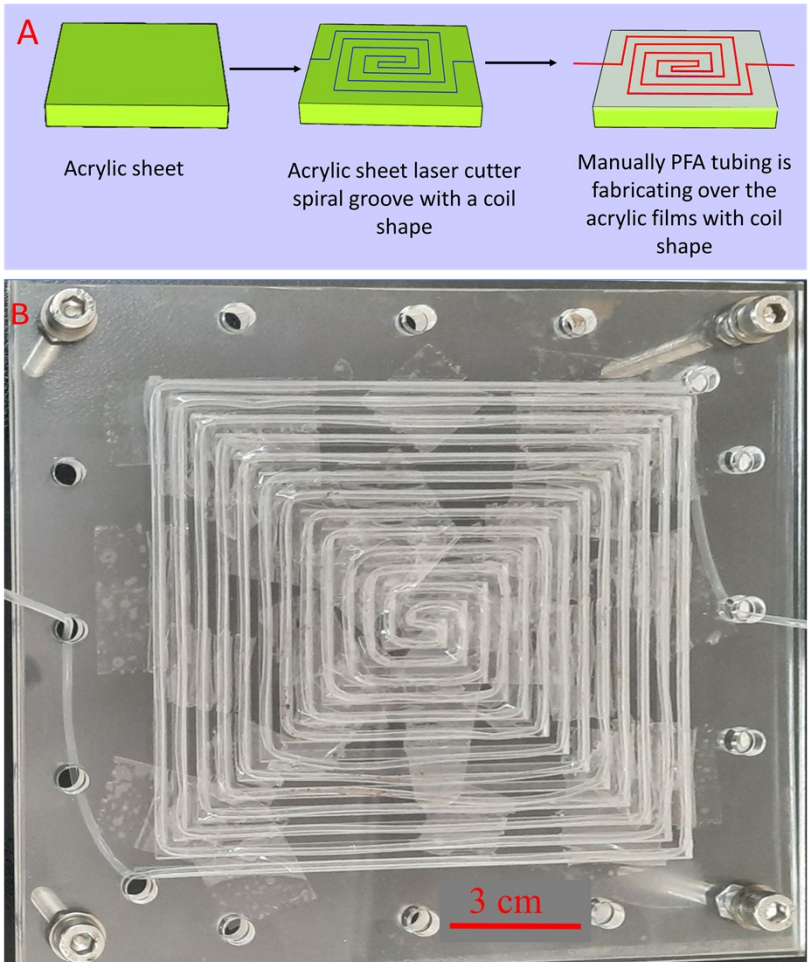


Fig S1. (A) Fabrication step for a µ-PFR (acrylic sheet size length 150 mm X width 150 mm X height 6 cm); (B) real image of fabricated µ-PFR.

3.2 Design of µ-PFR.

After fabrication of µ-PFR, we make the complete design **µ-PFR.** At the first layer was the acrylic sheet (α) with the dimensions (150 mm length x 150 mm width x 6 mm thickness) then the second layer kept homemade fabricated µ-PFR (β). Then the third layer PTFE Teflon (γ) films with dimensions (150 mm length x 150 mm width x 6 mm) were instructed to make a hole at all corners (1 mm diameter) as shown in Fig. S2. Next, layer the heating plate (δ) customized as per the reactor size (150 mm length x 150 mm width x 6 mm thickness). Then another layer of the same PTFE Teflon (γ) films was instructed to make a hole at all corners (1 mm diameter). At last kept Bakelite layer (π) with dimensions (150 mm length x 150 mm width x 12 mm thickness). After the all layers was aligned by inserting metal pins through the holes at the corners. Finally, the Bakelite and acrylic holder was tightly pressed by screw to seal the device with no leak. Solution A and Solution B mixed at T-junction and connected to designated µ-PFR for the Blue light reaction Fig. S2.

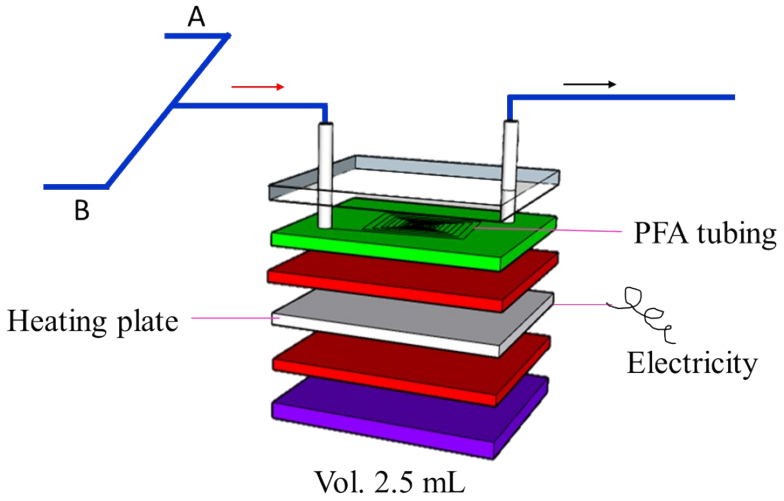
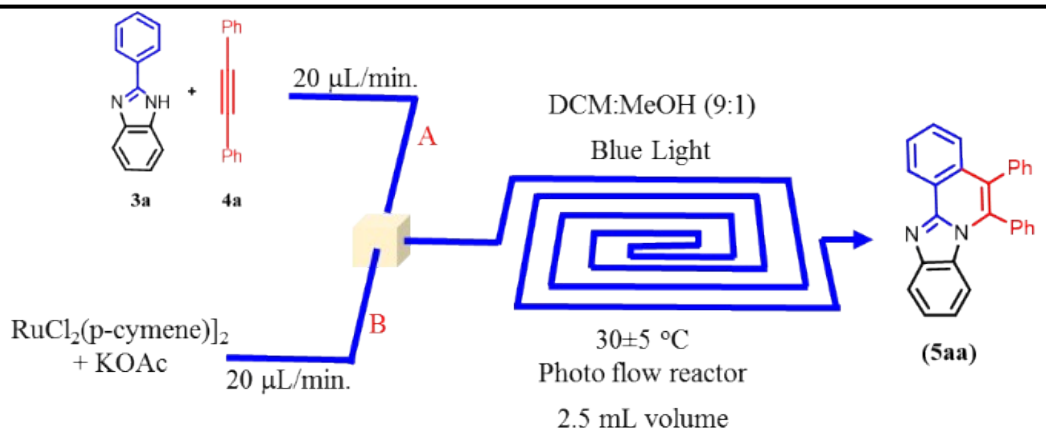


Fig. S2. Schematic set-up for the µ-PFR.

4. An integrated continuous μ-PFR platform for the synthesis, extraction and separation of annulated product.



Entry	Deviation from standard conditions	Yield (%)[a]
1	None	91
2	without light	NR
3	without $[RuCl_2(p\text{-cymene})]_2$	NR
4[b]	200 μL/min. instead 20 μL/min.	20
5[b]	100 μL/min. instead 20 μL/min.	65
6	DCE/MeOH instead DCM/MeOH	90
7	$CHCl_3$/MeOH instead DCM/MeOH	94
8[b]	K_2CO_3, instead KOAc	10
9[b]	NaOAc instead KOAc	50
10[b]	red, green instead of blue light	20, 70
11	60 °C, 80 °C instead 30 °C	NR
12	$Pd(OAc)_2$, $Co(acac)_2$, $NiBr_2(dme)$, instead $[RuCl_2(p\text{-cymene})]_2$	NR

Table S1. Selected optimization studies.

Reaction condition: (A) **3a**:**4a**: DCM: MeOH in molar ratio (1:2:700:123); (B) KOAc: $[RuCl_2(cymene)]_2$: DCM: MeOH in molar ratio (1:0.025:350:61), [a]yields are based on isolated yield, [b]$CHCl_3$/MeOH has been used as a solvent.

4.1 μ-PFR platform for annulation reaction.

Initially we proceed the model reaction of a solution A containing fused imidazole **3a**: alkyne **4a**: in $CHCl_3$: MeOH in a molar ratio (1:2:561:123) and solution B containing KOAc, $[RuCl_2(p\text{-cymene})]_2$ dissolved in $CHCl_3$: MeOH in a molar ratio (1:0.025:280:61) respectively. Both the solutions were introduced through T-mixer in a flow rate to maintain the stoichiometric ratio and pass through the fabricated μ–PFR (reactor volume 2.5 mL). The μ–PFR was placed under the visible light (blue LED, 34 W, 450-455 nm, 30 °C) Fig. S3. Finally, the outcome from the outlet of the μ–PFR was collected into a flask.

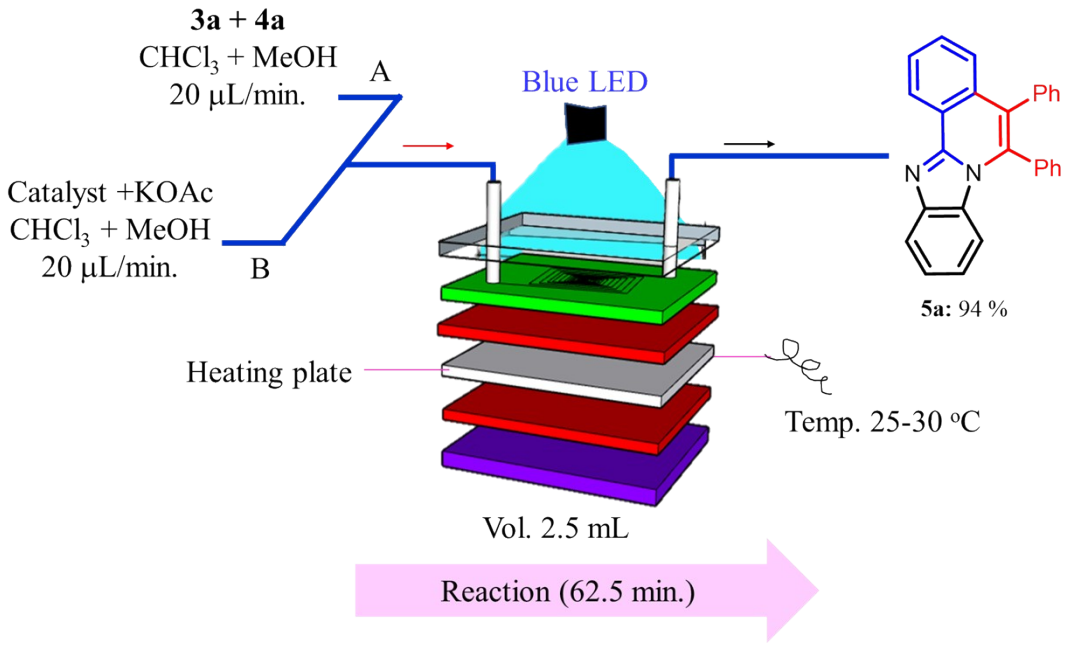


Fig. S3. Basic set up for the synthesis of imidazoisoquinolines: The stock solution **(A)** containing **3a**: **4a**: $CHCl_3$: MeOH in molar ratio (1:2:561:123); and the stock solution; **(B)** containing KOAc: $[RuCl_2(cymene)]_2$: $CHCl_3$: MeOH in molar ratio (1:0.025:280:61).

4.3 Light screening.

The stock solution **(A)** containing **3a**:**4a**: $CHCl_3$: MeOH in molar ratio (1:2:561:123); and the stock solution **(B)** containing KOAc: $[RuCl_2(cymene)]_2$: $CHCl_3$: MeOH in molar ratio (1:0.25:280:61). The two solution phases were mixed at T-mixer, then flowed through the μ–PFR (reactor volume 2.5 mL placed under the various visible light. (Table S1 entry 10).

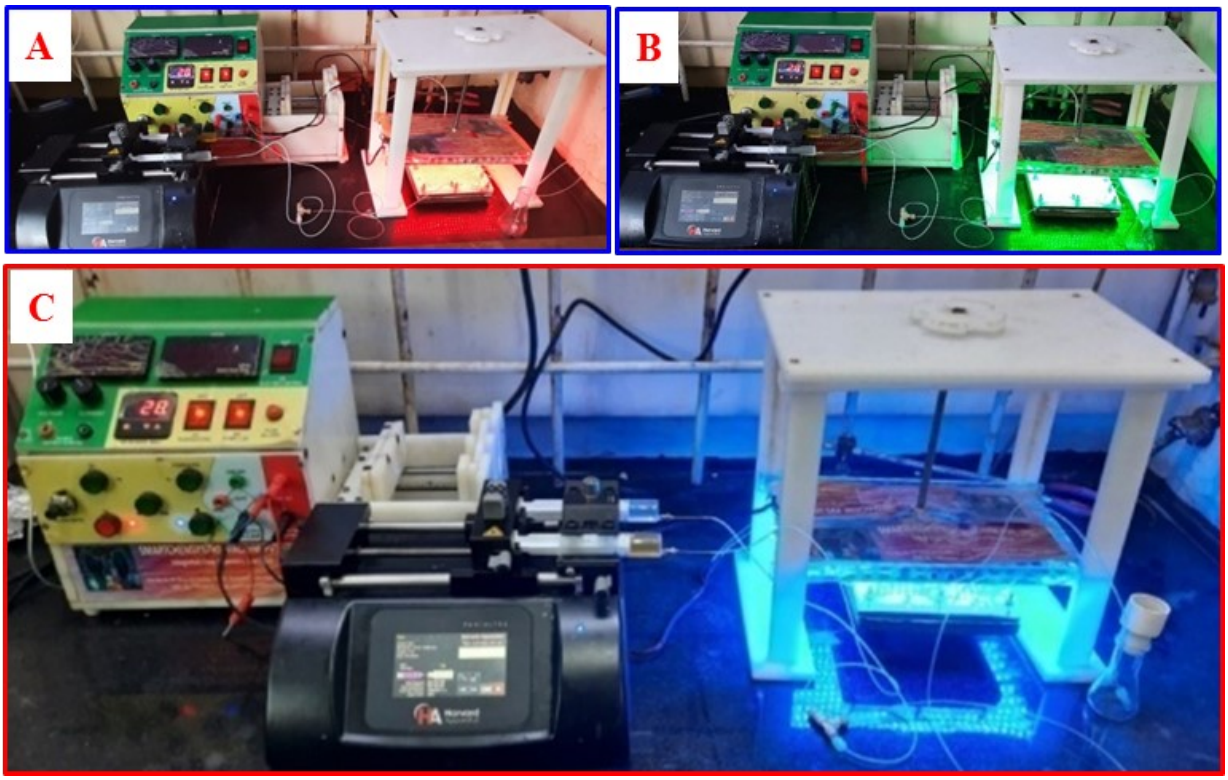


Fig. S4. Snapshot of the reactor set-up for the screening of annulation reaction; **(A)** red light; **(B)** green light; **(C)** blue light

4.2 Procedure for photo-flow synthesis of 4+2 annulation reaction with alkyne.

The stock solution **(A)** containing **3a**:**4a**: $CHCl_3$: MeOH in molar ratio (1:2:561:123); and the stock solution **(B)** containing KOAc: $[RuCl_2(cymene)]_2$: $CHCl_3$: MeOH in molar ratio (1:0.025:280:61). Both the solutions were introduced through T-mixer in a flow rate to maintain the stoichiometric ratio and pass through the fabricated μ–PFR (reactor volume 2.5 mL). The μ–PFR was placed under the visible light (Blue LED, 34 W, 450-455 nm, 30 °C) (Fig. S5). As mentioned in table 1, various reaction parameters (retention time, solvent, base, light, temperature, and catalyst) were optimized to performed the controlled reaction. Eventually, at the room temperature under the visible light (Blue LED, 34 W, 450-455 nm, 30 °C), and the 62.5 min. retention time, generated the best yield 94% of compound **5aa** (Table S1 entry 7).

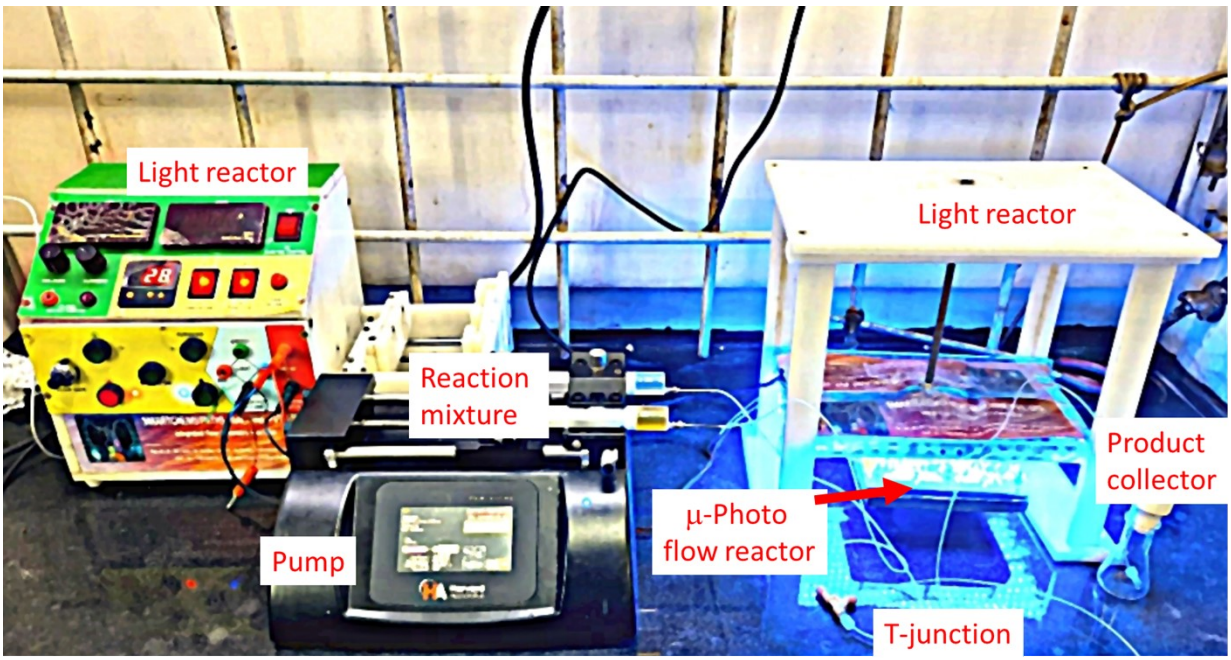


Fig. S5. Snapshot of photo-flow optimized reactor for the annulation reaction.

4.4 Fabrication of a dual channel micro-separator.

As shown in Fig. S6, laser ablation on PTFE film was employed to fabricate the proposed dual-channel device. First and foremost, layers of 1mm thick PTFE films were ablated by UV laser 355 nm, to form a serpentine microchannel (1 mm width, 1mm depth, and 20 cm length) as per our previously reported procedure[5]. The 4-corners of each film were holed (1 mm dia.) to align the film patterns. After laser ablation, the films were cleaned by washing with acetone under ultrasonic and dried. Polytetrafluoroethylene (PTFE) membrane (Whatman, 0.45 µm pore, 47 mm dia.) sandwiched by two sheets of PTFE film with the identical dimension of microchannel were placed between metal holders, which were aligned with each other by inserting metal pins through the holes at the film corners. Finally, the metal holder was tightly pressed by the screw to seal the device with no leak.

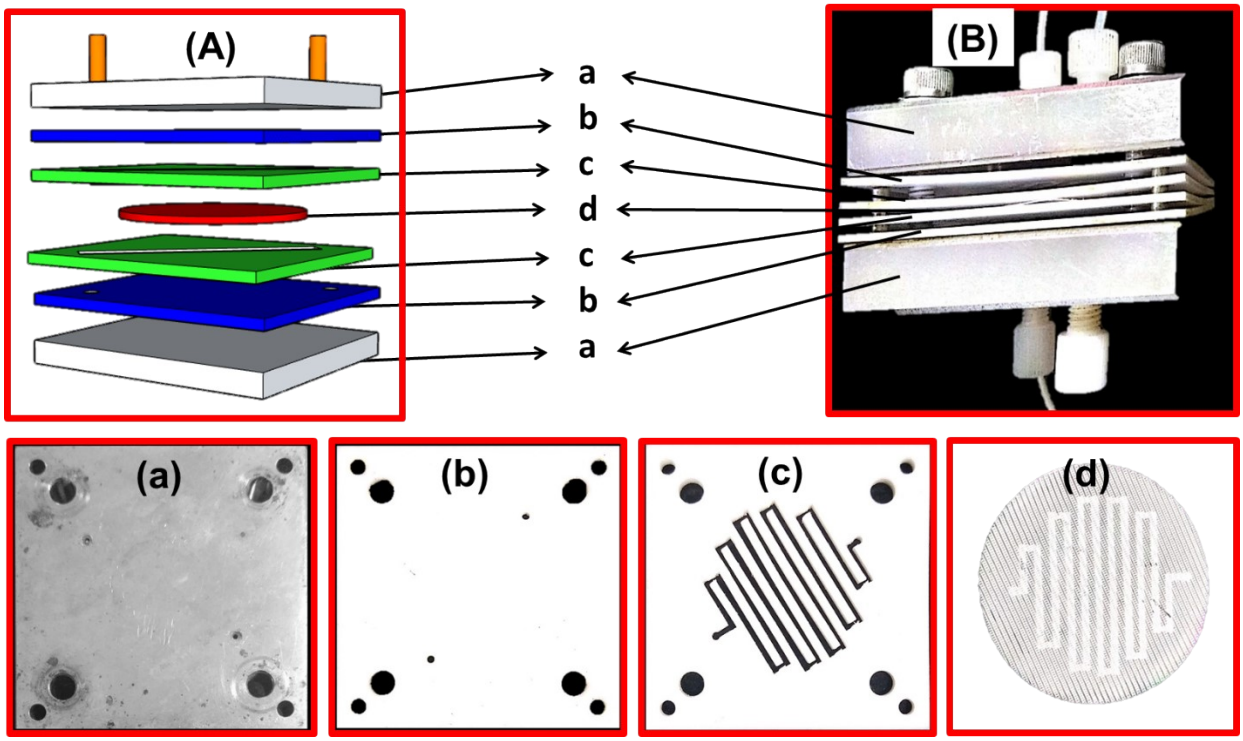


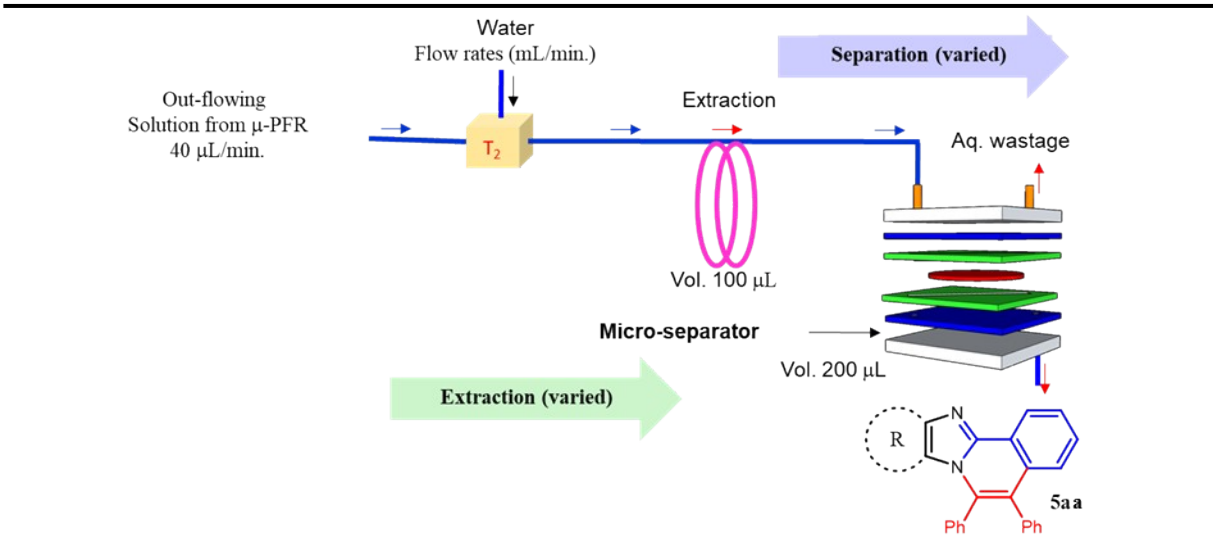
Fig. S6. Diagram of a fluoropolymer PTFE membrane based micro-separator, (A) 3D model; (B)

original photograph; (a) SS-metal body; (b) metal protecting PTFE layer; (c) laser grooved PTFE channel; (d) propylene coated PTFE membrane.

4.5 Solvent exchange optimization.

To exchange the solvent containing product from $CHCl_3$: MeOH to chloroform solvent, the additional PTFE membrane embedded phase separator was connected to the outlet of the µ-PFR reactor as shown in table S1. A continuous process of droplet formation, extraction and separation for purification of the out flowing the solution from µ-PFR was conducted in droplet microfluidics equipped with the PTFE membrane micro-separator, as explained in a stepwise manner. At first, formation of alternating organic-aqueous droplets by introducing water into the product mixture through T-junction was done. Secondly, extraction of reaction waste into aqueous stream by passing through a length of 0.1 m capillary during 6 sec. Finally, completion of the separation of the mixture of reactant, catalyst and product containing organic phase by wetting and crossing through thin PTFE membrane to the bottom of the separator wherein, the waste aq. MeOH: H_2O containing aqueous phase did not wet the membrane and passed through as the original stream.

Table S2. Solvent exchange through the micro-separator.



Entry	Flow rates (mL/min.)	Extraction	Separation	Yield %
	H_2O	Time (min.)	Time (min.)	
1	0.3	0.29	0.58	95
2	0.5	0.18	0.36	94
3	1	0.09	0.18	94
4	2	0.04	0.09	90
5	3	0.03	0.06	88
6	4	0.02	0.04	82

Isolated yields are based on average of two experiments.

5. An integrated continuous photo-flow synthesis of 5,6-diphenylbenzo [4,5] imidazo [2,1-a] isoquinoline (5aa).

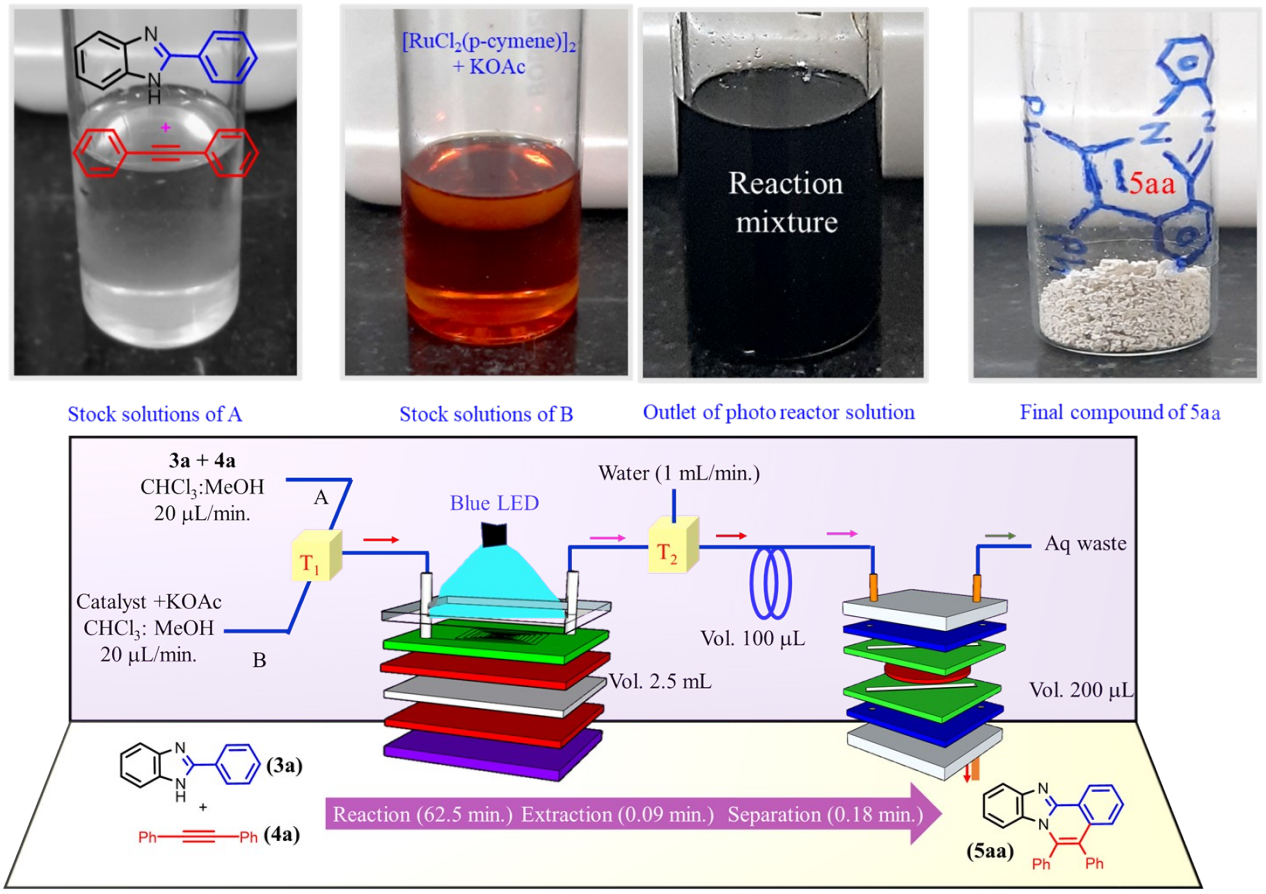
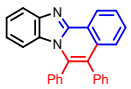


Fig. S7. Integrated continuous flow set-up for synthesis of **5aa**.

The stock solution **(A)** containing **3a**:**4a**: $CHCl_3$: MeOH in molar ratio (1:2:561:123); and the stock solution **(B)** containing KOAc: $[RuCl_2(cymene)]_2$: $CHCl_3$: MeOH in molar ratio (1:02:280:61) was taken in two separate syringes (Fig. S7) and connected with designed μ-PFR to perform the reaction. Two reactants were introduced into capillary micro-reactor through T- junction (T_1) in a flow rate molar ratio of 1:1 to maintain the stoichiometry and then passed through a μ-PFR (reactor volume 2.5 mL) for the synthesis of annulation product during 62.5 min of residence time. The μ-PFR solution was delivers to the micro separator by introducing water through additional T-junction to form organic-aqueous droplets. Complete extraction between organic-aqueous segments was accomplished for 0.09 min retention time by flowing through a PTFE capillary (id = 1000 μm, length = 0.1 m, vol. = 100 μL). The complete separation was achieving by passing through the micro separator under the optimized reaction condition. The organic layer was concentrated under vacuum to give the product and subsequent purification by column chromatography(*n*-Hexane: EtOAc = 5:1) on silica gel afforded the corresponding product **5aa**, 94% as a white solid and melting point is 275-277 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.99 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.60 – 7.55 (m, 1H), 7.43 – 7.32 (m, 7H), 7.29 (dd, *J* = 7.7, 6.0 Hz, 2H), 7.26 – 7.18 (m, 3H), 6.93 (ddd, *J* = 8.4, 7.2, 1.1 Hz, 1H), 6.01 (d, *J* = 8.5 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.7, 144.2, 135.6, 135.1, 133.7, 132.6, 131.5, 131.2, 130.6, 129.9, 129.2, 128.7, 128.0, 127.7, 127.2, 126.4, 125.0, 124.1, 123.5, 122.9, 121.2, 119.5, 114.1. **IR (V_{max}):** 3027, 1712, 1501, 1438, 1360, 1221, 748 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{27}H_{18}N_2$ $[M+H]^+$: 371.1543, found: 371.1541. The analytical data corresponds with those reported in the literature.[2, 6-9]

Table S3. Comparative table for synthesis of 5aa.

Product	Reaction condition	Ref.



Catalyst	Temp (^{o}C)	Time (min.)	Oxidant	Additive	
Ru	100	240	Electricity	1-AdCO_2H	9
Ru	110	720	Cu (II)	NO	8
Ni	160	1200	KOBu^t	NO	6
Rh	50	2888	Ag	NO	1
Co	60	300	Ag	NO	7
Rh	25-80	2880	Cu(II)	NBu_4F/ pivalic acid	10
Ru	100	2	Electricity	No	2
Ru	rt.	62.5	Visible Light	No	Our study

Productivity under optimized condition.

Molar solution = 0.02 M

Flow rate = 20 μL/min

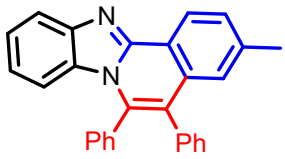
Product molecular weight = 370

Product yield = 94 %

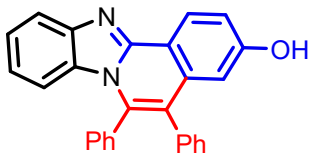
$$Productivity\ g/day\ = \frac{0.02_{X}0.02_{X}60_{X}24_{X}370_{X}0.94}{1000}$$

Productivity g/day =0.200 g/day

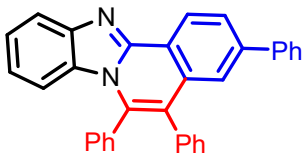
3-Methyl-5,6-diphenylbenzo [4,5] imidazo [2,1-a] isoquinoline (5ba): The product **(5ba)** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 75% yield of **5ba** as a white solid and melting point is 264-264 °C, **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.87 (d, *J* = 8.2 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.53 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.42 – 7.27 (m, 8H), 7.26 – 7.15 (m, 3H), 7.11 (s, 1H), 6.91 (ddd, *J* = 8.4, 7.1, 1.1 Hz, 1H), 5.98 (d, *J* = 8.5 Hz, 1H), 2.42 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.9, 144.3, 140.3, 135.7, 135.1, 133.8, 132.7, 131.5, 131.2, 130.6, 129.3, 129.1, 128.8, 128.0, 127.2, 126.1, 125.0, 124.00, 123.4, 121.0, 120.6, 119.4, 114.0, 22.0. **IR (V_{max}):** 3050, 2929, 1620, 1453, 1340, 1268, 745 cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{28}H_{20}N_2$ $[M+H]^+$: 385.1705, found: 385.1697. Verified the analytical data with those reported in the literature.[2, 7-9]



5,6-Diphenylbenzo[4,5]imidazo[2,1-a]isoquinolin-3-ol (5ca): The product **(5ca)** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 72% yield of **5ca** as a white solid and melting point is 340 °C, **^{1}H NMR (400 MHz, DMSO-d_6):** δ 9.91 (d, J = 2.0 Hz, 1H), 8.68 (dd, J = 8.7, 1.9 Hz, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.45 – 7.36 (m, 5H), 7.32 – 7.22 (m, 6H), 7.20 – 7.14 (m, 1H), 6.82 (t, J = 7.8 Hz, 1H), 6.63 (d, J = 2.0 Hz, 1H), 5.84 (d, J = 8.4 Hz, 1H). **^{13}C NMR (126 MHz, DMSO-d_6):** δ 155.04, 143.10, 139.72, 131.31, 130.87, 130.14, 129.22, 126.97, 126.38, 126.18, 125.05, 124.42, 123.73, 122.97, 122.37, 119.41, 117.95, 116.06, 114.49, 113.43, 110.53, 109.02, 105.84· **IR (V_{max}):** 3383, 1652, 994, 756. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{27}H_{18}N_2O$ $[M+H]^+$: 387.1488, found: 387.1487

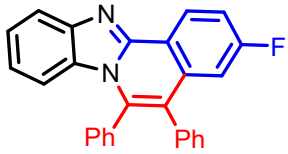


3,5,6-Triphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (5da): The product **(5da)** was prepared



according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 82% yield of **5da** as a white solid and melting point is 325-326 °C, **^{1}H NMR (300 MHz, $CDCl_3$):** δ 9.05 (d, J = 8.3 Hz, 1H), 8.03 – 7.91 (m, 2H), 7.56 (dd, J = 5.7, 1.5 Hz, 3H), 7.46 – 7.34 (m, 9H), 7.33 – 7.26 (m, 4H), 7.24 (s, 1H), 6.98 – 6.90 (m, 1H), 6.01 (d, J = 8.5 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.65, 144.40, 142.68, 140.48, 135.51, 133.73, 133.06, 131.50, 131.25, 130.62, 129.23, 128.87, 128.74, 128.08, 127.81, 127.39, 127.34, 127.01, 125.62, 124.56, 124.15, 123.66, 122.01, 121.88, 121.25, 119.53, 114.12. **IR (V_{max}):** 3025, 1447, 1216745, 672. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{33}H_{22}N_2$ $[M+H]^+$: 447.1860, found: 447.1854, Verified the analytical data with those reported in the literature.

3-Fluoro-5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinoline (5ea): The product **(5ea)** was



prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 85% yield of **5ea** as a white solid and melting point is 251-253 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.98 (dd, *J* = 8.9, 5.7 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.47 – 7.36 (m, 5H), 7.36 – 7.26 (m, 5H), 7.23 – 7.17 (m, 2H), 7.02 – 6.88 (m, 2H), 5.99 (d, *J* = 8.5 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 163.6 (d, $^1J_{C\text{-}F}$ = 251 Hz), 147.3, 144.20, 136.3, 135.1, 134.8 (d, $^3J_{C\text{-}F}$ = 10 Hz), 133.4, 131.3, 131.1, 130.4, 129.4, 128.8, 128.2, 127.7 (d, $^3J_{C\text{-}F}$ =9.0 Hz), 127.5, 124.3, 122.9 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 121.3, 119.5, 119.5, 116.4 (d, $^2J_{C\text{-}F}$ = 23 Hz), 114.1, 111.7 (d, ^{2}JC-F = 23 Hz). **^{19}F NMR (377 MHz, $CDCl_3$):** δ -108.4 (s). **IR (V_{max}):** 2986, 1738, 1451, 1318, 1269, 1154, 1033 cm^{-1}. **HRMS (ESI):** *m/z* calcd

for $C_{27}H_{17}FN_2$ $[M+H]^+$: 389.1449, found: 389.1449. Verified the analytical data with those reported in the literature.[2, 7-9]

3-Bromo-5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinoline(5fa): The product **5fa** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 65% yield of yield **5fa** as a white solid and melting point is 297-299 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.84 (d, *J* = 8.6 Hz, 1H), 7.97 (d, *J* = 8.1 Hz, 1H), 7.79 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.47 (d, *J* = 1.8 Hz, 1H), 7.44 – 7.36 (m, 4H), 7.34 – 7.27 (m, 5H), 7.22 – 7.18 (m, 2H), 6.94 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 5.99 (d, *J* = 8.5 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.2, 144.2, 136.3, 134.8, 134.1, 133.4, 131.4, 131.1, 131.0, 130.4, 129.4, 128.8, 128.8, 128.2, 127.6, 126.7, 124.6, 124.4, 122.5, 121.66, 121.6, 119.6, 114.1. **IR (V_{max}):** 2937, 1603, 1524, 1435, 1335, 1260, 747 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{27}H_{17}BrN_2$ $[M+H]^+$: 449.0653, found: 449.0652. Verified the analytical data with those reported in the literature.[2, 7-9]

5,6-Diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile (5ga): The product **5ga** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 85% yield of **5ga** as a white solid and melting point is 272-274 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.07 (d, *J* = 8.3 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.66 (s, 1H), 7.43 (dd, *J* = 16.0, 8.3 Hz, 4H), 7.37 – 7.29 (m, 5H), 7.19 (d, *J* = 6.8 Hz, 2H), 7.00 (t, *J* = 7.8 Hz, 1H), 6.03 (d, *J* = 8.5 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 146.1, 144.3, 137.0, 134.2, 133.0, 132.5, 131.3, 131.1, 131.1, 130.3, 129.6, 129.5, 128.9, 128.4, 127.9, 125.9, 125.6, 124.8, 122.5, 122.4,

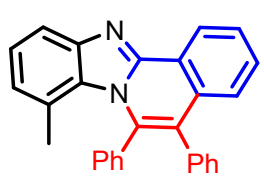
120.0, 118.7, 114.3, 113.0. **IR (V_{max}):** 2927, 1448, 1215, 752, 671 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{28}H_{17}N_3$ $[M+H]^+$: 396.1501, found: 396.1494. Verified the analytical data with those reported in the literature.[2, 7]

2-Methyl-5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinoline (5ha): The product **5h** was prepared according to the general procedure as described in section 5**.** The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 52% yield of **5h** as a white solid and melting point is 291-293 °C. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.81 (s, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.44 – 7.32 (m, 7H), 7.28 – 7.19 (m, 6H), 6.92 (dd, *J* = 11.5, 4.1 Hz, 1H), 6.01 (d, *J* = 8.4 Hz, 1H), 2.60 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.72, 144.2, 138.0, 135.8, 134.2, 133.8, 131.4, 131.4, 131.2, 130.7, 130.4, 129.1, 128.7, 127.9, 127.2, 126.3, 124.7, 124.0, 123.5, 122.8, 121.1, 119.5, 114.1, 21.5. **IR (V_{max}):** 3050, 2940, 1619, 1502, 1442, 1340, 1265, 1023, 828, 753 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{28}H_{20}N_2$ $[M+H]^+$: 385.1705, found: 385.161698. Verified the analytical data with those reported in the literature.[2]

5,6-Diphenyl-2-(trifluoromethyl) benzo [4,5] imidazo [2,1-a] isoquinoline (5ia): The product **5ia** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 55% yield of **5ia** as a white solid and melting point is 285-287 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.29 (s, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.75 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.47 – 7.38 (m, 5H), 7.37 – 7.27 (m, 5H), 7.21 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.00 – 6.95 (m, 1H), 6.02 (d, *J* = 8.5 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 146.9, 144.2, 137.2, 134.9, 134.8, 133.2, 131.4, 131.1, 130.3, 129.6 (q, $^2J_{C\text{-}F}$ = 25 Hz),

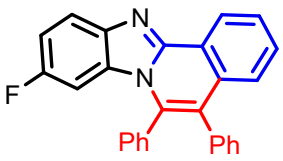
129.5, 128.9, 128.2, 127.6, 127.1, 125.8 (q, $^{3}J_{C\text{-}F}$ = 2.5 Hz), 125.1, 124.6, 124.6, 122.8 (q, $^{1}J_{C\text{-}F}$ = 10 Hz), 122.6 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 121.9, 119.8, 114.2. **^{19}F NMR (376 MHz, $CDCl_3$):** δ -62.20 (s). **IR (V_{max}):** 2925, 2859, 1439, 1315, 1132, 750 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{28}H_{17}F_3N_2$ $[M+H]^+$: 439.1422, found: 439.1417 found: 439.1417. Verified the analytical data with those reported in the literature.[2, 7-9]

8-Methyl-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (5ja): The product **(5ja)** was

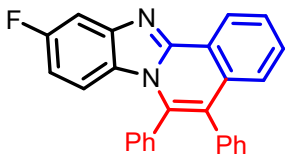


prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 51% yield of **5ja** as a white solid and melting point is 248-249 °C, **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.03 (dd, J = 8.0, 0.8 Hz, 1H), 7.67 (ddd, J = 8.1, 7.1, 1.1 Hz, 1H), 7.55 (ddd, J = 8.4, 7.2, 1.4 Hz, 1H), 7.41 – 7.35 (m, 3H), 7.34 – 7.30 (m, 3H), 7.29 – 7.26 (m, 2H), 7.25 – 7.20 (m, 3H), 7.18 – 7.15 (m, 1H), 6.82 (dd, J = 8.5, 7.2 Hz, 1H), 5.84 (d, J = 8.5 Hz, 1H), 2.85 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 147.13, 143.67, 135.80, 135.19, 133.78, 132.46, 131.53, 130.84, 130.66, 129.62, 129.47, 129.08, 128.63, 127.96, 127.55, 127.16, 126.24, 125.19, 124.18, 123.35, 123.13, 121.01, 111.58, 17.13. **IR (V_{max}):** 3027, 2923, 1441, 1349, 1276, 1216, 749. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{28}H_{20}N_2$ $[M+H]^+$: 385.1704, found: 385.1697

9-Fluoro-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (5ka): The product **(5ka)** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 53% yield of **5ka** as a white solid and melting point is 245-246 °C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.94 (dd, J = 8.0, 0.7 Hz, 1H), 7.90 (dd, J = 8.9, 5.1 Hz, 1H), 7.71 – 7.67 (m, 1H), 7.60 – 7.55 (m, 1H), 7.42 (ddd, J = 14.2, 5.9, 2.5 Hz, 3H), 7.37 – 7.27 (m, 6H), 7.23 – 7.19 (m, 2H), 7.13 (td, J = 9.1, 2.5 Hz, 1H), 5.64 (dd, J = 10.2, 2.4 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 140.62, 135.43, 134.73, 133.14, 132.49, 131.40, 130.53, 129.96, 129.50, 128.88, 128.06, 127.92, 127.35, 126.48, 124.82, 123.79, 122.97, 120.01, 119.91, 112.80, 112.55, 101.05, 100.75. **^{19}F NMR (376 MHz, $CDCl_3$):** δ -119.07 (s). **IR (V_{max}):** 3022, 2931, 1722, 1449, 1281, 1215, 744. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{27}H_{17}FN_2$ $[M+H]^+$: 389.1451, found: 389.1445

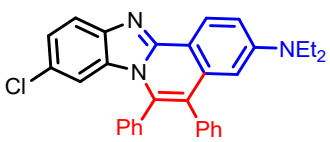


10-Fluoro-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (5la): The product **(5la)** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 42% yield of **5la** as a white solid and melting point is 285-286 °C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.96 (dd, J = 8.0, 0.8 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.63 – 7.57 (m, 2H), 7.44 – 7.38 (m, 3H), 7.34 (dd, J = 7.9, 6.6 Hz, 3H), 7.29 (ddd, J = 8.4, 4.1, 2.6 Hz, 3H), 7.23 – 7.20 (m, 2H), 6.68 (td, J = 9.2, 2.6 Hz, 1H), 5.90 (dd, J = 9.2, 4.8 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 149.02, 135.46, 134.83, 133.46, 132.61, 131.42, 130.55, 130.10, 129.37, 128.87, 128.05, 127.89, 127.34, 126.41, 125.06, 123.80, 122.60, 114.76, 114.66, 109.76, 109.51, 104.93, 104.70. **^{19}F NMR (376 MHz, $CDCl_3$):** δ -117.87 (s). **IR (V_{max}):** 3022, 1214, 740, 670 cm^{-1}. **HRMS (ESI):** *m/z* calcd for:



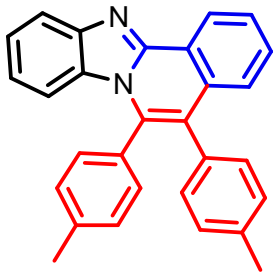
$C_{27}H_{17}FN_2$ $[M+H]^+$: 389.1451, found: 389.1446. Verified the analytical data with those reported in the literature [26]

***N*, *N* Diethyl-5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinolin-3 amine (5ma):** The product



5ma was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 67% yield of **5ma** as a white solid and melting point is 260-262 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.71 (d, *J* = 9.0 Hz, 1H), 7.83 (d, *J* = 2.0 Hz, 1H), 7.42 – 7.26 (m, 6H), 7.25 – 7.19 (m, 4H), 7.08 (dd, *J* = 9.1, 2.6 Hz, 1H), 6.78 (dd, *J* = 8.9, 2.1 Hz,1H), 6.31 (d, *J* = 2.5 Hz, 1H), 5.77 (d, *J* = 8.9 Hz, 1H), 3.30 (q, *J* = 7.1 Hz, 4H), 1.08 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 149.7, 149.0, 145.6, 136.0, 134.9, 134.6, 133.8, 131.3, 131.3, 130.6, 129.9, 129.1, 128.7, 127.9, 127.1, 126.7, 123.8, 120.2, 118.1, 114.2, 113.5, 111.5, 106.1, 44.6, 12.3. **IR (V_{max}):** 2962, 1610, 1480, 1355, 1259, 754 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{31}H_{26}ClN_3$ $[M+H]^+$: 476.1894, found: 476.1887. Verified the analytical data with those reported in the literature.[2]

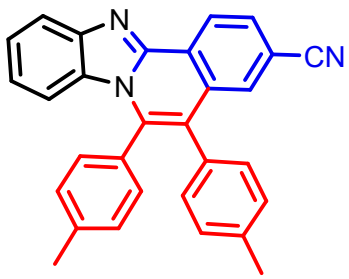
5,6-Di-p-tolylbenzo[4,5]imidazo[2,1-a]isoquinoline (5ab): The product **5ab** was prepared



according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 89% yield of **5ab** as a white solid and melting point is 272-274 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.97 (dd, J = 8.0, 0.8 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.58 – 7.53 (m, 1H), 7.36 (ddd, J = 14.5, 10.4, 4.2 Hz, 2H), 7.23 – 7.18 (m, 4H), 7.09 (s, 4H), 6.94 (ddd, J = 8.4, 7.2, 1.1 Hz, 1H), 6.03 (d, J = 8.5 Hz, 1H), 2.42 (s, 3H), 2.33 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.78, 144.54, 144.18, 138.97, 136.69, 135.22, 132.93, 132.67, 131.28,

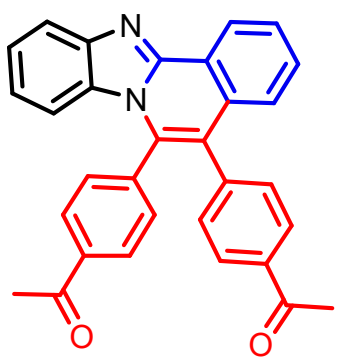
130.87, 130.41, 129.77, 129.44, 128.72, 127.57, 126.39, 124.98, 124.01, 123.50, 122.82, 121.10, 119.43, 114.28, 21.54, 21.25. **IR (V_{max}):** 3023, 1509, 1450, 1215, 749, 670. cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{29}H_{22}N_2$ $[M+H]^+$: 399.1850, found: 399.1848. Verified the analytical data with those reported in the literature.[10]

5,6-Di-p-tolylbenzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile (5gb): The product **5gb** was



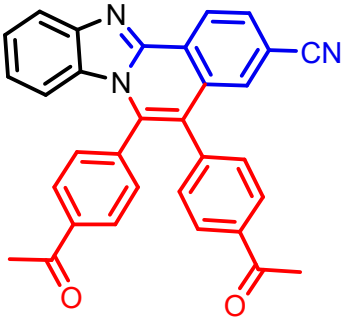
prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 87% yield of **5gb** as a white solid and melting point is 337-338 °C. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.05 (d, J = 8.3 Hz, 1H), 8.00 (d, J = 8.2 Hz, 1H), 7.85 (dd, J = 8.3, 1.5 Hz, 1H), 7.65 (d, J = 1.0 Hz, 1H), 7.41 (ddd, J = 8.2, 7.2, 0.9 Hz, 1H), 7.23 – 7.20 (m, 4H), 7.13 (d, J = 7.8 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 7.01 (ddd, J = 8.4, 7.1, 1.1 Hz, 1H), 6.06 (d, J = 8.5 Hz, 1H), 2.43 (s, 3H), 2.36 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 146.20, 144.29, 139.49, 137.50, 137.14, 135.72, 132.87, 131.28, 131.21, 131.09, 130.15, 130.08, 129.63, 129.27, 129.17, 125.84, 125.52, 124.69, 122.46, 122.23, 119.96, 118.77, 114.48, 112.90, 21.56, 21.26. **IR (V_{max}):** 3021, 2357, 1425, 1215, 741, 670. cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{30}H_{21}N_3$ $[M+H]^+$: 424.1805, found: 424.1804.

1,1'-(Benzo[4,5]imidazo[2,1-a]isoquinoline-5,6-diylbis(4,1-phenylene))bis(ethan-1-one)



(5ac): The product **5ac** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 84% yield of **5ac** as a white solid and melting point is 254-255 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.99 (d, J = 7.4 Hz, 1H), 8.07 (dd, J = 7.5, 2.1 Hz, 1H), 8.00 (d, J = 8.3 Hz, 2H), 7.89 (d, J = 8.2 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.62 – 7.57 (m, 1H), 7.51 (dd, J = 4.8, 2.5 Hz, 1H), 7.48 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 7.3 Hz, 1H), 7.33 (d, J = 8.2 Hz, 1H), 7.24 (s, 1H), 7.00 – 6.93 (m, 1H), 6.03 (d, J = 8.5 Hz, 1H), 2.66 (s, 3H), 2.60 (s, 3H)..**^{13}C NMR (75 MHz, $CDCl_3$):** δ 197.67, 197.34, 147.54, 144.16, 140.48, 137.81, 137.49, 136.14, 133.82, 131.73, 130.97, 130.82, 130.22, 129.02, 128.80, 128.39, 128.23, 126.56, 126.03, 125.23, 124.52, 122.88, 121.72, 119.79, 113.69, 26.73, 26.63. **IR (V_{max}):** 3022, 1686, 1608, 1530, 1448, 1362, 1269, 841, 757. cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{31}H_{22}N_2O_2$ $[M+H]^+$: 455.1756, found: 455.1753.

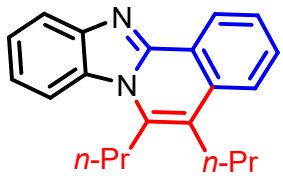
5,6-Bis(4-acetylphenyl)benzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile (5gc): The



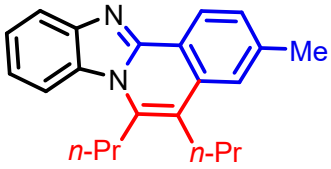
product **5gc** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 81% yield of **5gc** as a white solid and melting point is 320-321 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.09 (d, J = 8.3 Hz, 1H), 8.05 – 8.01 (m, 3H), 7.95 – 7.90 (m, 3H), 7.57 (d, J = 1.0 Hz, 1H), 7.50 – 7.43 (m, 3H), 7.32 (d, J = 8.3 Hz, 2H), 7.03 (ddd, J = 8.4, 7.2, 1.1 Hz, 1H), 6.05 (d, J = 8.5 Hz, 1H), 2.67 (s, 3H), 2.63 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 197.43, 197.14, 148.56, 146.00, 144.39, 139.01,

137.91, 137.06, 136.76, 135.89, 131.75, 131.65, 131.65, 130.92, 130.87, 130.57, 130.11, 129.01, 128.66, 126.24, 125.79, 125.22, 122.90, 120.46, 113.90, 113.47, 26.76, 26.69. **IR (V_{max}):** 3024, 1215, 741, 670. cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{32}H_{21}N_3O_2$ $[M+H]^+$: 480.1706, found: 480.1706.

5,6-Dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (5ad): The product **5ad** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 71% yield of **5ad** as a white solid and melting point is 140-142 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.92 (dd, *J* = 8.0, 1.1 Hz, 1H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.70 (ddd, *J* = 8.3, 7.2, 1.5 Hz, 1H), 7.66 – 7.57 (m, 1H), 7.55 – 7.43 (m, 1H), 7.37 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 3.41 – 3.32 (m, 2H), 3.01 – 2.94 (m, 2H), 1.96 – 1.86 (m, 2H), 1.76 – 1.68 (m, 2H), 1.24 (t, *J* = 7.4 Hz, 3H), 1.14 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 148.1, 144.4, 135.7, 131.5, 130.8, 129.9, 126.8, 125.6, 123.9, 123.5, 122.8, 121.6, 119.9, 118.6, 114.3, 31.07, 29.6, 23.8, 21.6, 14.5, 13.9. **IR (V_{max}):** 3063, 2956, 2878, 1625, 1526, 1455, 1354, 1281, 752 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{22}N_2$ $[M+H]^+$: 303.1861, found: 303.1855. Verified the analytical data with those reported in the literature.[2, 6]

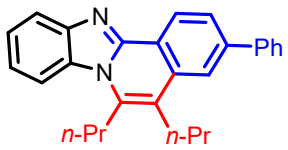


3-Methyl-5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (5bd): The product **5bd** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 63% yield of **5bd** as a white solid and melting point is 124-126 °C. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.80 (d, *J* = 8.1 Hz, 1H), 8.00 (dd, *J* = 8.1, 0.6 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.63 (s, 1H), 7.50



– 7.43 (m, 2H), 7.35 (ddd, *J* = 8.4, 7.1, 1.2 Hz, 1H), 3.40 – 3.34 (m, 2H), 2.99 – 2.93 (m, 2H), 2.58 (s, 3H), 1.97 – 1.86 (m, 2H), 1.78 – 1.70 (m, 2H), 1.24 (t, *J* = 7.3 Hz, 3H), 1.15 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 148.3, 144.4, 140.1, 135.8, 131.7, 130.8, 128.4, 125.5, 123.8, 123.3, 121.3, 120.5, 119.8, 118.5, 114.2, 31.1, 29.5, 23.8, 22.3, 21.6, 14.5, 13.9. **IR (V_{max}):** 3060, 2955, 2876, 1626, 1526, 1454, 1350, 1281, 752 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{24}N_2$ $[M+H]^+$: 317.2018, found: 317.2017. Verified the analytical data with those reported in the literature.[2]

3-Phenyl-5,6-dipropylbenzo[4,5]imidazo[2,1-a]isoquinoline (5dd): The product **5dd** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 77% yield of **5dd** as a white solid and melting point is 132-133 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.98 (d, J = 8.3 Hz, 1H), 8.06 – 8.01 (m, 2H), 7.94 (d, J = 8.5 Hz, 1H), 7.87 (dd, J = 8.3, 1.6 Hz, 1H), 7.74 (dd, J = 5.2, 3.3 Hz, 2H), 7.55 – 7.48 (m, 3H), 7.46 – 7.34 (m, 2H), 3.44 – 3.38 (m, 2H), 3.07 – 3.01 (m, 2H), 1.94 (dd, J = 16.0, 7.7 Hz, 2H), 1.79 (dd, J = 15.8, 7.7 Hz, 2H), 1.26 (t, J = 7.3 Hz, 3H), 1.16 (t, J = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.97, 144.51, 142.80, 141.06, 136.19, 131.91, 130.87, 129.00, 127.83, 127.52, 126.19, 126.14, 124.02, 121.90, 121.63, 121.32, 119.96, 118.70, 114.26, 31.14, 29.55, 23.89, 21.59, 14.55, 13.89. **IR (V_{max}):** 2962, 1462, 1216, 749, 671. cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{27}H_{26}N_2$ $[M+H]^+$: 379.2166, found: 379.2165.

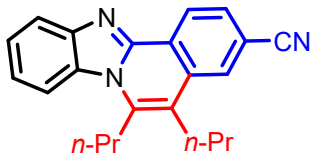


3-Fluoro-5,6-dipropylbenzo [4,5] imidazo [2,1-a] isoquinoline (5ed): The product **5ed** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 75% yield of **5ed** as a white solid and melting point is 155-157 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.91 (dd, *J* = 8.9, 6.0 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.40 – 7.31 (m, 2H), 3.41 – 3.32 (m, 2H), 2.95 – 2.87 (m, 2H), 1.96 – 1.86 (m, 2H), 1.72 (m, 2H), 1.25 (t, *J* = 7.3 Hz, 3H), 1.15 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 164.0 (d, $^1J_{C\text{-}F}$ = 249 Hz), 147.63, 144.34, 137.08, 133.81 (d, $^3J_{C\text{-}F}$ = 9 Hz), 130.72, 128.2 (d, $^3J_{C\text{-}F}$ = 9 Hz), 124.15, 121.69, 119.91 119.41, 118.03 (d, $^4J_{C\text{-}F}$ = 3 Hz), 115.4 (d, $^2J_{C\text{-}F}$ = 23 Hz), 114.22, 109.0 (d, $^2J_{C\text{-}F}$ = 23 Hz), 31.13, 29.71, 23.61, 21.49, 14.46, 13.88. **^{19}F NMR (376 MHz, $CDCl_3$):** δ -108.89 (s). **IR (V_{max}):** 2955, 2881, 1622, 1453, 1345, 1370, 1191, 832, 749 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{21}FN_2$ $[M+H]^+$: 321.1767, found: 321.1760. Verified the analytical data with those reported in the literature.[2]

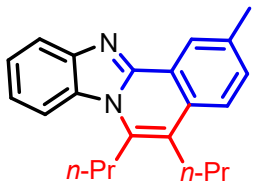
3-Bromo-5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (5fd): The product **5fd** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 79% yield of **5fd** as a white solid and melting point is 158-160°C**. ^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.77 (d, *J* = 8.6 Hz, 1H), 8.01 (d, *J* = 7.7 Hz, 1H), 7.97 (d, *J* = 1.8 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.72 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.50 (ddd, *J* = 8.1, 7.2, 0.8 Hz, 1H), 7.41 – 7.35 (m, 1H), 3.41 – 3.31 (m, 2H), 2.95 – 2.88 (m, 2H), 1.95 – 1.87 (m, 2H), 1.7-1.69 (m, 2H), 1.25 (t, *J* = 7.3 Hz, 3H), 1.15 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.5, 144.3, 137.1, 133.1, 130.7, 130.0, 127.2,

126.2, 124.7, 124.2, 121.9, 121.5, 120.1, 117.6, 114.3, 31.1, 29.4, 23.7, 21.5, 14.5, 13.8. **IR (V_{max}):** 2953, 1707, 1617, 1528, 1450, 1341, 1265, 1090, 825, 754 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{21}BrN_2$ $[M+H]^+$: 381.0966, found: 381.0964. Verified the analytical data with those reported in the literature.[2]

5,6-Dipropylbenzo [4,5] imidazo [2,1-a] isoquinoline-3-carbonitrile (5gd): The product **5gd** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 69% yield of **5gd** as a white solid and melting point is 194-196 °C. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.01 (d, *J* = 8.3 Hz, 1H), 8.16 (d, *J* = 1.0 Hz, 1H), 8.06 (dd, *J* = 8.2, 0.5 Hz, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 7.82 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.45 (ddd, *J* = 8.4, 7.1, 1.2 Hz, 1H), 3.40 (dd, *J* = 9.5, 7.2 Hz, 2H), 3.00 – 2.93 (m, 2H), 1.97 – 1.89 (m, 2H), 1.76 – 1.68 (m, 2H), 1.27 (t, *J* = 7.4 Hz, 3H), 1.17 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 146.4, 144.4, 137.9, 131.4, 130.7, 128.6, 128.4, 126.5, 125.6, 124.7, 122.8, 120.5, 119.0, 117.6, 114.4, 113.1, 31.1, 29.4, 23.9, 21.4, 14.4, 13.9. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{21}N_3$ $[M+H]^+$: 328.1814, found: 328.1807. Verified the analytical data with those reported in the literature.[2]

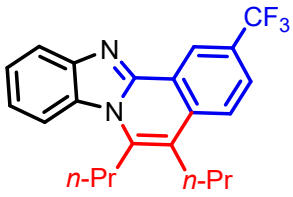


2-Methyl-5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (5hd): The product **5hd** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 61% yield of **5hd** as a white solid and melting point is 168-170 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.73 (s, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.49 (dd, *J* = 17.6, 8.5 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 1H), 3.42 – 3.31 (m, 2H), 2.99 – 2.91 (m, 2H), 2.58 (s, 3H), 1.96 – 1.86



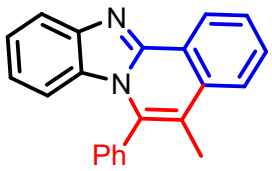
(m, 2H), 1.76-1.71 (m, 2H), 1.24 (t, J = 7.3 Hz, 3H), 1.13 (t, J = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 148.1, 144.3, 136.9, 134.8, 131.5, 130.8, 129.3, 125.2, 123.9, 123.4, 122.7, 121.4, 119.9, 118.7, 114.2, 31.0, 29.6, 23.9, 21.6, 21.3, 14.5, 13.8. **IR (V_{max}):** 2954, 1625, 1518, 1454, 1353, 749 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{24}N_2$ $[M+H]^+$: 317.2018, found: 317.2008. Verified the analytical data with those reported in the literature.[2]

5,6-Dipropyl-2-(trifluoromethyl) benzo [4,5] imidazo [2,1-a] isoquinoline (5id): The product

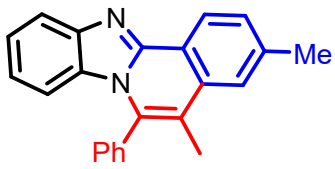


5id was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 65% yield of **5id** as a white solid and melting point is 137 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.22 (s, 1H), 8.09 – 8.01 (m, 1H), 7.95 (t, J = 8.0 Hz, 2H), 7.88 (dd, J = 8.7, 1.7 Hz, 1H), 7.57 – 7.49 (m, 1H), 7.42 (ddd, J = 8.4, 7.2, 1.2 Hz, 1H), 3.45 – 3.34 (m, 2H), 3.04 – 2.93 (m, 2H), 1.99 – 1.88 (m, 2H), 1.78-1.68 (m, 2H), 1.26 (t, J = 7.3 Hz, 3H), 1.16 (t, J = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 147.29, 144.34, 138.09, 133.77, 130.75, 128.89, 128.56, 125.9 (q, $^3J_{C\text{-}F}$ = 3 Hz) 124.50, 124.33, 123.2 (q, $^3J_{C\text{-}F}$ = 4 Hz), 122.75, 122.30, 120.31, 118.07, 114.39, 31.22, 29.60, 23.82, 21.50, 14.49, 13.93. **^{19}F NMR (376 MHz, $CDCl_3$):** δ -62.14 (s). **IR (V_{max}):** 2952, 1441, 1328, 1135, 752 cm^{-1}. **HRMS (ESI):** *m/z* calcd for$C_{22}H_{21}F_3N_2$ $[M+H]^+$: 371.1735, found: 371.1727. Verified the analytical data with those reported in the literature.[2]

5-Methyl-6-phenylbenzo [4,5] imidazo[2,1-a] isoquinoline (5ae): The product **5ae** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 85% yield of **5ae** as a white solid and melting point is 238-240 °C. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.97 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.94 (t, *J* = 7.3 Hz, 2H), 7.78-7.63 (m, 5H), 7.52 – 7.46 (m, 2H), 7.35 – 7.31 (m, 1H), 6.92 – 6.89 (m, 1H), 5.93 (d, *J* = 8.5 Hz, 1H), 2.32 (s, 3H)**. ^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.5, 143.9, 134.5, 134.3, 132.3, 131.1, 130.2, 130.0, 129.7, 129.5, 127.6, 125.4, 124.0, 123.8, 123.1, 121.0, 119.4, 115.5, 113.8, 14.5. **IR (V_{max}):** 2929, 1626, 1456, 1354, 1273, 1194, 757 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{16}N_2$ $[M+H]^+$: 309.1392, found: 309.1391. Verified the analytical data with those reported in the literature.[2, 6, 9]



3,5-Dimethyl-6-phenylbenzo [4,5] imidazo[2,1-a] isoquinoline (5be): The product **5be** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 77% yield of **5be** as a white solid and melting point is 179-181 °C**. ^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.84 (d, *J* = 8.2 Hz, 1H), 7.93 – 7.90 (m, 1H), 7.71 (s, 1H), 7.68 – 7.62 (m, 3H), 7.55 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.32 (ddd, *J* = 8.2, 7.1, 1.0 Hz, 1H), 6.89 (ddd, *J* = 8.4, 7.1, 1.2 Hz, 1H), 5.92 (d, *J* = 8.5 Hz, 1H), 2.61 (s, 3H), 2.29 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.7, 144.0, 140.3, 134.6, 134.3, 132.4, 131.1, 130.2, 129.7, 129.5, 129.1, 125.3, 124.0, 123.7, 120.8, 120.8, 119.2, 115.3, 113.7, 22.2, 14.5. **IR (V_{max}):** 3192, 2930, 2862, 1721, 1627, 1453, 1350, 1273, 754 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{23}H_{18}N_2$ $[M+H]^+$: 322.1549, found: 322.1547. Verified the analytical data with those reported in the literature.[2]

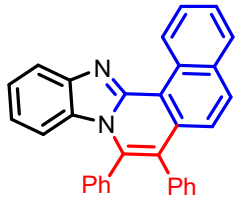


3-Fluoro-5-methyl-6-phenylbenzo [4,5] imidazo[2,1-a] isoquinoline (5ee): The product **5ee** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 82% yield of **5ee** as a white solid and melting point is 168-170 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.96 (dd, *J* = 8.9, 5.8 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.72 – 7.62 (m, 3H), 7.55 (dd, *J* = 10.5, 2.4 Hz, 1H), 7.51 – 7.37 (m, 3H), 7.34 (ddd, *J* = 8.2, 7.2, 1.0 Hz, 1H), 6.91 (ddd, *J* = 8.4, 7.2, 1.1 Hz, 1H), 5.92 (d, *J* = 8.5 Hz, 1H), 2.27 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 163.9 (d, $^1J_{C\text{-}F}$ = 250 Hz), 147.1, 144.0, 135.5, 134.5 (d, $^3J_{C\text{-}F}$ = 9 Hz), 134.2, 131.0, 130.0, 129.9, 129.6, 128.0 (d, $^3J_{C\text{-}F}$ = 10 Hz), 124.0, 121.1, 119.7, 119.4, 116.1 (d, $^4J_{C\text{-}F}$ = 24 Hz), 114.8 (d, $^2J_{C\text{-}F}$ = 3 Hz), 113.8, 109.7 (d, $^2J_{C\text{-}F}$ = 22 Hz), 14.5. **IR (V_{max}):** 3022, 1433, 1256, 743, 671 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{15}FN_2$ $[M+H]^+$: 327.1298, found: 327.1298. Verified the analytical data with those reported in the literature.[2]

Benzo[4,5]imidazo[2,1-a]isoquinoline-5,6-diyldimethanol (5af): The product **5af** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 51% yield of **5af** as a white solid and melting point is >340 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.01 (d, J = 13.6 Hz, 1H), 7.92 – 7.66 (m, 2H), 7.52 (d, J = 14.0 Hz, 3H), 7.28 (s, 1H), 7.21 (s, 1H), 6.13 (dd, J = 52.5, 14.9 Hz, 1H), 4.77 – 4.59 (m, 1H), 4.27 – 3.93 (m, 1H), 3.24 (dd, J = 79.1, 18.3 Hz, 1H), 2.81 (d, J = 13.7 Hz, 1H), 2.62 (t, J = 17.5 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 148.91, 130.57, 130.39, 129.29, 128.66, 123.32, 123.02, 122.43, 121.89, 121.78, 120.73, 110.36, 109.90, 99.29, 99.12,

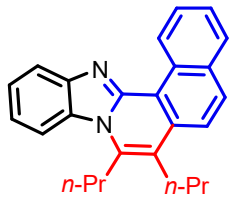
74.97, 46.30. **IR (V_{max}):** 3023, 1215, 741, 670. cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{14}N_2O_2$ $[M+H]^+$: 279.1129, found: 279.1121.

7, 8-Diphenylbenzo[h]benzo [4,5] imidazo[2,1-a] isoquinoline (5na): The product **5na** was



prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 63% yield of **5na** as a white solid and melting point is 236-238 °C**. ^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.14 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 8.1 Hz, 1H), 8.00 – 7.91 (m, 3H), 7.75 – 7.70 (m, 1H), 7.45-7.34 (m, 7H), 7.33-7.28 (m, 3H), 7.25 – 7.23 (m, 2H), 6.97-6.93 (m 1H), 6.08 (d, *J* = 8.5 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 147.8, 144.7, 136.4, 136.0, 134.0, 132.5, 132.4, 131.7, 130.7, 130.5, 130.2, 129.8, 129.1, 128.7, 128.2, 128.2, 128.0, 127.2, 126.8, 124.3, 123.9, 121.0, 119.8, 118.1, 114.4. **IR (V_{max}):** 3058, 2927, 2855, 1482, 1375, 1278, 1088, 1029, 753 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{31}H_{20}N_2$ $[M+H]^+$: 421.1699, found: 421.1695. Verified the analytical data with those reported in the literature.[2, 7-9]

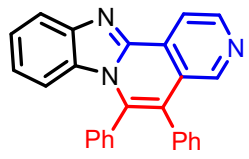
7,8-Dipropylbenzo[h]benzo [4,5] imidazo[2,1-a] isoquinoline (5nd): The product **5nd** was



prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 61% yield of **5nd** as a white solid and melting point is 117-119 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.09 (d, *J* = 8.7 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 9.0 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.98 (t, *J* = 8.7 Hz, 2H), 7.91 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.57-7.54 (m, 1H), 7.43-7.39 (m, 1H), 3.54 – 3.45 (m, 2H), 3.14 – 3.06 (m, 2H), 2.03 – 1.92 (m, 2H), 1.84 – 1.74 (m, 2H), 1.28 (t, *J* = 7.3 Hz, 3H), 1.18 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ

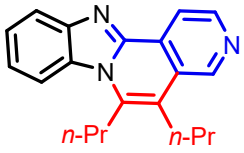
148.1, 144.8, 136.9, 132.1, 131.7, 131.1, 130.6, 129.4, 129.2, 128.1, 128.0, 126.4, 124.2, 121.5, 121.5, 120.4, 119.1, 117.9, 114.6, 31.4, 30.2, 24.1, 21.5, 14.6, 14.0. **IR (V_{max}):** 3062, 2951, 1728, 1461, 1373, 1278, 1090, 810, 747 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{25}H_{24}N_2$ $[M+H]^+$: 352.2018, found: 352.2018. Verified the analytical data with those reported in the literature.[2]

5,6-Diphenylbenzo [4,5] imidazo [2,1-a] [2,6] naphthyridine (5oa): The product **5oa** was



prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 71% yield of **5oa** as a white solid and melting point is 268-270 °C. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.85 (d, *J* = 5.3 Hz, 1H), 8.75 – 8.69 (m, 2H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.48 – 7.40 (m, 4H), 7.36 – 7.28 (m, 5H), 7.25 – 7.23 (m, 2H), 7.03 – 6.99 (m, 1H), 6.06 (d, *J* = 8.5 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 149.4, 146.9, 145.5, 144.2, 136.7, 133.9, 132.9, 131.3, 131.1, 130.4, 129.6, 128.9, 128.2, 127.9, 127.7, 127.0, 124.7, 122.5, 121.8, 120.2, 117.2, 114.4. **IR (V_{max}):** 3055, 2932, 1593, 1533, 1439, 1330, 847, 757 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{26}H_{17}N_3$ $[M+H]^+$: 372.1501, found: 372.1494. Verified the analytical data with those reported in the literature.[2, 7]

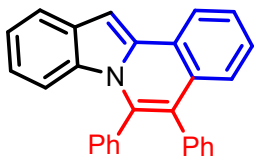
5,6-Dipropylbenzo [4,5] imidazo[2,1-a] [2,6] naphthyridine (5od): The product **5od** was



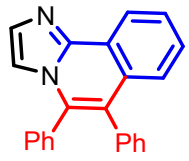
prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 61% yield of **5od** as a white solid and melting point is 167-169 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.27 (s, 1H), 8.78 (d, *J* = 5.1 Hz, 1H), 8.64 (d, *J* = 5.3 Hz, 1H), 8.06 (d, *J* = 8.1 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.9 Hz, 1H), 3.42 – 3.33 (m, 2H), 3.09 – 2.99 (m, 2H), 1.96 - 1.86 (m, 2H), 1.82 – 1.72 (m, 2H), 1.26 (t, *J* = 7.3 Hz, 3H), 1.16 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR**

(101 MHz, $CDCl_3$): δ 146.9, 145.9, 145.7, 144.2, 137.4, 130.7, 127.8, 125.8, 124.5, 122.8, 120.6, 117.6, 117.2, 114.4, 30.8, 28.8, 24.1, 21.4, 14.4, 13.8 cm^{-1}. **IR (V_{max}):** 3050, 2954, 1529, 1435, 1359, 846, 746 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{21}N_3$ $[M+H]^+$: 304.1814, found: 304.1811. Verified the analytical data with those reported in the literature.[2]

5,6-Diphenylindolo[2,1-a] isoquinoline (5pa): The product **5pa** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 70% yield of **5pa** as a green solid and melting point is 225-227 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.30 (dd, *J* = 8.0, 0.7 Hz, 1H), 7.78 (d, *J* = 8 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.41 (d, *J* = 0.5 Hz, 1H), 7.33 (m, 6H), 7.25 – 7.05 (m, 7H), 6.80 (m, 1H), 5.99 (dd, *J* = 8.7, 0.6 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 136.7, 136.0, 135.9, 135.3, 132.7, 131.8, 130.8, 130.2, 129.6, 128.7, 128.6, 127.8, 127.3, 127.0, 126.7, 126.1, 125.4, 123.2, 121.6, 121.4, 120.2, 120.1, 114.6, 94.2. **IR (V_{max}):** 3295, 3053, 2703, 1603, 1449, 1346, 751, 696 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{28}H_{19}N$ $[M+H]^+$: 370.1595 found: 370.1587. Verified the analytical data with those reported in the literature.[2, 6, 11]

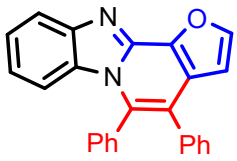


5,6-Diphenylimidazo[2,1-a] isoquinoline (5qa): The product **5qa** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 59% yield of **5qa** as a white solid and melting point is 237-239 °C. **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 8.76 (d, *J* = 7.5 Hz, 1H), 7.66 – 7.63 (m, 1H), 7.54 (d, *J* = 1.2 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.33 -7.31 (m, 3H), 7.31 – 7.27 (m, 4H), 7.25 – 7.19 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 143.1, 135.9, 133.5, 133.4, 131.404, 130.824, 130.6, 130.2, 128.8, 128.6, 128.0, 127.8, 127.3, 126.4, 124.4, 123.2, 123.2, 113.9. **IR**



(V_{max}): 2934, 1490, 1449, 1311, 760, 704 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{23}H_{16}N_2$ $[M+H]^+$: 321.1392, found: 321.1389. Verified the analytical data with those reported in the literature.[2, 6,7]

4,5-Diphenylbenzo[4,5]imidazo[1,2-a]furo[2,3-c]pyridine (5ra): The product **5ra** was prepared



according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 5:1), 92% yield of **5ra** as a yellow solid and melting point is 240-241 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.94 (d, J = 8.2 Hz, 1H), 7.61 (d, J = 5.3 Hz, 1H), 7.46 – 7.34 (m, 6H), 7.23 (ddd, J = 11.2, 6.4, 3.5 Hz, 4H), 7.05 (d, J = 5.1 Hz, 1H), 6.91 (ddd, J = 8.4, 7.2, 1.1 Hz, 1H), 6.07 (d, J = 8.6 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 145.19, 144.82, 140.34, 136.09, 134.95, 133.19, 130.81, 130.77, 129.38, 129.21, 128.84, 127.98, 127.27, 125.64, 125.25, 124.53, 121.55, 120.69, 119.38, 114.42. **IR (V_{max}):** 3022, 1428, 1214, 741, 670 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{25}H_{16}N_2O$ $[M+H]^+$: 361.1325, found: 361.1321.

6. An integrated continuous photo-flow synthesis of 9-methyl-5,6-diphenyl-11-propylpyrazolo [4',3':4,5] pyrimido[2,1-a] isoquinolin-8(9H)-one (8aa).

6.1 Synthesis of pyrazolo pyrimidines (7a-7l). Previously reported method has been applied for the synthesis of pyrazolo pyrimidines (7a-7l).[12] A dry round bottom flask (25 mL) was charged with 4-amino-2-methyl-5-propyl-2H pyrazole-3-carboxylic acid amide (0.18 M), benzaldehyde (0.18 M) and $K_2S_2O_8$ (0.36 M) in a mixture of ACN: H_2O (1:1, 6 mL) at room temperature and stirred. After the completion of reaction, the reaction mixture was dried on rotator evaporator, dissolved in ethyl acetate and washed with H_2O (3 times). The organic phases were combined and concentrated on rotator evaporator. The crude residue was purified by normal phase silica gel chromatography eluted with the mixture of n-Hex/EtOAc (60:40) to afford the pure desired products.

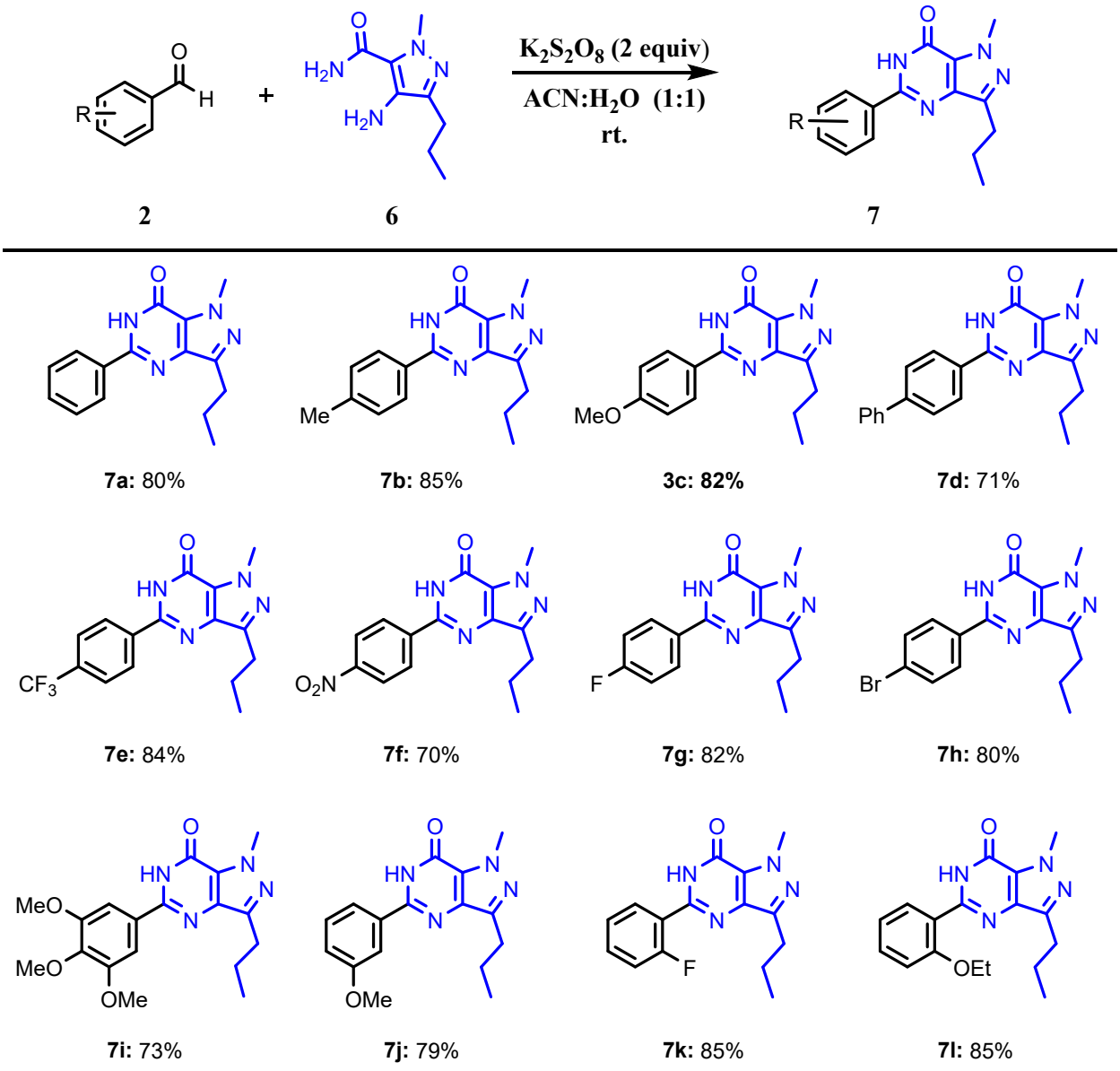
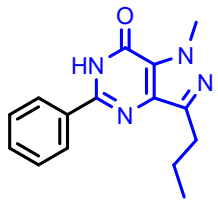


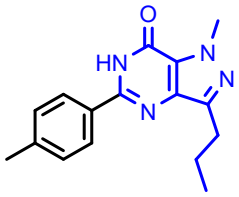
Fig. S8. Synthesis of substituted pyrazolo pyrimidines reaction condition: 0.18 M Substituted benzaldehyde (**2**), (0.18 M 4-amino-2-methyl-5-propyl-2Hpyrazole-3-carboxylic acid amide (**6**)), $K_2S_2O_8$ (0.36 M) and solvent ACN: H_2O (1:1, 6 mL), time 6 -12 h at room temperature Yields are based on isolated yield.

1-Methyl-5-phenyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7a):

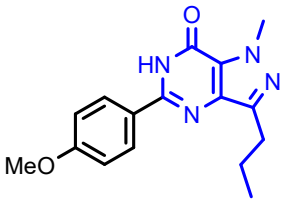


Starting material **7a** was prepared according to general procedure mentioned in section **6.1.** The crude material was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 80% yield of **7a** as a white solid and melting point is 221-223 °C. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 11.06 (s, 1H), 8.15 – 8.10 (m, 2H), 7.53 (d, J = 1.8 Hz, 3H), 4.29 (s, 3H), 2.96 – 2.92 (m, 2H), 1.87 (dt, J = 14.8, 7.4 Hz, 2H), 1.04 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 155.60, 149.45, 146.88, 139.24, 132.91, 131.02, 128.90, 127.07, 124.39, 38.16, 27.74, 22.36, 14.03. **IR (V_{max}):** 3022, 1531, 1215, 741, 670 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{16}N_4O$ $[M+H]^+$: 269.1402 found: 269.1399. Verified the analytical data with those reported in the literature.[4, 13]

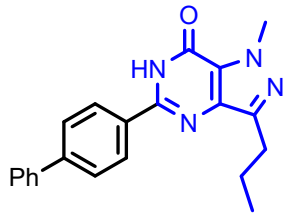
1-Methyl-3-propyl-5-(p-tolyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7b):



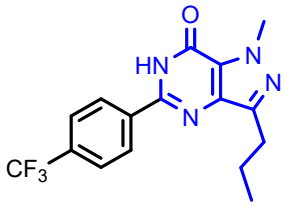
Starting material **7b** was prepared according to general procedure mentioned in section **6.1.** The crude material was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 85 % yield **7b** as a white solid and melting point is 239–242 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 10.85 (s, 1H), 8.01 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 4.29 (s, 3H), 2.97 – 2.89 (m, 2H), 2.44 (s, 3H), 1.87 (dd, J = 15.1, 7.5 Hz, 2H), 1.03 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 155.58, 149.48, 146.75, 141.44, 139.31, 130.09, 129.60, 126.92, 124.34, 38.17, 27.73, 22.36, 21.45, 14.04. **IR (V_{max}):** 3032, 1215,742, 670 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{18}N_4O$ $[M+H]^+$: 283.1559 found: 283.15542. Verified the analytical data with those reported in the literature.[13, 14]



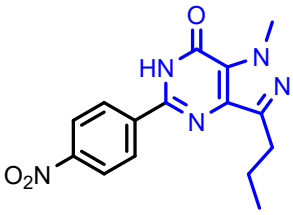
5-(4-Methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7c): Starting material **7c** was prepared according to general procedure mentioned in section **6.1.** The crude material was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 82% yield **7c** as a white solid and melting point is 247–249 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.11 (s, 1H), 8.15 – 8.06 (m, 2H), 7.07 – 6.96 (m, 2H), 4.28 (s, 3H), 3.89 (s, 3H), 2.97 – 2.89 (m, 2H), 1.87 (dd, J = 15.1, 7.5 Hz, 2H), 1.03 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 161.88, 155.74, 149.31, 146.59, 139.41, 128.67, 125.35, 124.15, 114.19, 55.47, 38.13, 27.74, 22.35, 14.04. **IR (V_{max}):** 3024, 2366, 1676, 1215, 1019, 743, 670 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{18}N_4O_2$ $[M+H]^+$: 299.1505 found: 299.1503. Verified the analytical data with those reported in the literature.[13, 14]



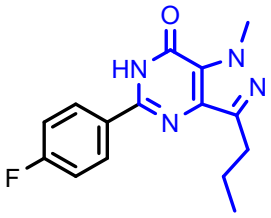
5-([1,1'-Biphenyl]-4-yl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7d): Starting material **7d** was prepared according to general procedure mentioned in section **6.1.** The crude material was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 71% yield **7c** as a white solid and melting point is 209-210 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 10.93 (s, 1H), 8.59 (s, 1H), 8.19 (d, J = 7.1 Hz, 2H), 7.88 (d, J = 8.3 Hz, 1H), 7.73 (dd, J = 8.2, 6.3 Hz, 3H), 7.64 (dd, J = 10.5, 3.2 Hz, 3H), 7.53 – 7.45 (m, 3H), 7.44 – 7.37 (m, 2H), 4.25 (d, J = 36.4 Hz, 5H), 2.99 – 2.92 (m, 2H), 2.79 – 2.72 (m, 1H), 1.94 – 1.72 (m, 3H), 1.04 (dt, J = 9.4, 7.4 Hz, 5H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 161.76, 159.30, 155.32, 149.05, 146.90, 144.58, 143.85, 139.93, 134.83, 131.63, 128.97, 128.77, 128.06, 127.67, 127.61, 127.37, 127.15, 39.2, 28.65. 22.15, 14.05. **IR (V_{max}):** 3021, 3236, 1532, 1215, 742, 670 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{21}H_{20}N_4O$ $[M+H]^+$: 345.1715 found: 345.1708.

1-Methyl-3-propyl-5-(4-(trifluoromethyl)phenyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7e): 

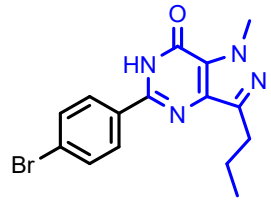
Starting material **7e** was prepared according to general procedure mentioned in section **6.1.** The crude material was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 84% yield **7e** as a white solid and melting point is 244-245 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.58 (s, 1H), 8.31 (d, J = 8.2 Hz, 2H), 7.78 (d, J = 8.3 Hz, 2H), 4.30 (s, 3H), 2.99 – 2.92 (m, 2H), 1.88 (dd, J = 15.0, 7.5 Hz, 2H), 1.04 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 155.78, 147.94, 147.23, 139.13, 136.15, 132.87, 132.54, 127.61, 125.80, 125.76, 124.39, 38.22, 27.72, 22.35, 14.02. **IR (V_{max}):** 3023, 2404, 1714, 1215, 740, 669 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{15}F_3N_4O$ $[M+H]^+$: 337.1276 found: 337.1268.

1-Methyl-5-(4-nitrophenyl)-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7f): 

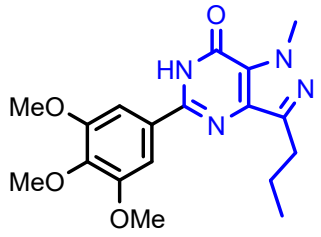
Starting material **7f** was prepared according to general procedure mentioned in section **6.1.** The crude material was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 70% yield **7f** as a yellowish white solid and melting point is 229-231 °C. **^{1}H NMR (500 MHz, DMSO-d_6):** δ 12.71 (s, 1H), 8.33 (q, J = 9.0 Hz, 4H), 4.17 (s, 3H), 2.82 (t, J = 7.5 Hz, 2H), 1.78 (dd, J = 14.9, 7.4 Hz, 2H), 0.96 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, DMSO-d_6):** δ 154.42, 148.48, 148.26, 145.39, 138.62, 137.55, 128.93, 124.54, 123.60, 37.89, 27.13, 21.65, 13.84. **IR (V_{max}):** 3023, 1693, 1520, 1354, 1215, 744, 670 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{15}N_5O_3$ $[M+H]^+$: 314.1250 found: 314.1249. Verified the analytical data with those reported in the literature.[14]



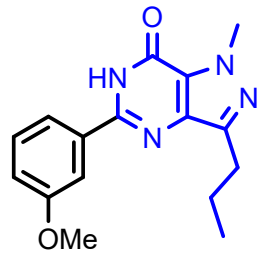
5-(4-Fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7g): Starting material **7g** was prepared according to general procedure mentioned in section **6.1.** The crude material was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 82% yield **7g** as a white solid and melting point is 206-208 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 11.06 (s, 1H), 8.14 (dd, J = 8.7, 5.2 Hz, 2H), 7.21 (t, J = 8.5 Hz, 2H), 4.29 (s, 3H), 2.93 (t, J = 7.6 Hz, 2H), 1.87 (dd, J = 15.0, 7.4 Hz, 2H), 1.03 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 155.60, 148.49, 146.88, 145.48, 139.20, 129.32, 129.24, 129.13, 124.22, 116.13, 115.91, 38.20, 27.72, 22.36, 14.03. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -108.88 (s). **IR (V_{max}):** 2930, 1689, 1497, 1219, 836, 743, 672 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{15}FN_4O$ $[M+H]^+$: 287.1305 found: 287.1304. Verified the analytical data with those reported in the literature.[4]



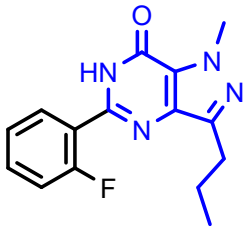
5-(4-Bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7h): Starting material **7h** was prepared according to general procedure mentioned in section **6.1.** The crude material was oncentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 80% yield **7h** as a white solid and melting point is 246-248 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.24 (s, 1H), 8.09 – 8.01 (m, 2H), 7.68 – 7.63 (m, 2H), 4.29 (s, 3H), 2.96 – 2.91 (m, 2H), 1.87 (dd, J = 15.1, 7.5 Hz, 2H), 1.03 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 155.58, 148.36, 146.99, 139.15, 132.11, 131.75, 128.57, 125.74, 124.29, 38.25, 27.71, 22.34, 14.03. **IR (V_{max}):** 2974, 2361, 1214, 739, 666, 568 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{15}BrN_4O$ $[M+H]^+$: 347.0501 found: 347.0502. Verified the analytical data with those reported in the literature.[4]



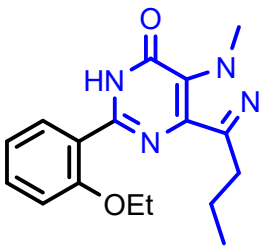
1-Methyl-3-propyl-5-(3,4,5-trimethoxyphenyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7i): Starting material **7i** was prepared according to general procedure mentioned in section **6.1.** The crude material was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 60:40), 73% yield **7i** as a white solid and melting point is 204-206 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 10.66 (s, 1H), 7.26 (s, 2H), 4.25 (s, 3H), 3.99 (s, 6H), 3.92 (s, 3H), 2.96 – 2.91 (m, 2H), 1.87 (dd, *J* = 15.0, 7.5 Hz, 2H), 1.04 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 155.27, 153.63, 149.36, 146.79, 140.78, 139.13, 128.33, 124.24, 104.64, 61.00, 56.48, 38.26, 27.64, 22.33, 14.03. **IR (V_{max}):** 3024, 3266, 1215, 740, 670 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{22}N_4O_4$ $[M+H]^+$: 359.1713 found: 359.1712.



5-(3-Methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7j): Starting material **7j** was prepared according to general procedure mentioned in section **6.1.** The crude material was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 79% yield **7j** as a white solid and melting point is 175-176 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 10.84 (s, 1H), 7.69 – 7.62 (m, 2H), 7.43 (t, J = 8.0 Hz, 1H), 7.09 – 7.03 (m, 1H), 4.29 (s, 3H), 3.91 (s, 3H), 2.96 – 2.91 (m, 2H), 1.87 (dd, J = 15.1, 7.5 Hz, 2H), 1.04 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 160.10, 155.36, 149.20, 146.87, 139.11, 134.27, 130.01, 124.46, 119.12, 116.51, 112.87, 55.48, 38.19, 27.72, 22.36, 14.04. **IR (V_{max}):** 3024, 2366, 1215, 740, 670 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{18}N_4O_2$ $[M+H]^+$: 299.1505 found: 299.1501.



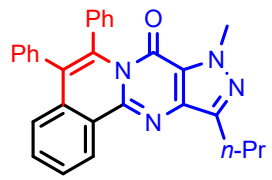
5-(2-Fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7k): Starting material **7k** was prepared according to general procedure mentioned in section **6.1.** The crude material was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 85% yield **7k** as a white solid and melting point is 148-149 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.80 (d, *J* = 8.7 Hz, 1H), 8.30 (td, *J* = 8.0, 1.7 Hz, 1H), 7.55 – 7.47 (m, 1H), 7.37 – 7.31 (m, 1H), 7.22 (dd, *J* = 12.6, 8.3 Hz, 1H), 4.27 (s, 3H), 2.95 – 2.90 (m, 2H), 1.86 (dd, *J* = 15.0, 7.5 Hz, 2H), 1.03 (t, *J* = 7.4 Hz, 3H).**^{13}C NMR (101 MHz, $CDCl_3$):** δ 161.61, 159.15, 153.88, 147.00, 145.66, 138.35, 132.98, 132.89, 131.16, 125.32, 124.52, 116.68, 116.45, 38.32, 27.76, 22.41, 14.06. **^{19}F NMR (376 MHz, $CDCl_3$):** δ -116.07 (s). **IR (V_{max}):** 3023, 2366, 1705, 1215, 741, 669 cm^{-1}. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{15}FN_4O$ $[M+H]^+$: 287.1308, found: 287.13064.



5-(2-Ethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7l): Starting material **7l** was prepared according to general procedure mentioned in section **6.1.** The crude material was purified by silica gel column chromatography (n-Hexane: EtOAc = 70:30), 85% yield **7l** as a white solid and melting point is 122-124 °C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 11.12 (s, 1H), 8.47 (dd, J = 7.9, 1.8 Hz, 1H), 7.45 (ddd, J = 8.5, 7.4, 1.8 Hz, 1H), 7.17 – 7.11 (m, 1H), 7.03 (d, J = 8.4 Hz, 1H), 4.33 – 4.28 (m, 2H), 4.27 (d, J = 2.9 Hz, 3H), 2.96 – 2.91 (m, 2H), 1.88 (dd, J = 15.1, 7.5 Hz, 2H), 1.60 (t, J = 7.0 Hz, 3H), 1.03 (t, J = 7.4 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 156.45, 153.90, 148.35, 146.60, 138.69, 132.35, 131.02, 124.43, 121.82, 120.19, 112.89, 65.26, 38.14, 27.79, 22.36, 14.70, 14.05. **IR (V_{max}):** 3064, 1644, 1552, 1479, 1296, 1239,

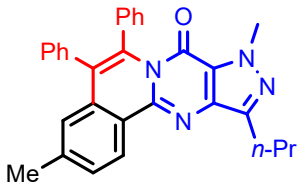
1164, 1033, 761, 702 cm^{-1} **HRMS (ESI):** *m/z* calcd for $C_{17}H_{20}N_4O_2$ $[M+H]^+$: 313.164 found: 313.1655. Verified the analytical data with those reported in the literature[4].

6.2. An integrated continuous photo-flow synthesis of 9-Methyl-5,6-diphenyl-11-propylpyrazolo [4',3':4,5] pyrimido[2,1-a] isoquinolin-8(9H)-one (8aa).



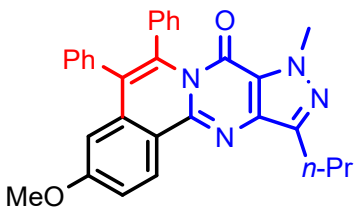
The product **8aa** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1). 82% yield of **8aa** as a white solid and melting point is 217-218 °C, **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.14 – 9.05 (m, 1H), 7.65 – 7.60 (m, 2H), 7.39 – 7.32 (m, 4H), 7.18 (d, J = 7.2 Hz, 1H), 7.13 – 7.03 (m, 6H), 4.32 (s, 3H), 1.47 (dd, J = 9.0, 6.7 Hz, 2H), 1.31 – 1.26 (m, 2H), 0.66 (t, J = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 160.91, 151.85, 141.21, 136.00, 135.79, 134.44, 134.03, 132.57, 131.05, 130.83, 128.75, 128.58, 128.51, 128.32, 128.06, 127.75, 126.74, 126.67, 125.97, 125.58, 77.00, 38.02, 30.37, 21.79, 13.63. **IR (Vmax):** 30.23, 1707, 1215, 742, 672 cm-1. **HRMS (ESI):** m/z calcd for: $C_{29}H_{24}N_4O$ [M+H]+: 445.2027, found: 445.2020.

3,9-Mimethyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8ba): The product **8ba** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 85% yield of **8ba** as a white solid and melting point is 223-224 °C, **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.94 (d, J = 8.3 Hz, 1H), 7.42 (dd, J = 8.3, 1.2 Hz, 1H), 7.26 – 7.24 (m, 3H), 7.10 (dt, J = 6.0, 2.2 Hz, 3H), 7.06 – 7.01 (m, 4H), 6.91 (s, 1H), 4.12 (s, 3H), 3.07 – 3.02 (m, 2H), 2.36 (s, 3H), 1.97 (dd, J = 15.0, 7.5 Hz, 2H), 1.10 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 153.68, 146.32, 145.64, 141.63, 137.41, 136.48, 135.77, 135.39, 133.05, 131.09, 129.72, 128.34, 128.07, 127.90, 127.04, 126.66, 126.61, 126.02, 125.71, 123.60,

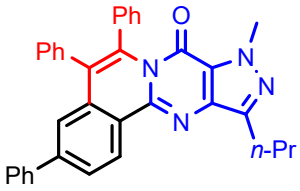


38.26, 27.90, 22.46, 21.84, 14.16. **IR (V_{max}):** 3022, 1705, 1215, 741, 670, cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{30}H_{26}N_4O$ $[M+H]^+$: 459.2193, found: 459.2197.

3-Methoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8ca): The product **8ca** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 89% yield of **8ca** as a white solid and melting point is 209-210 °C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.99 (d, J = 9.0 Hz, 1H), 7.26 – 7.22 (m, 3H), 7.17 (dd, J = 9.0, 2.6 Hz, 1H), 7.13 – 7.09 (m, 3H), 7.07 – 7.01 (m, 4H), 6.54 (d, J = 2.5 Hz, 1H), 4.12 (s, 3H), 3.71 (s, 3H), 3.06 – 3.00 (m, 2H), 1.96 (dd, J = 15.0, 7.5 Hz, 2H), 1.09 (t, J = 7.4 Hz, 3H).. **^{13}C NMR (101 MHz, $CDCl_3$):** δ 161.89, 153.70, 146.29, 145.46, 137.40, 136.63, 136.00, 135.71, 134.92, 130.99, 128.76, 128.30, 127.98, 127.17, 127.06, 126.67, 123.36, 121.57, 116.36, 108.78, 55.30, 38.26, 27.91, 22.46, 14.16. **IR (V_{max}):** 3022, 1706, 1216, 741, 671 cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{30}H_{26}N_4O_2$ $[M+H]^+$: 475.2142, found: 475.2143.

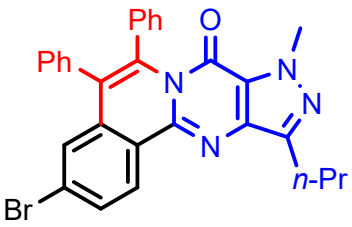


9-Methyl-3,5,6-triphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8da): The product **8da** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 77% yield of **8da** as a white solid and melting point is 265-266 °C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.11 (d, J = 8.4 Hz, 1H), 7.84 (dd, J = 8.5, 1.8 Hz, 1H), 7.49 (dd, J = 5.3, 3.3 Hz, 2H), 7.43 – 7.33 (m, 4H), 7.25 (dd, J = 4.3, 2.8 Hz, 3H), 7.14 – 7.05 (m, 7H), 4.14 (s, 3H), 3.09 – 3.04 (m, 2H), 2.05 – 1.96 (m, 2H), 1.11 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 153.62, 146.06, 145.81, 143.78, 140.03, 137.31, 137.25, 136.46, 136.38, 135.78, 135.54, 133.49,

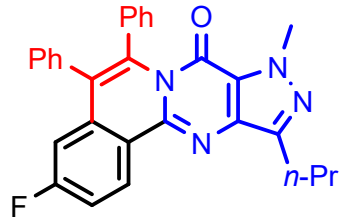


131.06, 128.90, 128.35, 128.18, 128.02, 127.26, 127.26, 127.09, 127.03, 126.72, 124.33, 123.68, 38.30, 27.93, 22.49, 14.17. **IR (V_{max}):** 3022, 1705, 1215, 741, 670 cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{35}H_{28}N_2O$ $[M+H]^+$: 521.2341, found: 521.2342.

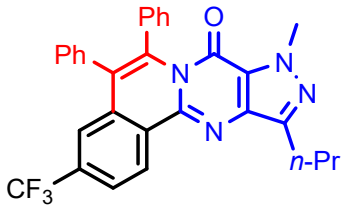
3-Bromo-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8ea): The product **(8ea)** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 83% yield of **8ea** as a white solid and melting point is 161-162 °C, **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.90 (d, J = 8.7 Hz, 1H), 7.69 (dd, J = 8.7, 2.0 Hz, 1H), 7.27 (d, J = 2.1 Hz, 2H), 7.26 (s, 2H), 7.13 – 7.10 (m, 3H), 7.05 – 7.01 (m, 4H), 4.12 (s, 3H), 3.05 – 3.01 (m, 2H), 1.96 (dd, J = 15.0, 7.5 Hz, 2H), 1.09 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 153.44, 145.89, 145.57, 136.93, 136.74, 136.19, 134.87, 134.60, 131.48, 130.97, 128.56, 128.46, 128.24, 128.19, 127.48, 127.15, 126.92, 126.87, 126.15, 123.66, 38.31, 27.86, 22.47, 14.14. **IR (V_{max}):** 3021, 1215, 741, 671. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{29}H_{23}BrN_4O$ $[M+H]^+$: 523.1130, found: 523.1129.



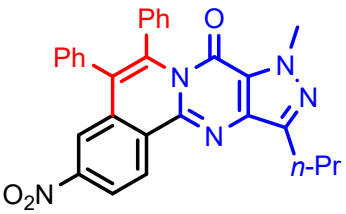
3-Fluoro-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8fa): The product **8fa** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 74% yield of **8fa** as a white solid and melting point is 210-211 °C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.07 (dd, J = 9.0, 5.8 Hz, 1H), 7.32 – 7.25 (m, 5H), 7.14 – 7.10 (m, 3H), 7.07 – 7.01 (m, 4H), 6.79 (dd, J = 10.0, 2.6 Hz, 1H), 4.12 (s, 3H), 3.05 – 3.01 (m, 2H), 1.96 (dd, J = 15.0, 7.5 Hz, 2H), 1.09 (t, J = 7.4 Hz, 3H).



^{13}C NMR (101 MHz, $CDCl_3$): δ 165.75, 163.25, 153.52, 145.67 (d *J* = 17.5 Hz), 137.00, 136.85 (d, *J* = 28.3 Hz), 136.30, 135.52, 135.00, 130.91, 129.66 (d, *J* = 9.2 Hz), 128.20 (d, *J* = 7.0 Hz), 127.76, 126.95, 126.90, 124.46, 123.52, 116.52 (d, *J* = 23.1 Hz), 111.84, 111.60, 38.29, 27.88, 22.47, 14.14. **^{19}F NMR (376 MHz, $CDCl_3$):** δ -107.39 (s). **IR (V_{max}):** 3022, 1215, 741, 671 cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{29}H_{23}FN_4O$ $[M+H]^+$: 463.1930, found: 463.1928.

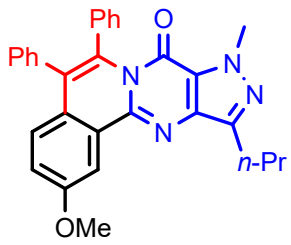


9-Methyl-5,6-diphenyl-11-propyl-3-(trifluoromethyl)pyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8ga): The product **8ga** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 70% yield of **8ga** as a white solid and melting point is 199-200 °C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.17 (d, J = 8.5 Hz, 1H), 7.79 (dd, J = 8.5, 1.4 Hz, 1H), 7.39 (s, 1H), 7.32 – 7.26 (m, 3H), 7.16 – 7.11 (m, 3H), 7.09 – 7.01 (m, 4H), 4.14 (s, 3H), 3.09 – 3.03 (m, 2H), 1.96 (dt, J = 14.8, 7.4 Hz, 2H), 1.10 (t, J = 7.4 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 153.34, 146.18, 145.00, 136.89, 136.79, 136.06, 134.64, 133.25, 132.80, 132.54, 130.94, 130.59, 128.26, 127.64, 127.28, 127.20, 127.03, 124.35, 123.84, 123.12, 123.08, 38.34, 27.87, 22.47, 14.13. **^{19}F NMR (376 MHz, $CDCl_3$):** δ -62.85 (s). **IR (V_{max}):** 2956, 1712, 1548, 1491, 1435, 1319, 1258, 1140, 768, 704. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{30}H_{23}F_3N_4O$ $[M+H]^+$: 513.1910, found: 513.1913.



9-Methyl-3-nitro-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8 (9H)-one (8ha): The product **8ha** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc

= 4:1), 75% yield of **8ha** as a yellowish white solid and melting point is 233-234 °C, **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.20 (d, J = 8.9 Hz, 1H), 8.35 (dd, J = 8.9, 2.3 Hz, 1H), 7.99 (d, J = 2.2 Hz, 1H), 7.32 – 7.29 (m, 3H), 7.17 – 7.12 (m, 3H), 7.08 – 7.03 (m, 4H), 4.14 (s, 3H), 3.08 – 3.04 (m, 2H), 1.97 (dd, J = 15.0, 7.5 Hz, 2H), 1.10 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 153.14, 149.26, 146.49, 144.44, 137.76, 136.45, 135.97, 134.20, 133.89, 132.48, 130.87, 128.48, 128.19, 127.92, 127.28, 127.24, 126.92, 123.85, 122.09, 121.34, 38.37, 27.85, 22.47, 14.12. **IR (V_{max}):** 3023, 1709, 1345, 1216, 742, 672. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{29}H_{23}N_5O_3$ $[M+H]^+$: 490.1885, found: 490.1888.

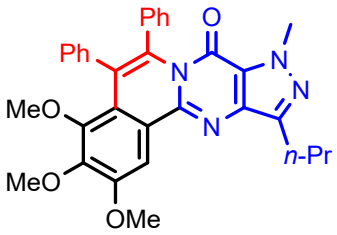


2-methoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8ia): The product **8ia** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 68% yield of **8ia** as a white solid and melting point is 190-191°C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.85 (s, 1H), 7.33 (dd, J = 8.2, 1.5 Hz, 1H), 7.24 (dt, J = 4.8, 2.2 Hz, 3H), 7.12 – 7.08 (m, 3H), 7.04 (dt, J = 3.9, 1.6 Hz, 5H), 4.13 (s, 3H), 3.09 – 3.03 (m, 2H), 2.57 (s, 3H), 1.98 (dd, J = 15.0, 7.5 Hz, 2H), 1.11 (t, J = 7.4 Hz, 3H).). **^{13}C NMR (126 MHz, $CDCl_3$):** 13C NMR (126 MHz, CDCl3) δ 159.61, 153.72, 145.89, 145.76, 137.43, 136.33, 135.97, 133.22, 131.06, 129.52, 129.08, 128.47, 127.96, 127.13, 127.09, 126.87, 126.60, 123.76, 120.08, 108.28, 55.72, 38.32, 27.92, 22.48, 14.21. **IR (V_{max}):** 2934, 1705, 1489, 1217, 1028 cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{30}H_{26}N_4O_2$ $[M+H]^+$: 475.2132, found: 475.2130.

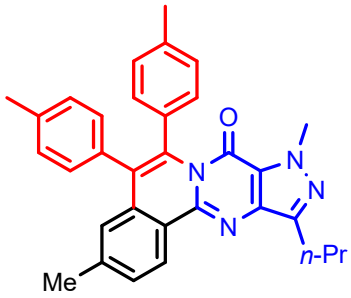
1-Fluoro-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8ja): The product **8ja** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 65% yield of **8ja** as a white solid and melting point is 197-198 °C, **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.43 (td, J = 8.1, 4.7 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.26 – 7.24 (m, 3H), 7.16 – 7.08 (m, 3H), 7.08 – 6.99 (m, 4H), 6.95 (d, J = 8.0 Hz, 1H), 4.12 (s, 3H), 3.07 – 3.01 (m, 2H), 2.03 – 1.95 (m, 2H), 1.09 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 162.21, 160.10, 153.51, 146.42, 143.47, 136.92, 136.31, 136.11, 135.79 (d, J = 15.7 Hz), 131.46 (d, J = 9.8 Hz), 131.08, 128.13 (d, J = 16.9 Hz), 127.86, 127.07, 127.03, 126.90, 123.70, 122.20 (d, J = 3.9 Hz), 116.78, 116.55, 116.43 (d, J = 23.4 Hz), 38.28, 27.96, 22.13, 14.12. **^{19}F NMR (376 MHz, CDCl3):** δ -104.28. **IR (V_{max}):** 3022, 1707, 1215, 741, 670. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{29}H_{23}FN_4O$ $[M+H]^+$: 463.1923, found: 463.1922.

1-Ethoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a] isoquinolin-8 (9H)-one (8ka): The product **8ka** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 63% yield of **8ka** as a white solid and melting point is 147-148 °C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 (t, J = 8.1 Hz, 1H), 7.26 – 7.21 (m, 3H), 7.13 – 7.00 (m, 8H), 6.76 (dd, J = 8.0, 1.0 Hz, 1H), 4.32 (q, J = 6.9 Hz, 2H), 4.11 (s, 3H), 3.07 – 3.02 (m, 2H), 1.98 (dd, J = 15.3, 7.6 Hz, 2H), 1.72 (t, J = 6.9 Hz, 3H), 1.10 (t, J = 7.4 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 158.80, 153.86, 146.29, 145.24, 137.31, 136.37, 136.22, 136.03, 135.65,

131.36, 131.20, 128.25, 128.16, 127.92, 127.11, 126.70, 123.57, 119.05, 117.11, 113.07, 65.49, 38.22, 28.02, 22.61, 15.14, 14.22. **IR (V_{max}):** 3023, 1215, 741, 671. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{31}H_{28}N_4O_2$ $[M+H]^+$: 489.22801, found: 489.22809.

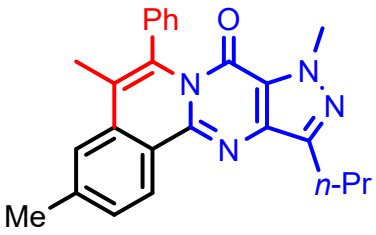


2,3,4-Trimethoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8la): The product **8la** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 68% yield of **8la** as a white solid and melting point is 191-192 °C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.40 (s, 1H), 7.15 – 7.00 (m, 10H), 4.10 (d, J = 7.5 Hz, 6H), 3.86 (s, 3H), 3.06 (s, 3H), 3.03 (d, J = 7.6 Hz, 2H), 1.96 (dt, J = 14.7, 7.4 Hz, 2H), 1.10 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 154.07, 153.46, 150.52, 146.22, 145.85, 145.57, 138.67, 137.13, 136.51, 134.54, 130.91, 128.91, 126.84, 126.65, 126.49, 126.23, 126.08, 125.30, 123.59, 121.91, 103.84, 60.74, 60.21, 56.10, 38.21, 27.85, 22.37, 14.16. **IR (V_{max}):** 3021, 1709, 1478, 1215, 1131, 747, 680. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{32}H_{30}N_4O_4$ $[M+H]^+$: 535.2333, found: 535.2332.

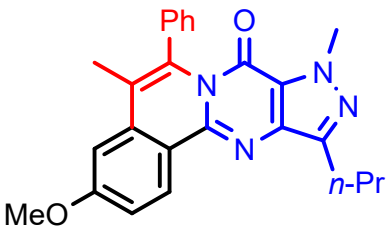


3,9-Dimethyl-11-propyl-5,6-di-p-tolylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8bb): The product **8bb** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 88% yield of **8bb** as a white solid and melting point is 196-197 °C, **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.91 (d, J = 8.3 Hz, 1H), 7.39 (dd, J = 8.3, 1.1 Hz, 1H), 7.07 (d, J = 7.7 Hz, 2H), 6.94 – 6.89 (m, 7H), 4.12 (s, 3H),

3.06 – 3.01 (m, 2H), 2.35 (d, J = 4.1 Hz, 6H), 2.26 (s, 3H), 1.97 (dd, J = 15.0, 7.5 Hz, 2H), 1.10 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 153.83, 146.51, 145.58, 141.51, 136.56, 136.50, 136.07, 135.44, 134.48, 133.39, 132.75, 130.88, 129.53, 128.65, 128.11, 127.96, 127.88, 126.56, 126.05, 125.64, 123.69, 38.25, 27.91, 22.47, 21.84, 21.36, 21.30, 14.17. **IR (V_{max}):** 2942, 1709, 1549, 1497, 831, 763. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{32}H_{30}N_4O$ $[M+H]^+$: 487.2489, found: 487.2488.



3,5,9-Trimethyl-6-phenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8be): The product **8be** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 70% yield of **8be** as a white solid and melting point is 141-142 °C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.90 (d, J = 8.3 Hz, 1H), 7.55 (s, 1H), 7.48 – 7.36 (m, 4H), 7.32 – 7.28 (m, 2H), 4.10 (s, 3H), 3.05 – 2.97 (m, 2H), 2.55 (s, 3H), 2.18 (d, J = 6.5 Hz, 3H), 1.94 (dd, J = 15.0, 7.5 Hz, 2H), 1.08 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 153.52, 146.18, 145.51, 141.69, 138.15, 137.74, 136.38, 134.39, 132.98, 129.52, 128.38, 127.75, 127.23, 126.85, 125.86, 123.91, 120.21, 38.21, 27.88, 22.43, 22.00, 15.24, 14.16. **IR (V_{max}):** 2940, 1705, 1547, 1490, 1217, 755. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{25}H_{24}N_4O$ $[M+H]^+$: 397.2020, found: 397.2019.

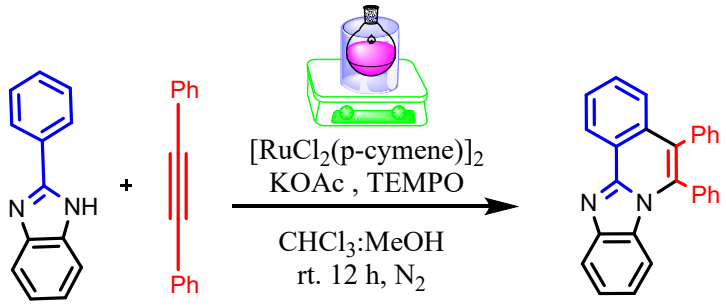


3-Methoxy-5,9-dimethyl-6-phenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one (8ce): The product **8ce** was prepared according to the general procedure as described in section 5. The extracted mixture was concentrated under vacuum and purified by silica gel column chromatography (n-Hexane: EtOAc = 4:1), 71% yield of **8ce** as a

white solid and melting point is 190-191 °C, **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.94 (d, J = 9.0 Hz, 1H), 7.46 – 7.37 (m, 3H), 7.34 – 7.28 (m, 2H), 7.20 (dd, J = 9.0, 2.5 Hz, 1H), 7.14 (d, J = 2.5 Hz, 1H), 4.09 (s, 3H), 3.96 (s, 3H), 3.02 – 2.97 (m, 2H), 2.17 (s, 3H), 1.94 (dd, J = 15.0, 7.5 Hz, 2H), 1.07 (t, J = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 162.11, 153.51, 146.10, 145.30, 138.13, 136.52, 135.06, 134.76, 128.96, 128.32, 127.76, 127.26, 123.41, 121.72, 119.95, 116.14, 106.52, 55.55, 38.19, 27.88, 22.42, 15.33, 14.15. **IR (V_{max}):** 3022, 1215, 741, 671. cm^{-1}. **HRMS (ESI):** *m/z* calcd for: $C_{25}H_{24}N_4O_2$ $[M+H]^+$: 413.1968, found: 413.1966.

7. Mechanistic studies

7.1 Radical scavenger experiments.



3a 4a 5aa: 82%

An oven dried test tube or round bottom flask charged with magnetic stirrer was added **3a:4a:** $[RuCl_2(cymene)]_2$: KOAc: TEMPO: $CHCl_3$: MeOH in molar ratio (1:2:0.05:2:1.5:561:123) under air. The flask was evacuated and purged with under N_2 (approx. 1 atm). The reaction mixture was kept under irradiation of blue light (34 W) at room temperature for 12 hours. The crude residue was purified by normal phase silica gel chromatography eluted with the mixture of n-Hexane: EtOAc = 5:1 to afforded the corresponding 5,6-diphenylbenzo [4,5] imidazo [2,1-a] isoquinoline **(5aa)** in 82 % of yield.

7.2 Deuterium-labelling experiments (Kinetic Isotope Effects).

Step 1. H/D Exchange Experiment.

The stock solution **(A)** containing **3a**:**4a**: $CHCl_3$: MeOH in a molar ratio 1:2:561:123 and the stock solution **(B)** having KOAc: catalyst dissolved in $CHCl_3$: MeOH: D_2O as a molar ratio 1:0.02:249:61:137 was taken in two syringes and connected with designed photo-flow reactor to perform the reaction as described in Fig. S9. The solution was introduced into capillary micro reactor with T-junction and passed through photo-flow reactor (reactor volume 2.5 mL) containing light held at 30 °C with 62.5 min. residence time and the solvent was removed under reduced pressure to give the residue and purified by column chromatography (*n*-hexane: EtOAc = 8:2), yield $[D]_n$-**3a** (65%) as a white solid and $[D]_n$-**5aa** (31%) as a white solid. The D-incorporation was estimated by ^1H NMR spectroscopy.

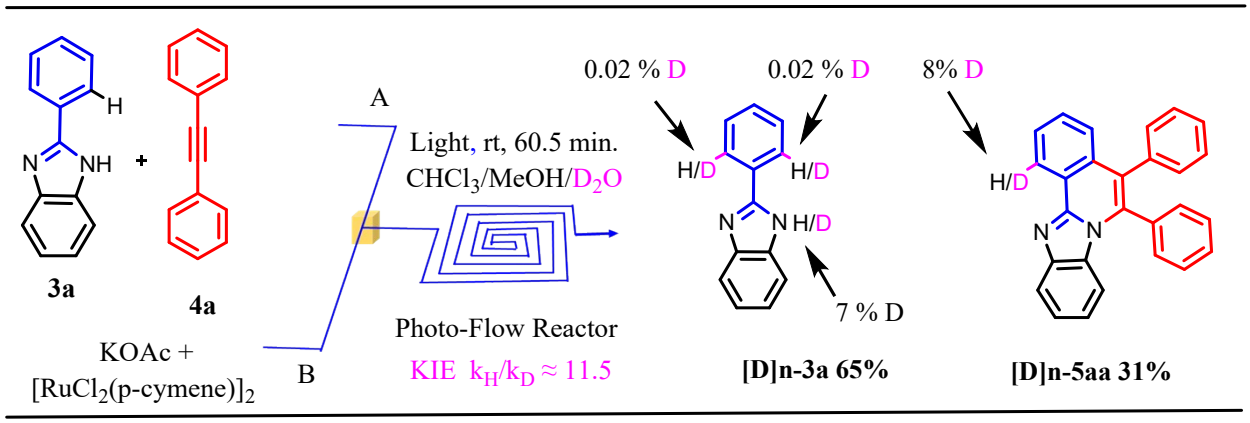


Fig. S9. The synthesis of H/D exchange: The stock solution **(A)** containing **3a**:**4a**: $CHCl_3$: MeOH in a molar ratio 1:2:561:123 and the stock solution **(B)** having KOAc: catalyst dissolved in $CHCl_3$: MeOH: D_2O as a molar ratio 1:0.02:249:61:137. Yields are based on isolated yield.

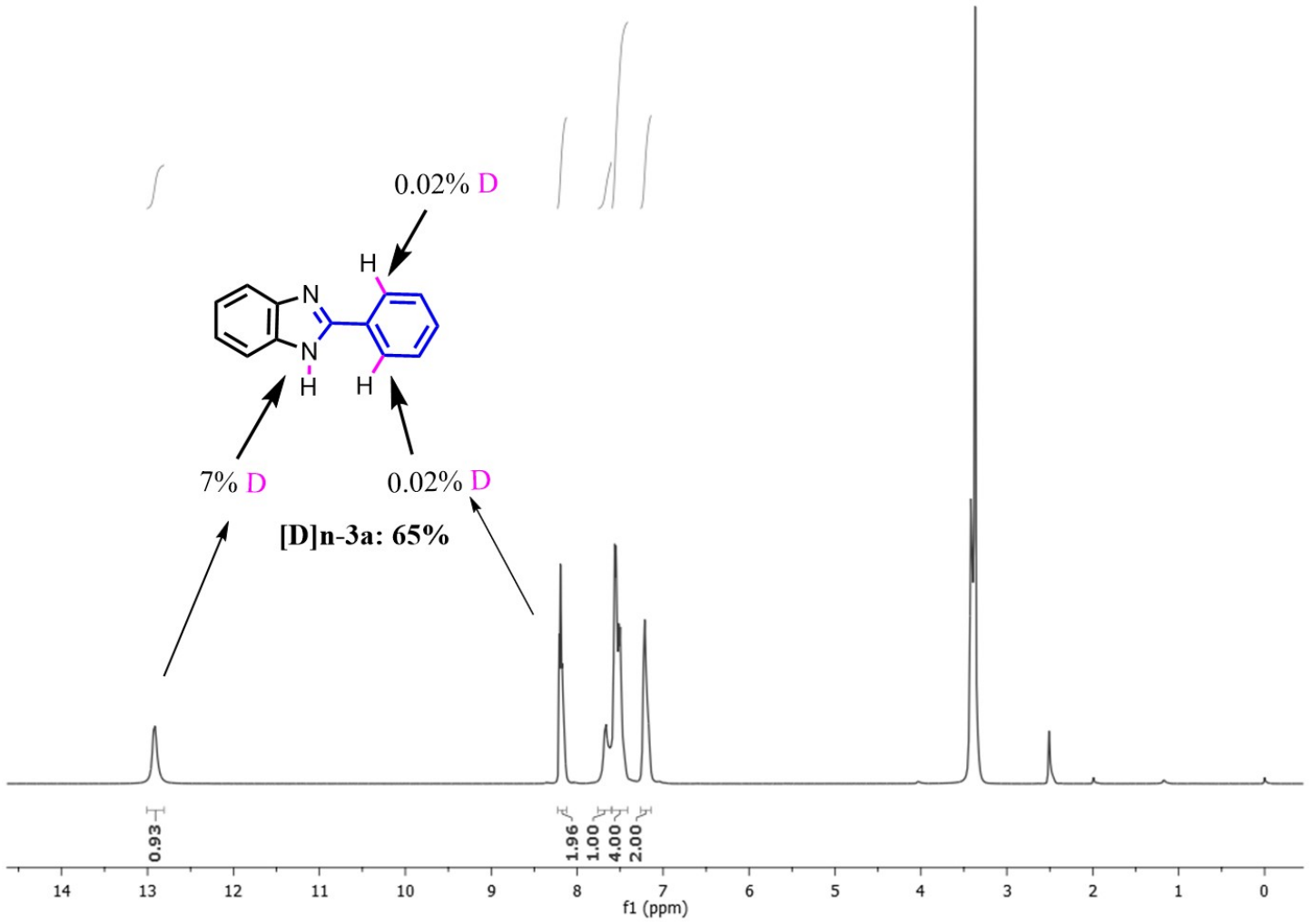


Fig. S10. ^{1}H NMR spectra of 2-(phenyl-2,6-d2)-1H-benzo[d]imidazole-1-d, in $CDCl_3$

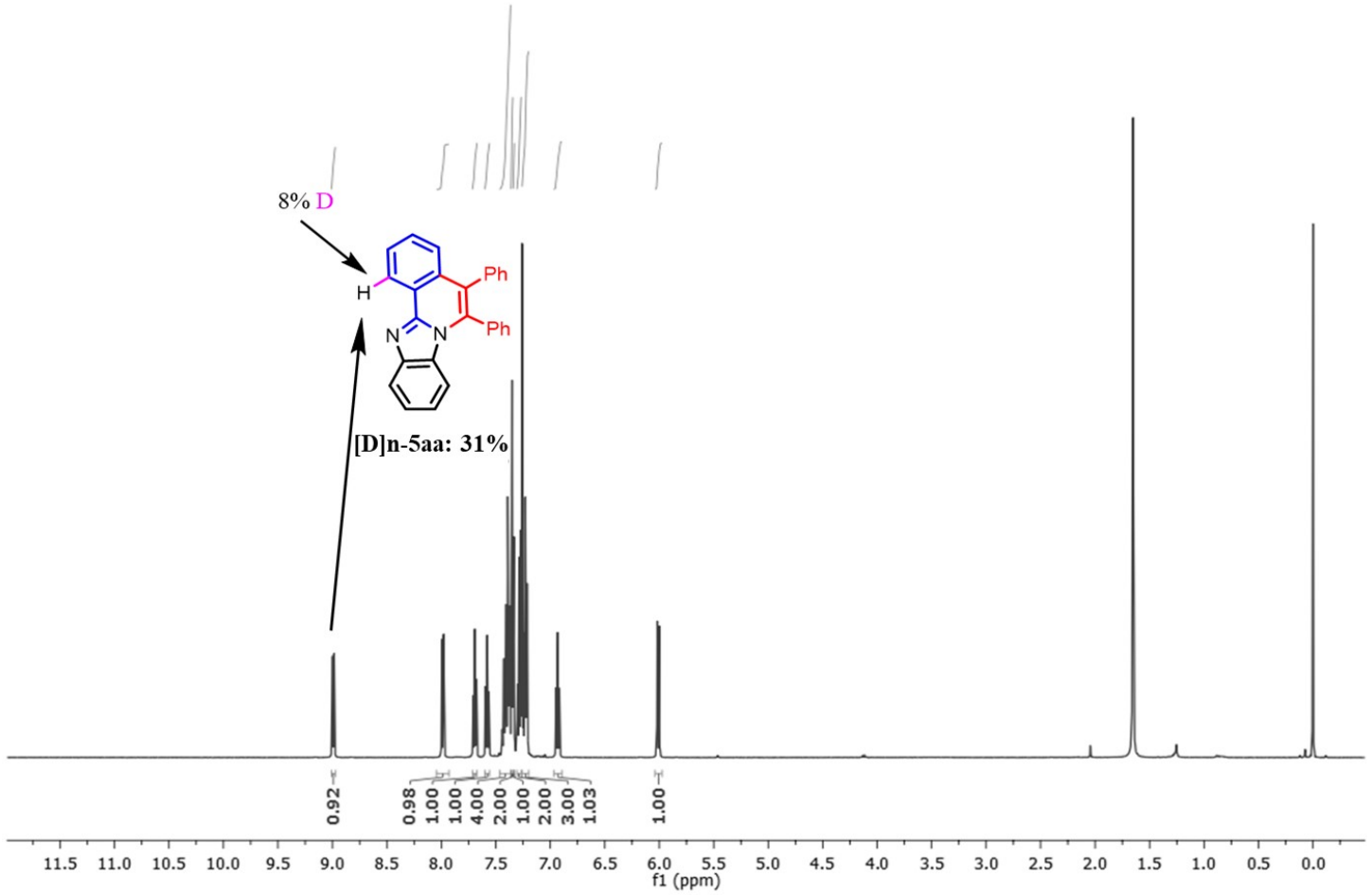
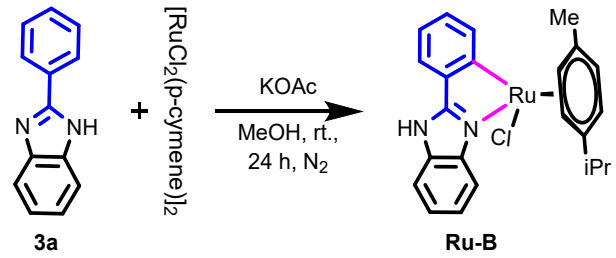


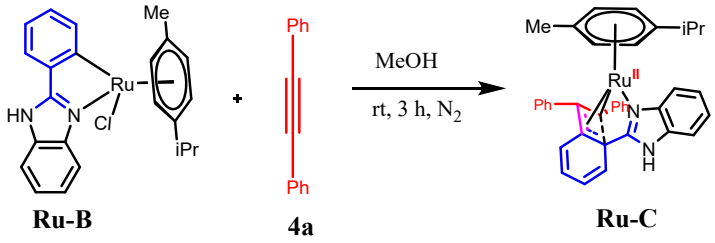
Fig. S11. ^{1}H NMR spectra of 5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinoline-1-d, in $CDCl_3$.

Step 2. Synthesis of key intermediate of Ru-B.



The following key intermediate of Ru-B were synthesized according to previously described methods.[2] A 15 mL Schlenk tube was charged with **3a** (39 mg, 0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (61.5 mg, 0.1 mmol), KOAc (39 mg, 0.40 mmol), and MeOH (20 mL). The mixture was stirred at ambient temperature for 24 h under N_2 and then MeOH was removed in vacuum. After column chromatography on silica gel (CH_2Cl_2: MeOH = 50:1) and crystallization (CH_2Cl_2 and n-hexane), **Ru-B** was isolated as a red solid (83 mg, 89%). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 11.06 (s, 1H), 8.15 (d, *J* = 7.4 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 6.86 – 6.80 (m, 2H), 6.72 (d, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 1H), 6.14 (s, 1H), 5.85 (d, *J* = 5.8 Hz, 1H), 5.72 (d, *J* = 5.7 Hz, 1H), 5.39 (d, *J* = 5.8 Hz, 1H), 5.17 (d, *J* = 5.7 Hz, 1H), 2.2 – 2.14 (m 1H), 2.06 (s, 3H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.68 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 177.4, 159.0, 141.3, 138.6, 133.6, 133.4, 128.8, 123.5, 122.8, 122.6, 121.9, 114.7, 112.9, 100.5, 97.5, 89.5, 88.0, 81.6, 80.2, 30.7, 22.4, 21.7, 18.9. **IR (V_{max}):** 3102, 3052, 2964, 2922, 2859, 1593, 1458, 1378, 1276, 1012, 741, 668 cm^{-1}. **HRMS (ESI)** m/z calcd for $C_{23}H_{22}N_2Ru$ $[M\text{-}Cl]^+$: 429.0905 found: 429.0903. Verified the analytical data with those reported in the literature.[2]

Step 3. Synthesis of second key intermediate Ru-C.



Ru-B **4a** **Ru-C**

The following key intermediate of **Ru-C** were synthesized according to previously described methods.[2] A 15 mL Schlenk tube was charged with **Ru-B** (93.0 mg, 0.20 mmol), **4a** (36.0 mg, 0.20 mmol) and MeOH (20 mL). The mixture was stirred at ambient temperature for 3 h, and then MeOH was removed in vacuum. After column chromatography on silica gel (CH_2Cl_2: MeOH = 50 : 1), **Ru-C** was isolated as yellow solid (117.0 mg, 91%), **^{1}H NMR (700 MHz, CD_3OD):** δ 8.12 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 7.1 Hz, 1H), 7.79 – 7.74 (m, 2H), 7.71 – 7.61 (m, 6H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 7.7 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 2H), 7.1 (t, *J* = 7.1 Hz, 1H), 5.25 (d, *J* = 5.2 Hz, 1H), 4.60 (d, *J* = 5.5 Hz, 1H), 4.29 (d, *J* = 5.0 Hz, 1H), 4.13 (s, 1H), 3.28 (d, *J* = 5.2 Hz, 1H), 2.24 (s, 3H), 1.31 (d, *J* = 6.4 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (176 MHz, CD_3OD):** δ 175.8, 155.7, 143.7, 143.6, 141.3, 135.8, 135.4, 133.9, 133.8, 132.1, 131.9, 131.6, 130.7, 130.0, 129.2, 128.9, 128.4, 128.1, 125.96, 125.4, 119.5, 114.8, 114.0, 109.4, 92.4, 88.9, 84.3, 84.2, 83.4, 32.4, 25.2, 21.7, 18.7. **IR (V_{max}):** 3391, 3058, 3011, 2961, 1595, 1484, 1440, 1379, 1323, 1279, 1220, 866, 757, 699 cm^{-1}. **HRMS (ESI)** *m/z* calcd for $C_{37}H_{32}N_2Ru$ $[M\text{-}Cl]^+$: 607.1687 found: 607.1694. Verified the analytical data with those reported in the literature.[2]

7.3 Continuous flow IR study:

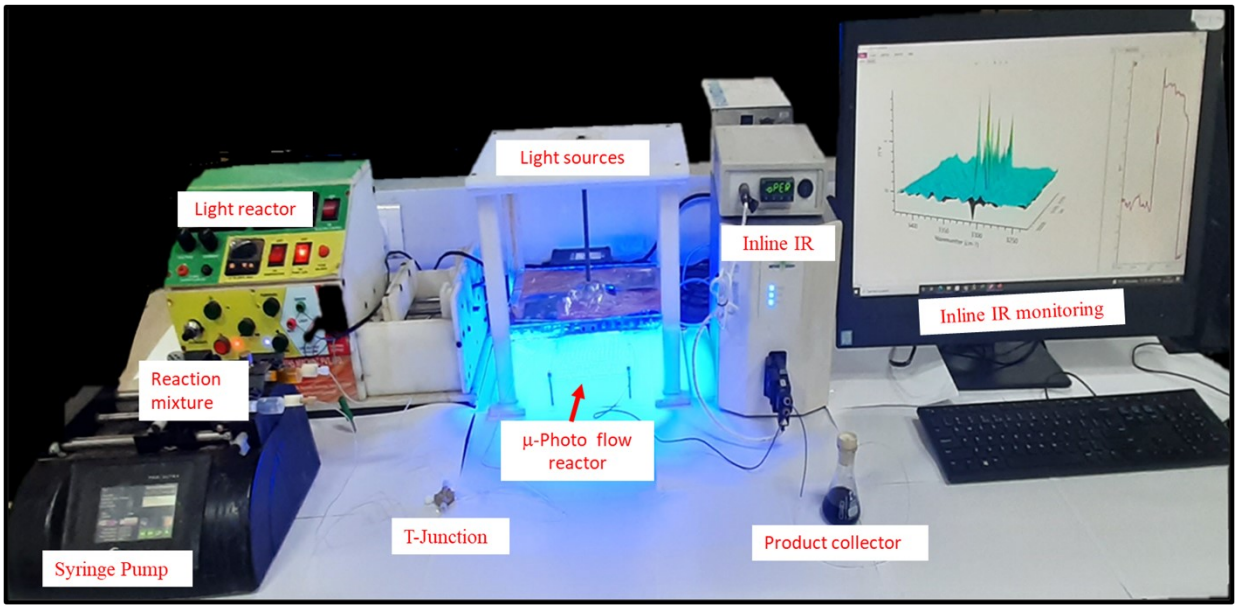


Fig. S12. Snapshot of the basic set up for the inline analysis.

Inline IR absorption spectrum measurement was conducted with React IR™ 15, mettler Toledo 7.1 Instrument, and iC IR 7.1.84.0 software. For below the all experiments, with presence of liquid nitrogen were operating. The Inline-IR were recorded at room temperature in a mixture of chloroform and methanol at a require substrate. All solutions were saturated with N_2 before the measurement and an over-pressure of N_2 was maintained throughout the experiment. The scan rate is 125 in 15 sec. Deviations from the general experimental setup as indicated in the Fig. 13 and descriptions. When we are checking the inline-IR of reaction mixture in absence of light (dark light) that time N-H asymmetric stretching shows 3250 cm^{-1}. Due to the large peak to peak separation, it appears unlikely that these belong to N-H asymmetric stretching. Upon addition of the light (blue LED), then peak 3250 cm^{-1} will be disappeared (Fig. S13).

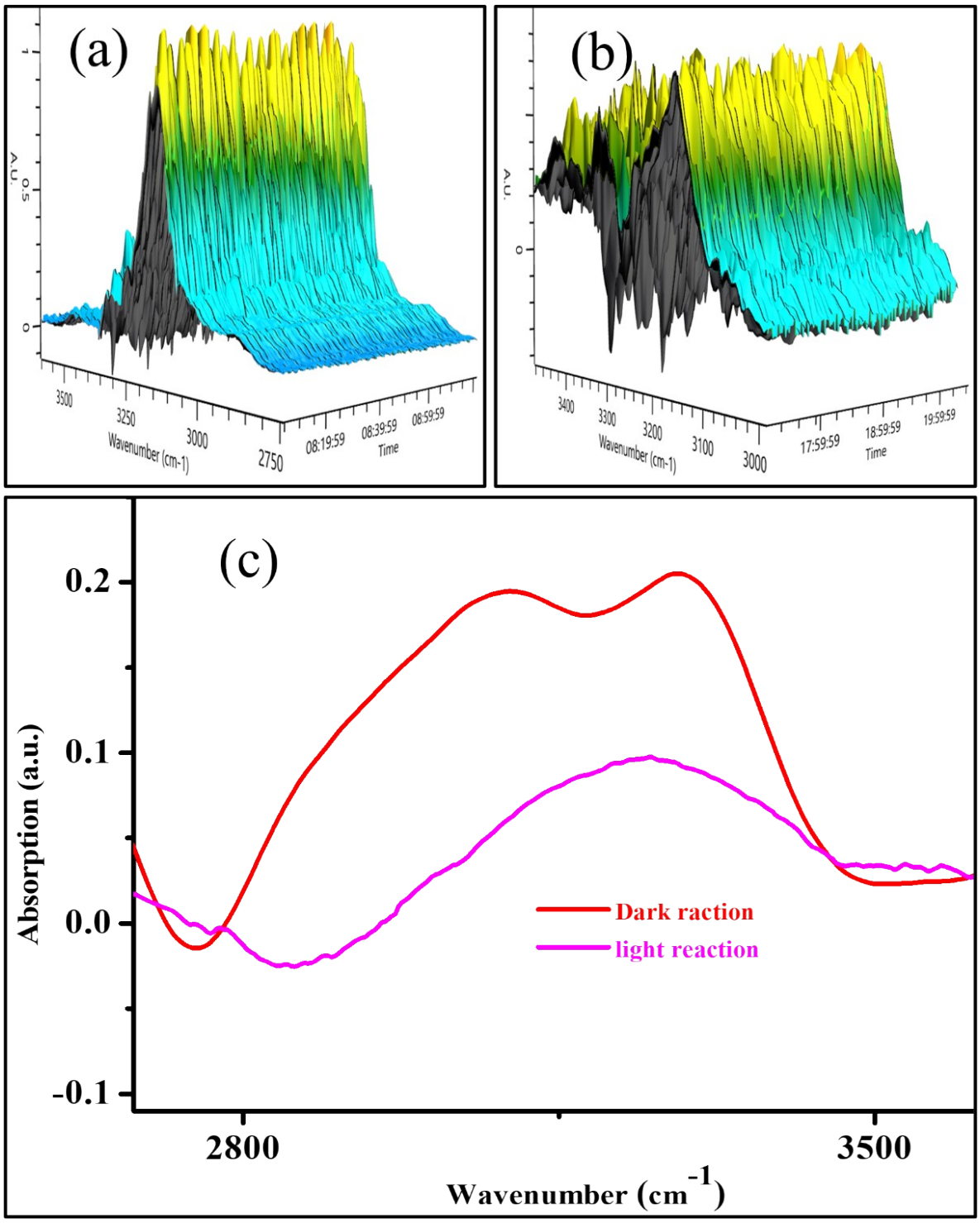
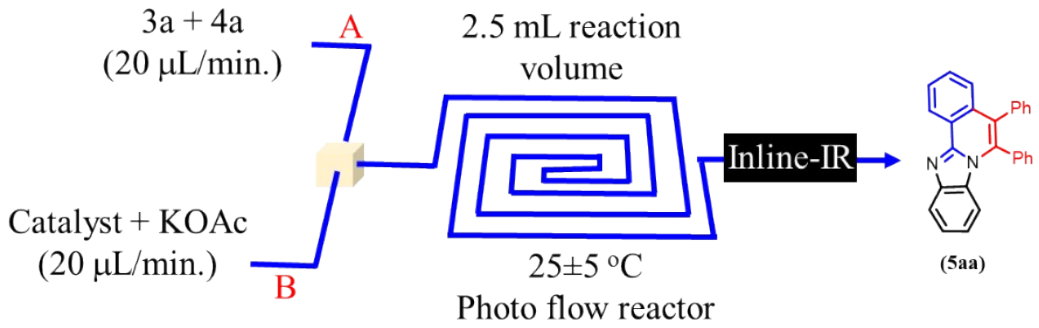


Fig. S13. N-H asymmetric stretching; **(a)** solution flow without light; **(b** solution flow with blue light; **(c)** comparative graph.



The stock solution **(A)** containing 3a:4a: $CHCl_3$: MeOH in molar ratio (1:2:561:123); and the stock solution **(B)** containing KOAc: $[RuCl_2(cymene)]_2$: $CHCl_3$: MeOH in molar ratio (1:02:280:61) were taken in two separate syringes and connected with designed µ-PFR to perform the reaction. Two reactants were introduced into capillary micro-reactor through T- junction (T_1) in a flow rate molar ratio of 1:1 to maintain the stoichiometry and then passed through a µ-PFR (reactor volume 2.5 mL) for the synthesis of annulation product during 62.5 min of residence time. The outlet of µ-PFR solution was achieved by passing through the Inline-IR instrument and analyzed of the corresponding peaks. The screening of Inline-IR of the photo-induced annulation reaction with N-H asymmetric stretching frequency Fig. S14. Thus, we observed the room temperature, The Inline-IR of **3a** (black line) the N-H asymmetric stretching peak of 3250 cm^{-1}. The curve showed an N-H asymmetric stretching peak of the first intermediate (**Ru-B**) (violet line, Fig. S14) and the curve showed the second intermediate (**Ru-C**) (green line, Fig. S14). Furthermore, the photochemical annulation reaction, N-H asymmetric stretching peak analysis of Inline-IR from dark reaction and light reaction shows Fig. S14 (red line and pink line).

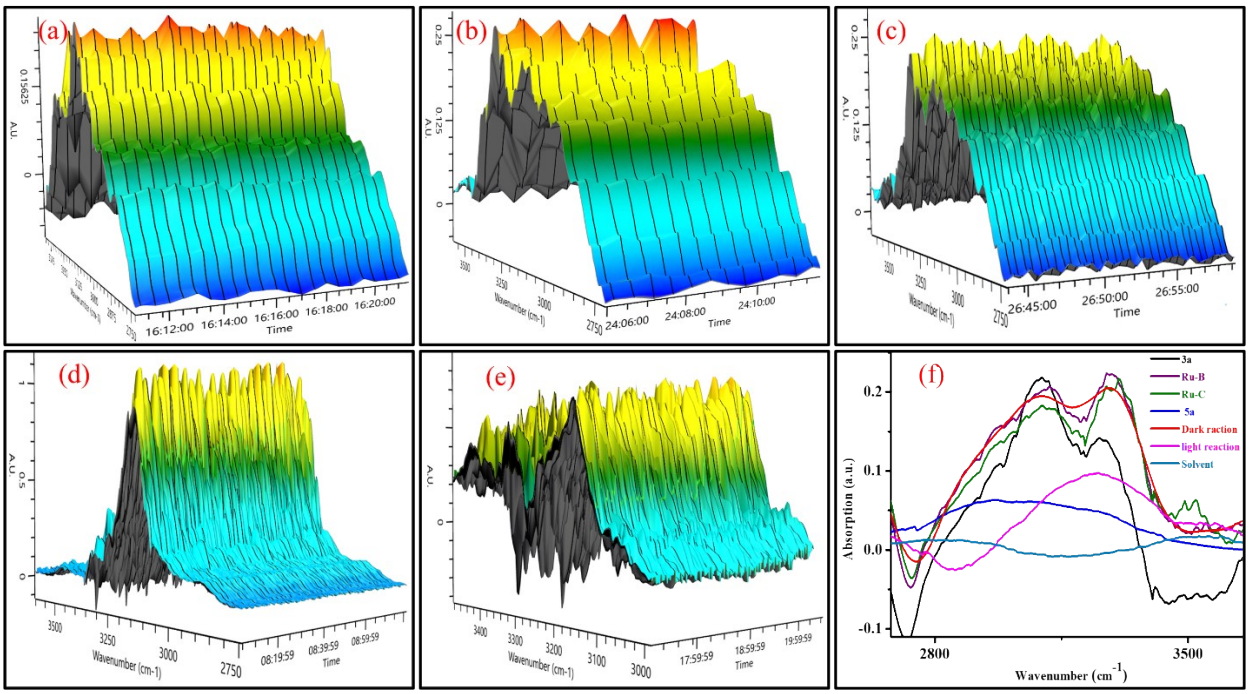


Fig. S14. Back ground of N-H stretching; **(a)** 2-phenylbenzimidazole **3a**; **(b)** 1st intermediate (**Ru-B**); **(c)** 2nd intermediate (**Ru-C**); **(c)** benzoimidazoisoquinolines (**5a**); **(d)** reaction mixture under without light; **(e)** reaction mixture after light exposure; **(f)** comparative data of **3a**, **Ru-B**, **Ru-C**, **5a**, absence of light and presence of light.

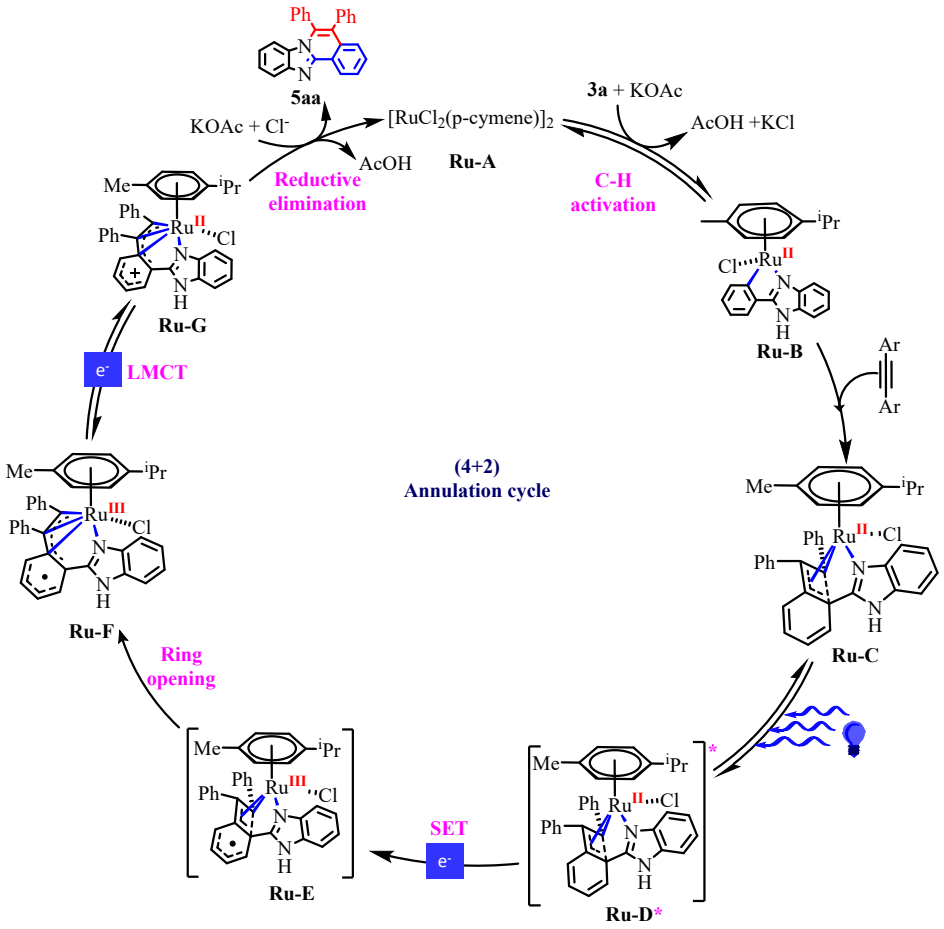


Fig. S15. Proposed mechanism for the photochemical-induced annulation.

7.4 ***Quantum efficiency or Quantum yield (ϕ):***

The values of number of incident photon ($N_{photons}$) were calculated using the following equations. Here,

$$N_{photon} = \frac{P\lambda t}{hc}$$

Area of lamp (a) = 448 cm^2 = 352 x 10^{-4} m^2

$$Power\ of\ the\ light\ (P) = \frac{34J\ s\text{-}1m\text{-}2}{448 \times 10\text{-}2m\text{-}2}$$

Power of the light (P) = 7.5J s^{-1}

λ = Wavelength of the light (420 nm) = 420 x 10^{-9} m

t = Duration of irradiation time, 62.5 min. = 3750s,

h = Planck's constant = 6.626 x 10^{-34} J s

c = Velocity of light = 3 x 10^8 m s^{-1}

No of photons incident per sec

$$N_{photon} = \frac{7.5\ J\ s^{-1} \times 420 \times 10^{-9}\ m \times 3750\ s}{6.626 \times 10^{-34}\ J\ s \times 3 \times 10^{8}\ m\ s^{-1}}$$

$$0.594249 \times 10^{23}$$

$$Number\ of\ moles\ of\ radiation\ energy\ absorbed = \frac{N\ photons}{N}$$

[N = Avogadro's number (6.02214076 × 10^{23})]

$$\frac{0.5942499 \times 1023}{6.02 \times 1023}$$

$= 9.87 \times 10^{-2}$ *moles*

Number of moles of product formed $= 2.3 \times 10^{-5}$ *moles*

$$\textbf{\textit{Quantum efficiency or Quantum yield (}}\phi\textbf{\textit{)}} = \frac{2.3 \times 10\text{-}5}{9.87 \times 10\text{-}2} \times 100$$

$$\phi = 0.023\ \%$$

8. Supporting references.

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9. Spectra

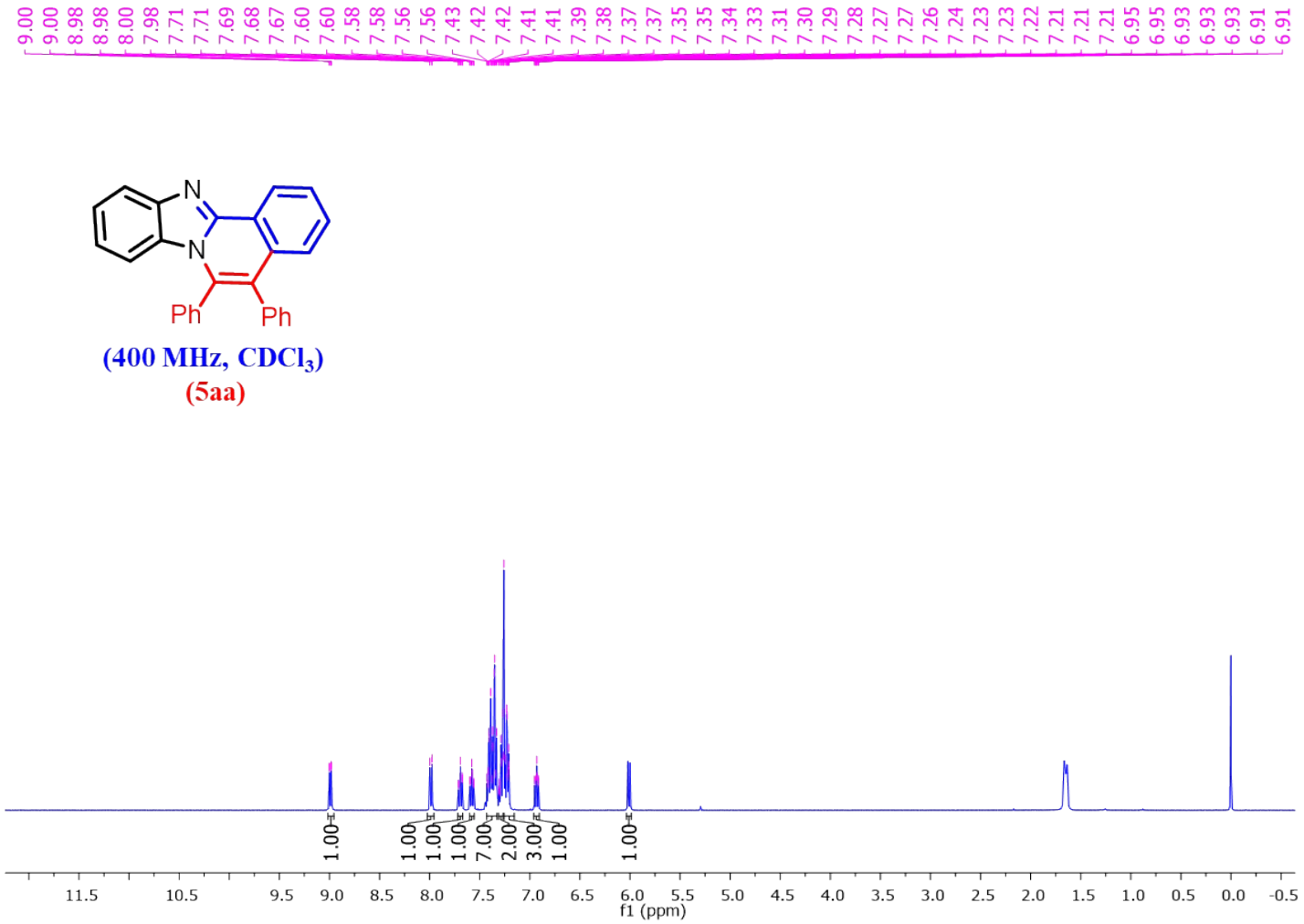


Fig. S16. ^{1}H NMR spectra of 5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5aa**) in $CDCl_3$.

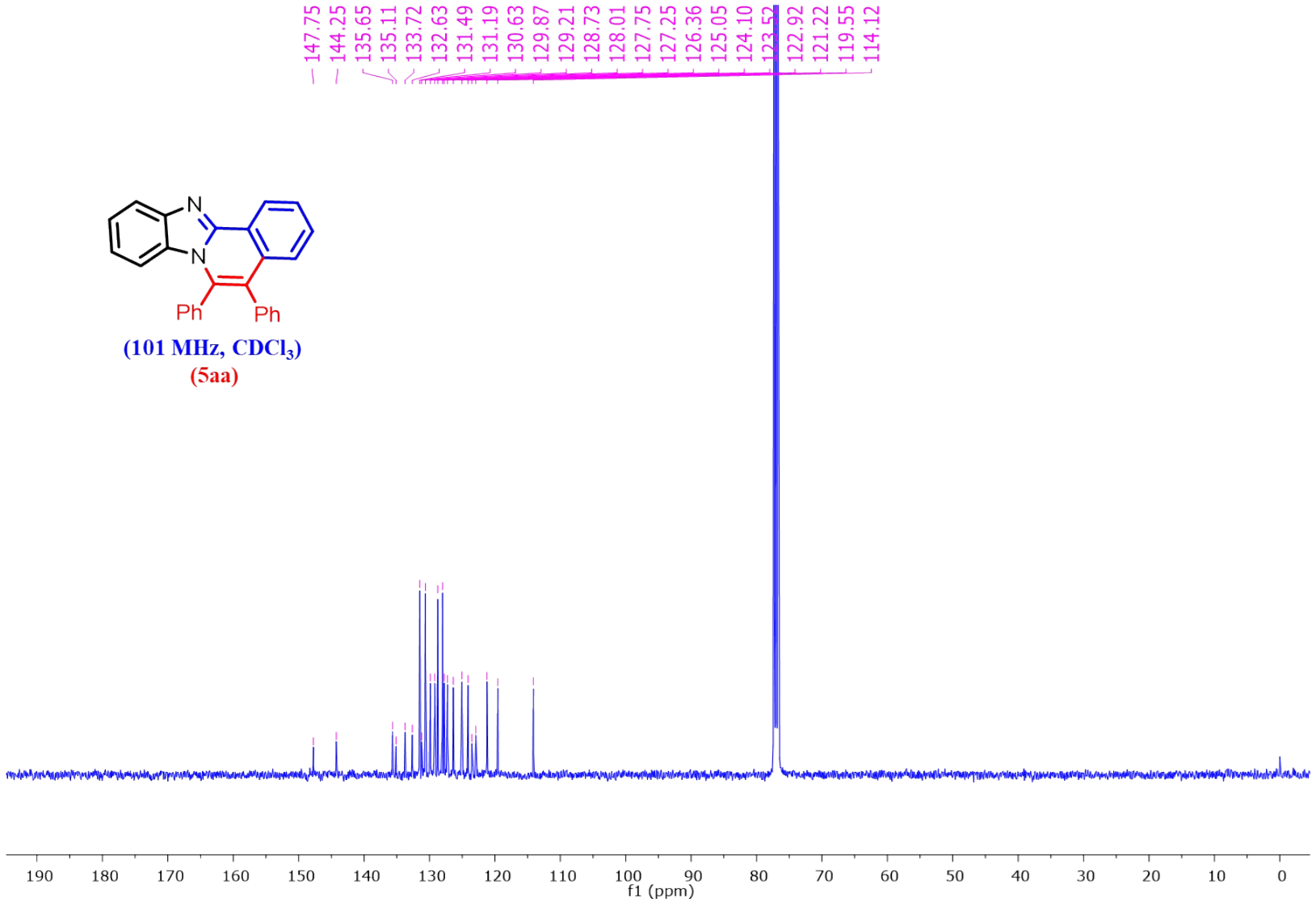


Fig. S17. ^{13}C NMR spectra of 5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5a**) in $CDCl_3$.

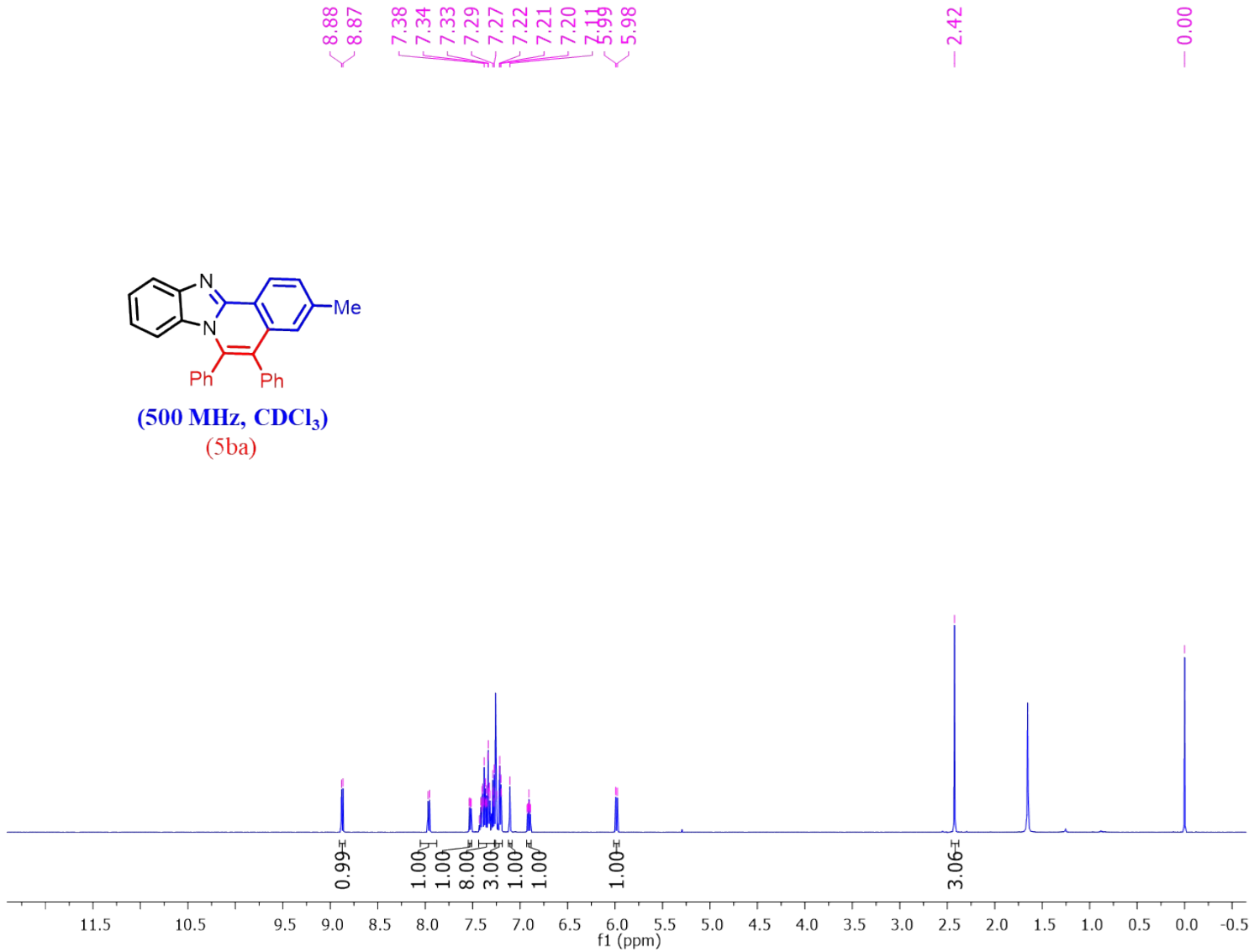


Fig. S18. ^{1}H NMR spectra of 3-methyl-5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5ba**) in $CDCl_3$.

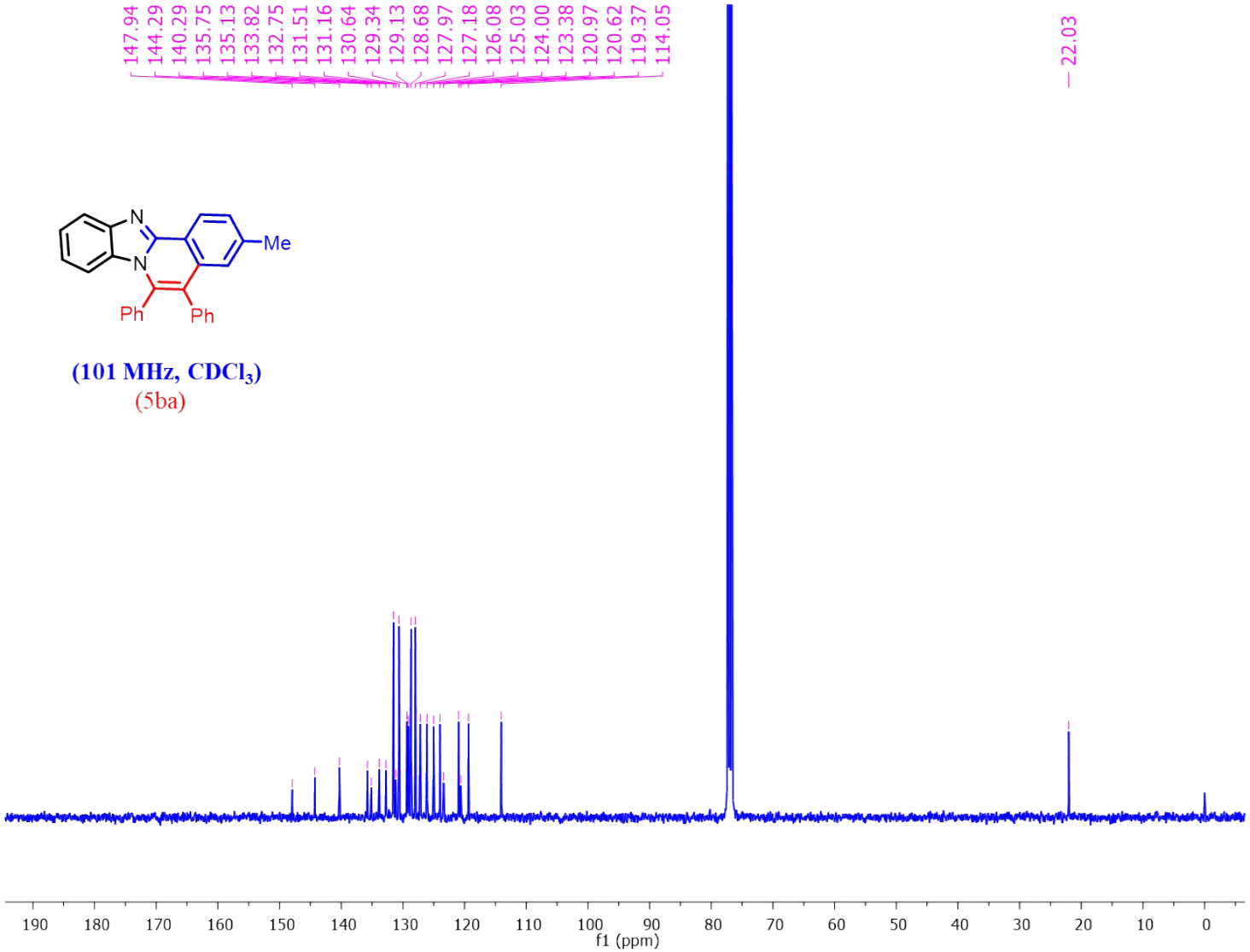


Fig. S19. ^{13}C NMR spectra of 3-methyl-5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5ba**) in $CDCl_3$.

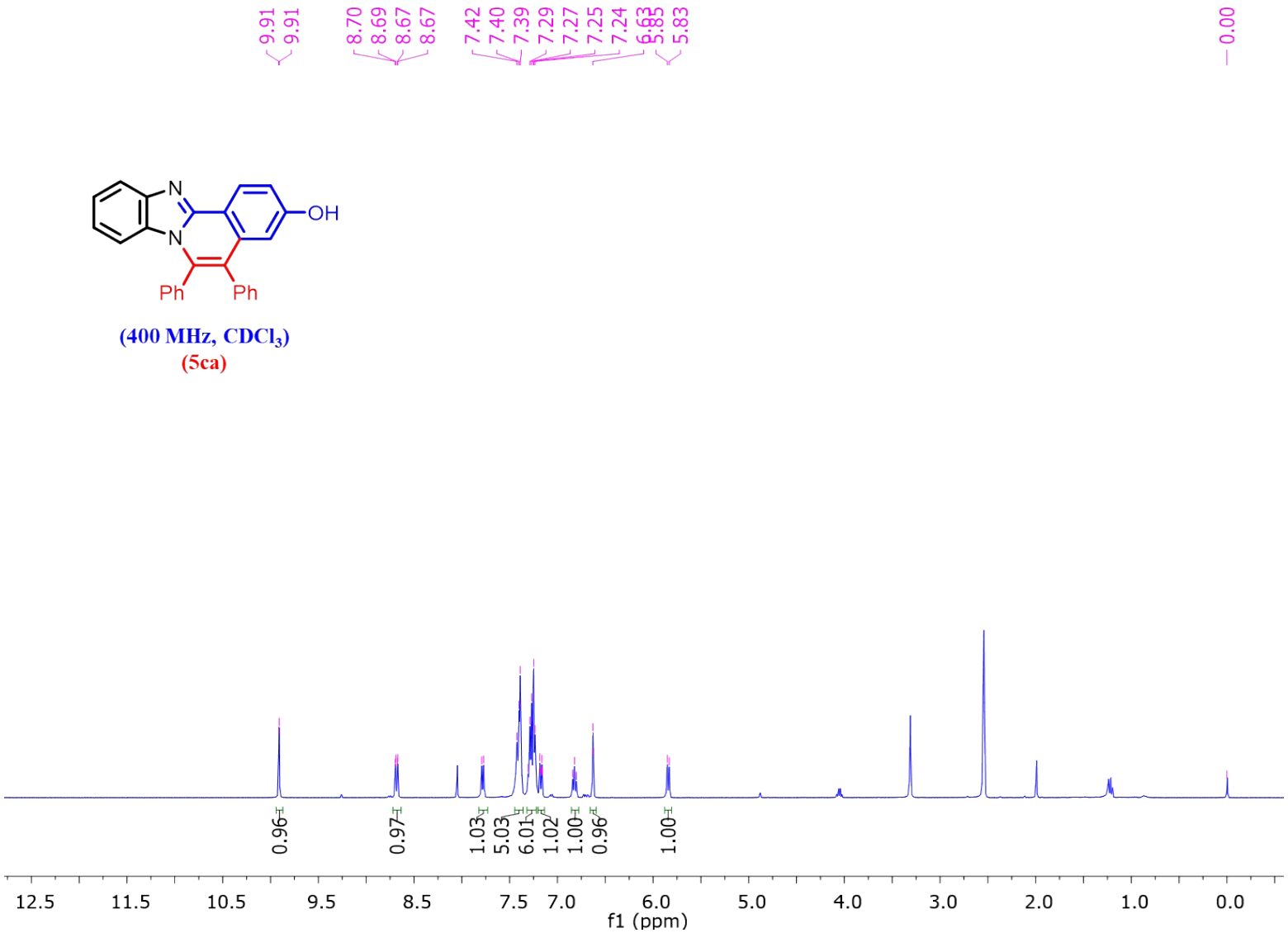


Fig. S20. ^{1}H NMR spectra of 5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinolin-3-ol (**5ca**) in DMSO-d_6.

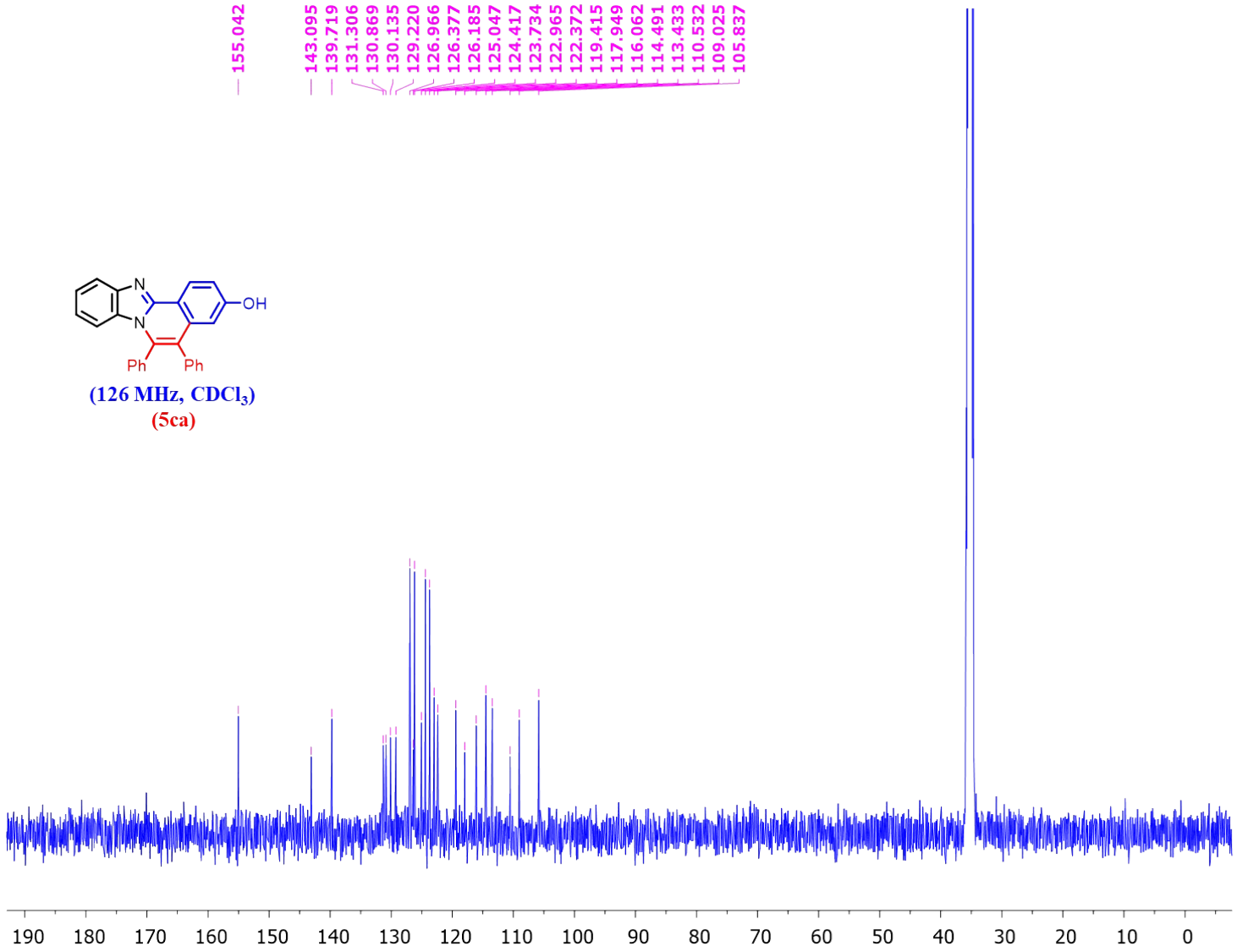


Fig. S21. ^{13}C NMR spectra of 5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinolin-3-ol (**5ca**) in DMSO-d_6.

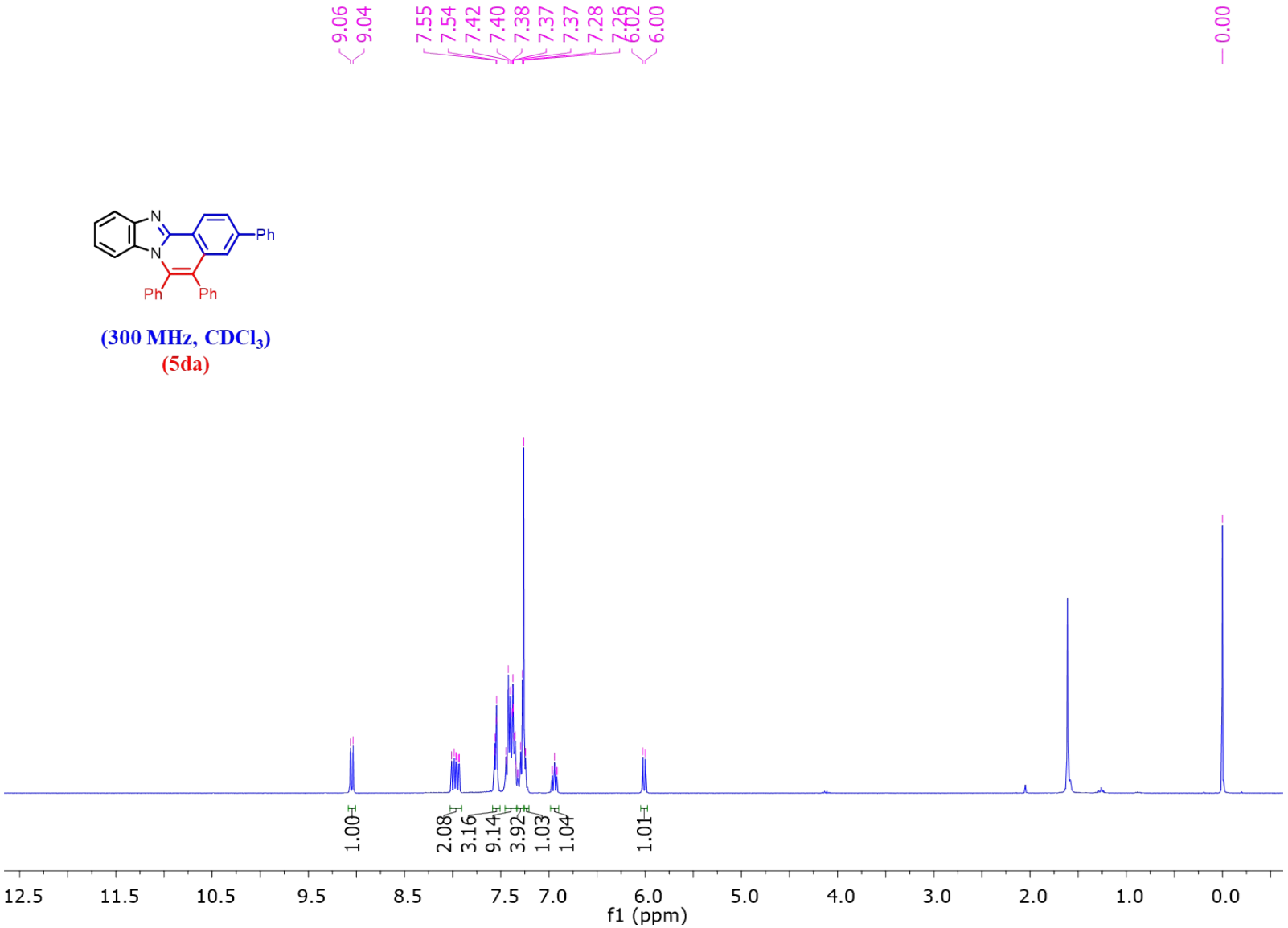


Fig. S22. ^{1}H NMR spectra of 3,5,6-triphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5da**) in $CDCl_3$.

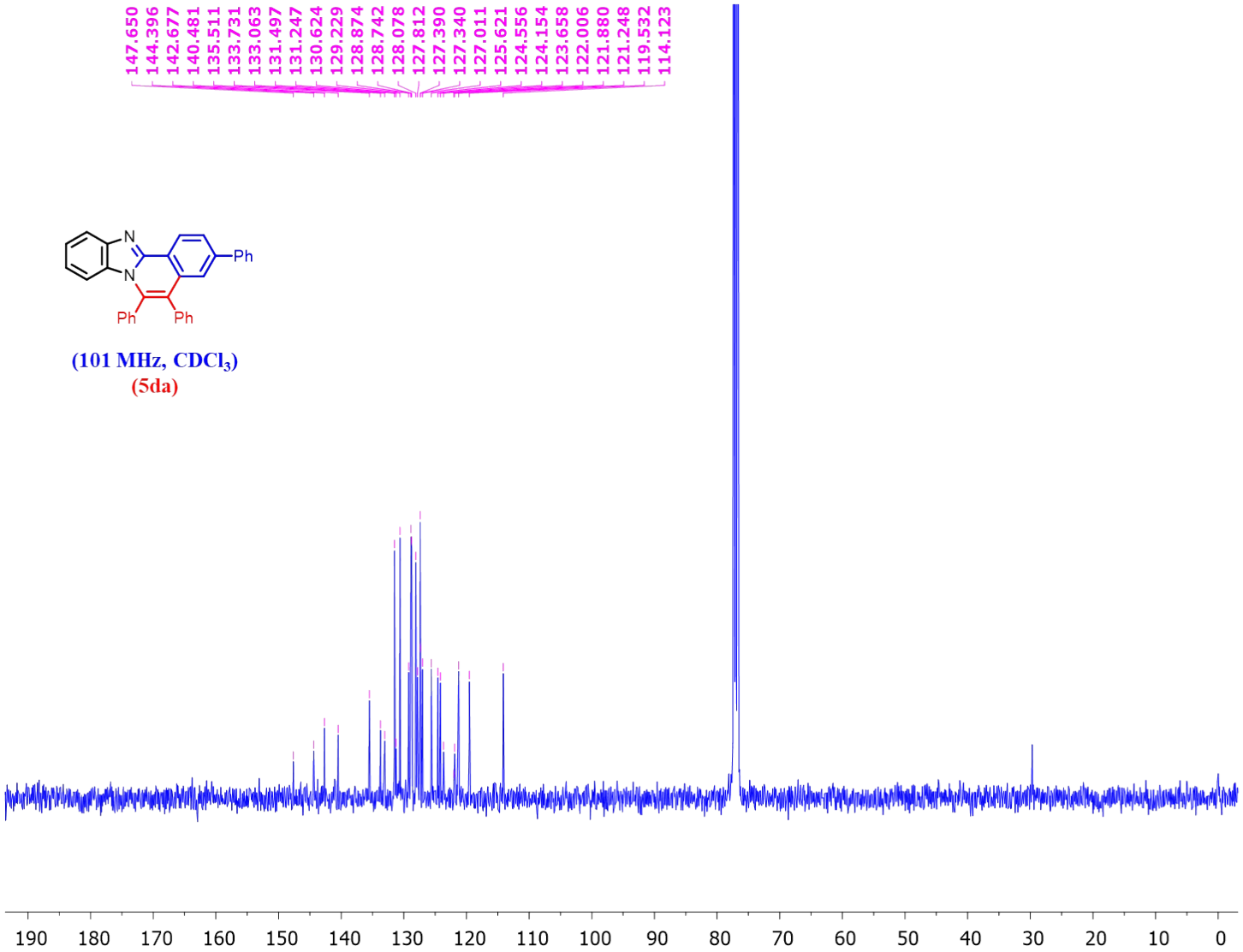


Fig. S23. ^{13}C NMR spectra of 3,5,6-triphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5da**) in $CDCl_3$.

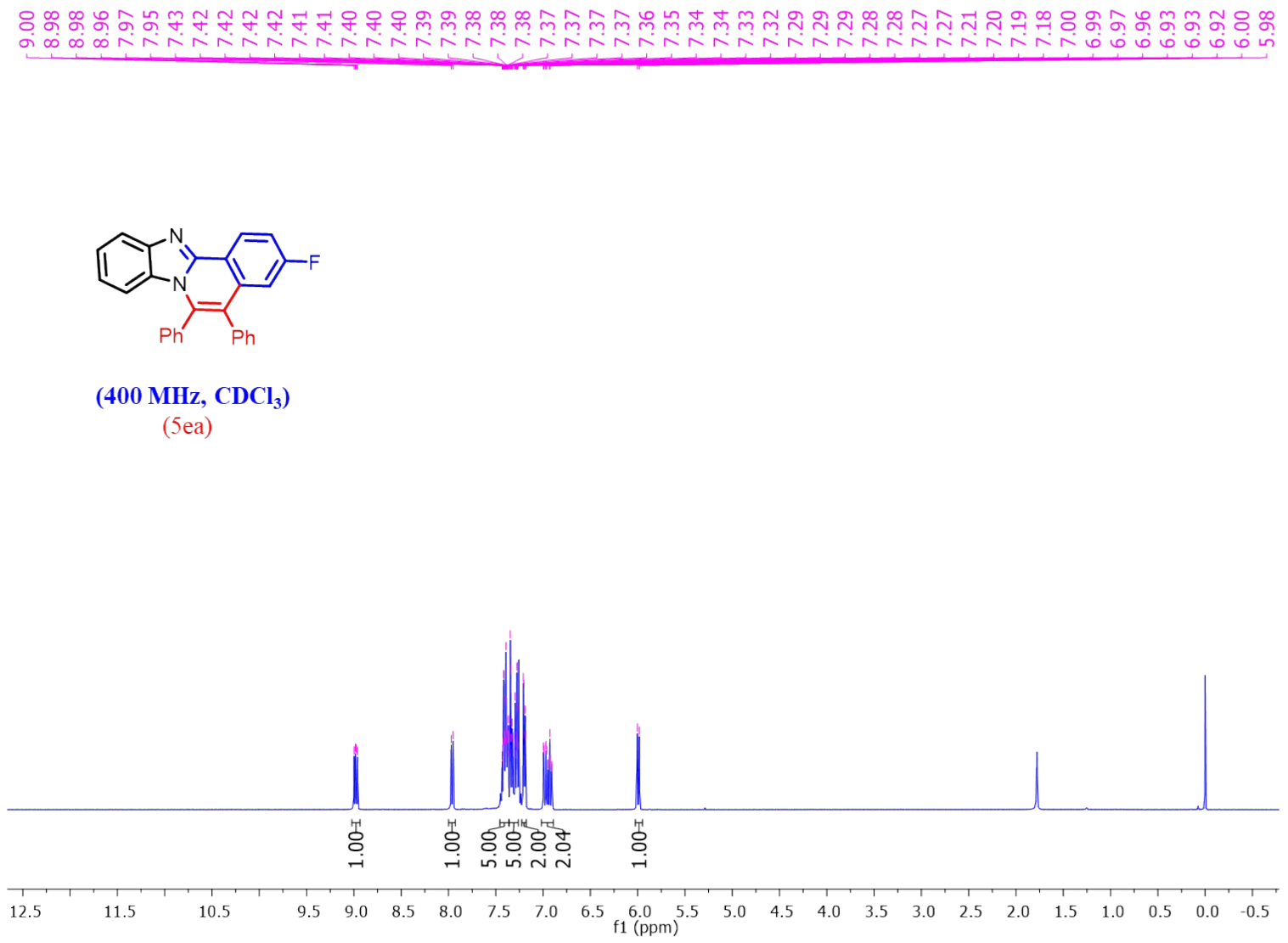


Fig. S24. ^{1}H NMR spectra of 3-fluoro-5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5ea**) in $CDCl_3$.

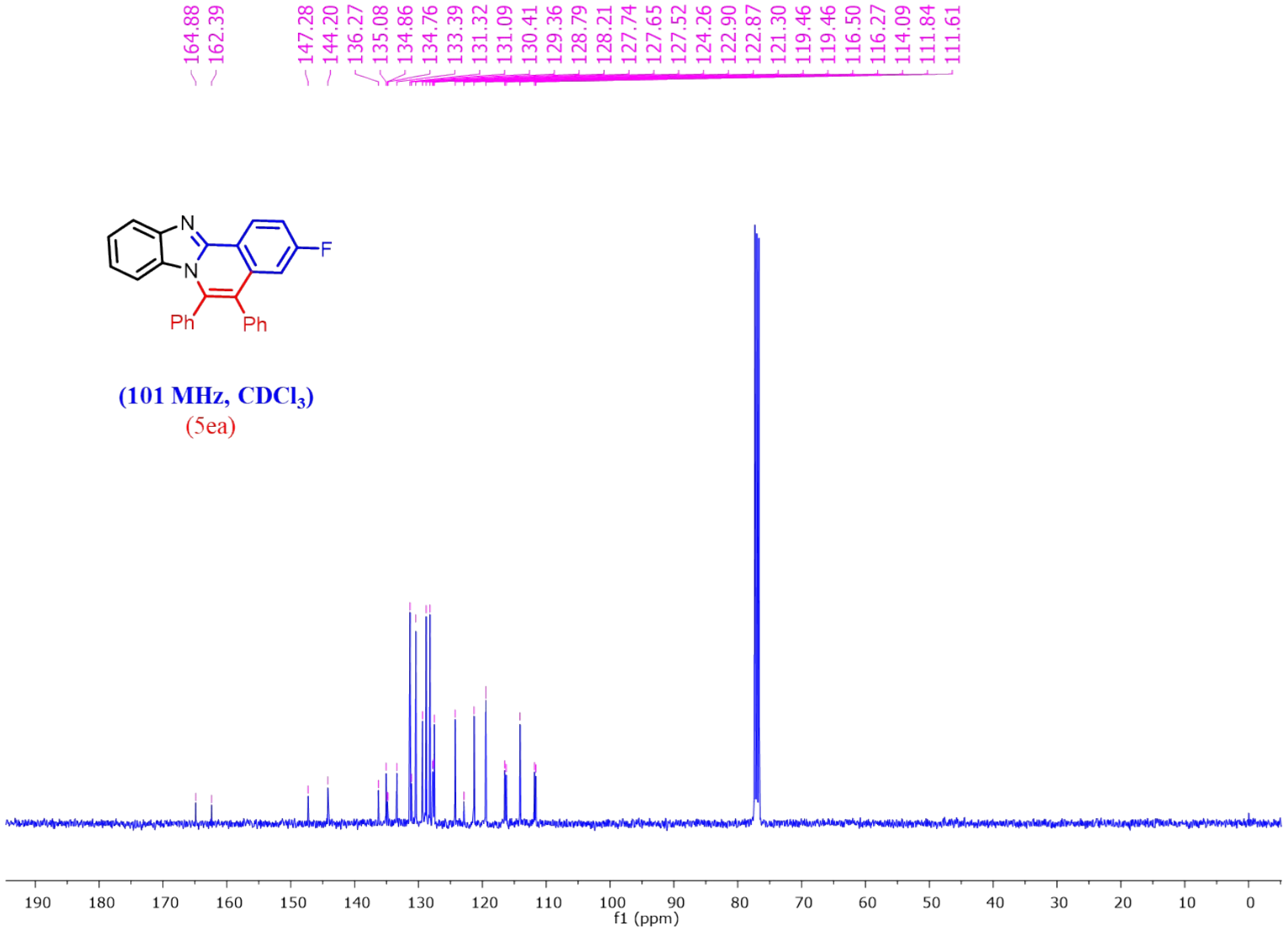


Fig. S25. ^{13}C NMR spectra of 3-fluoro-5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5ea**) in $CDCl_3$.

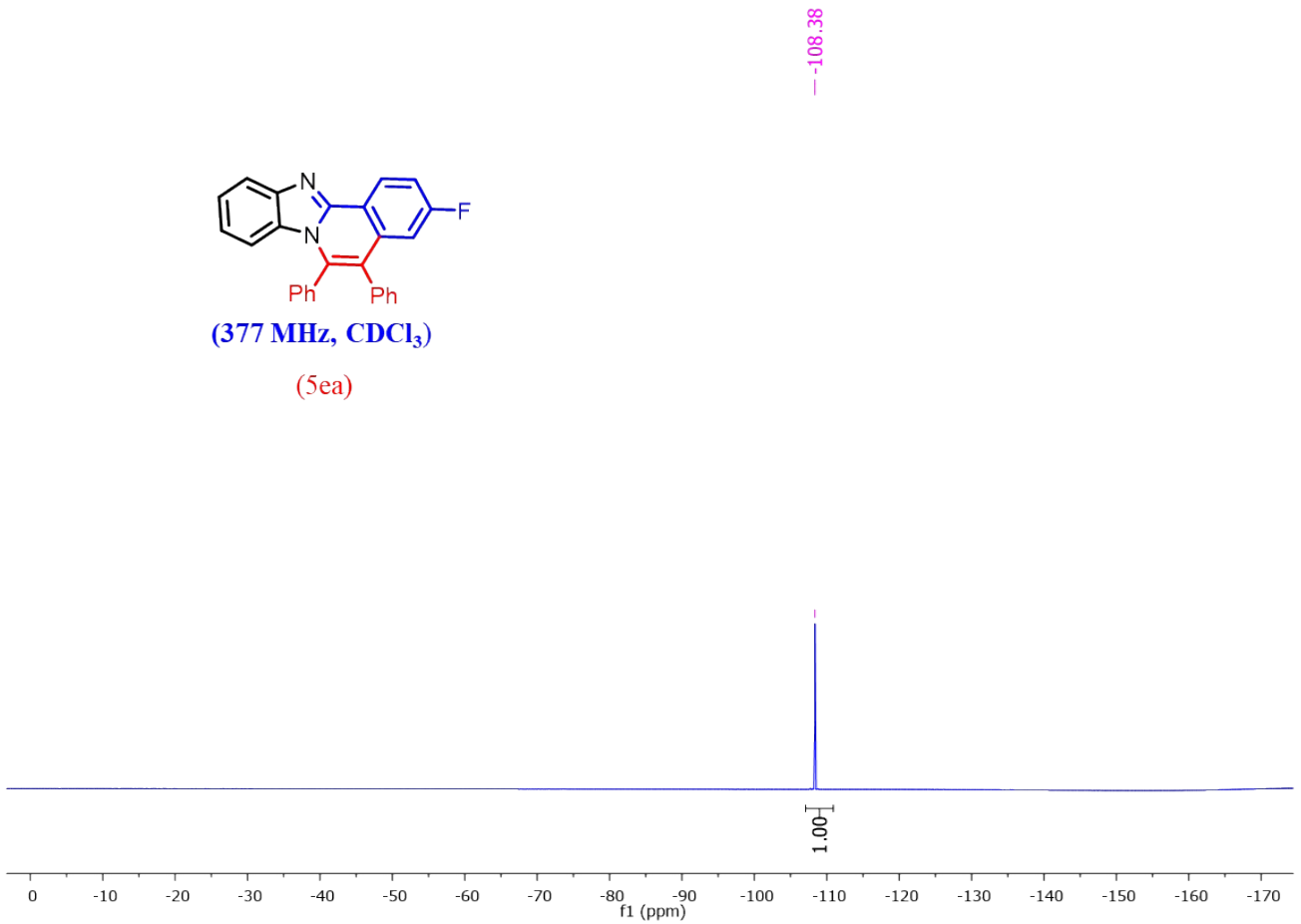


Fig. S26. ^{19}F NMR spectra of 3-fluoro-5,6-diphenylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5ea**) in $CDCl_3$.

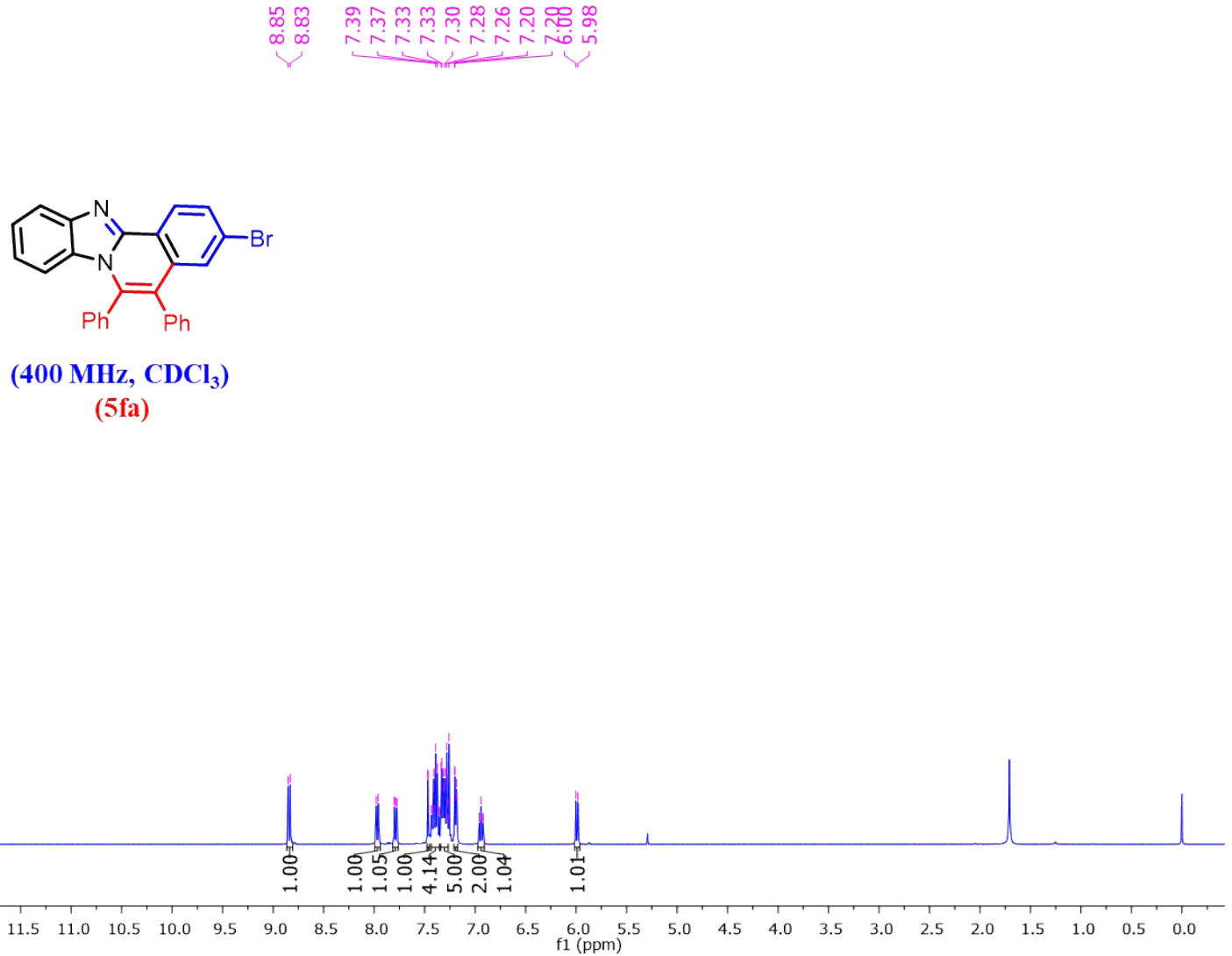


Fig. S27. ^{1}H NMR spectra of 3-bromo-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5f**) in $CDCl_3$.

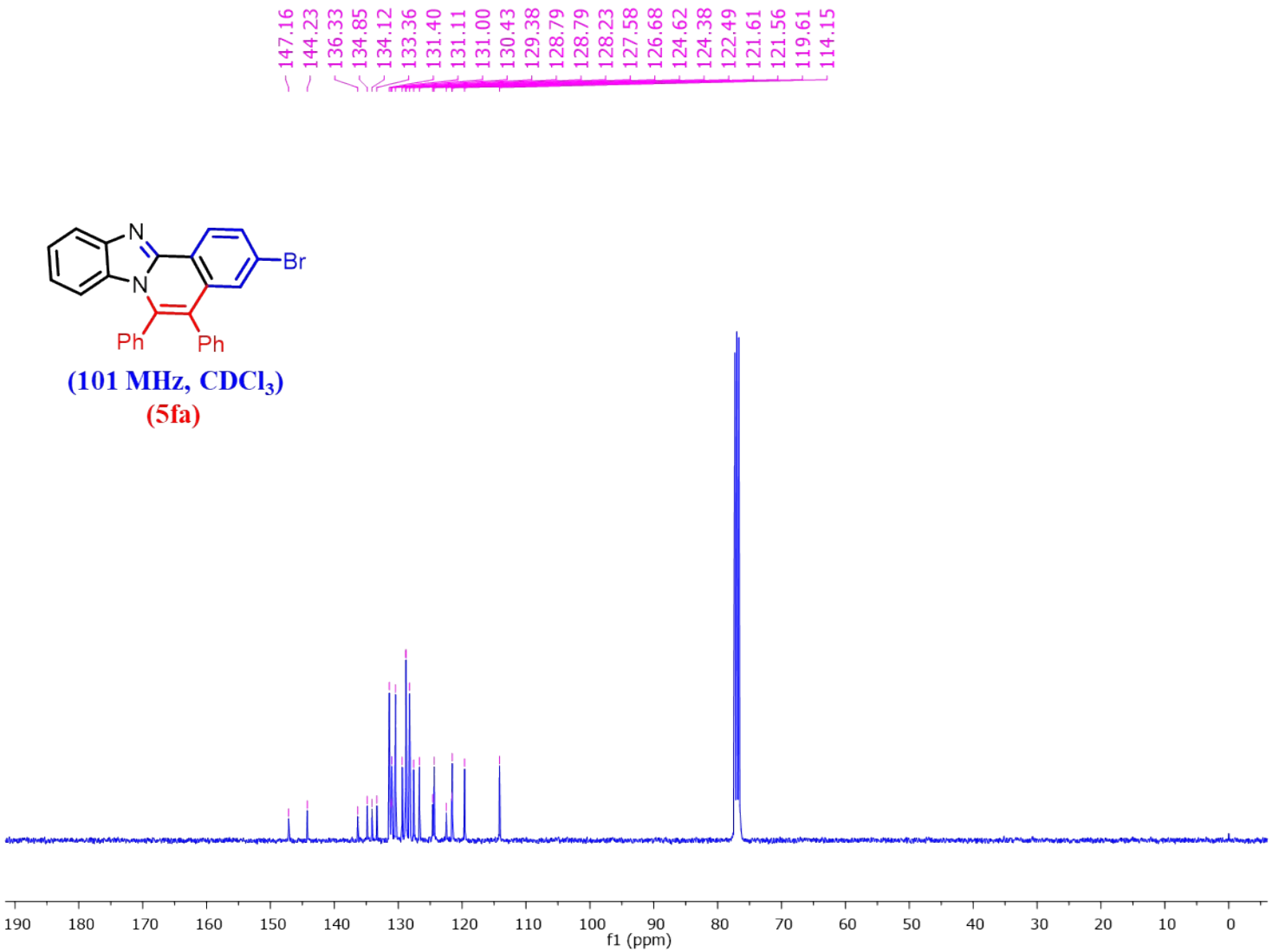


Fig. S28. ^{13}C NMR spectra of 3-bromo-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5f**) in $CDCl_3$.

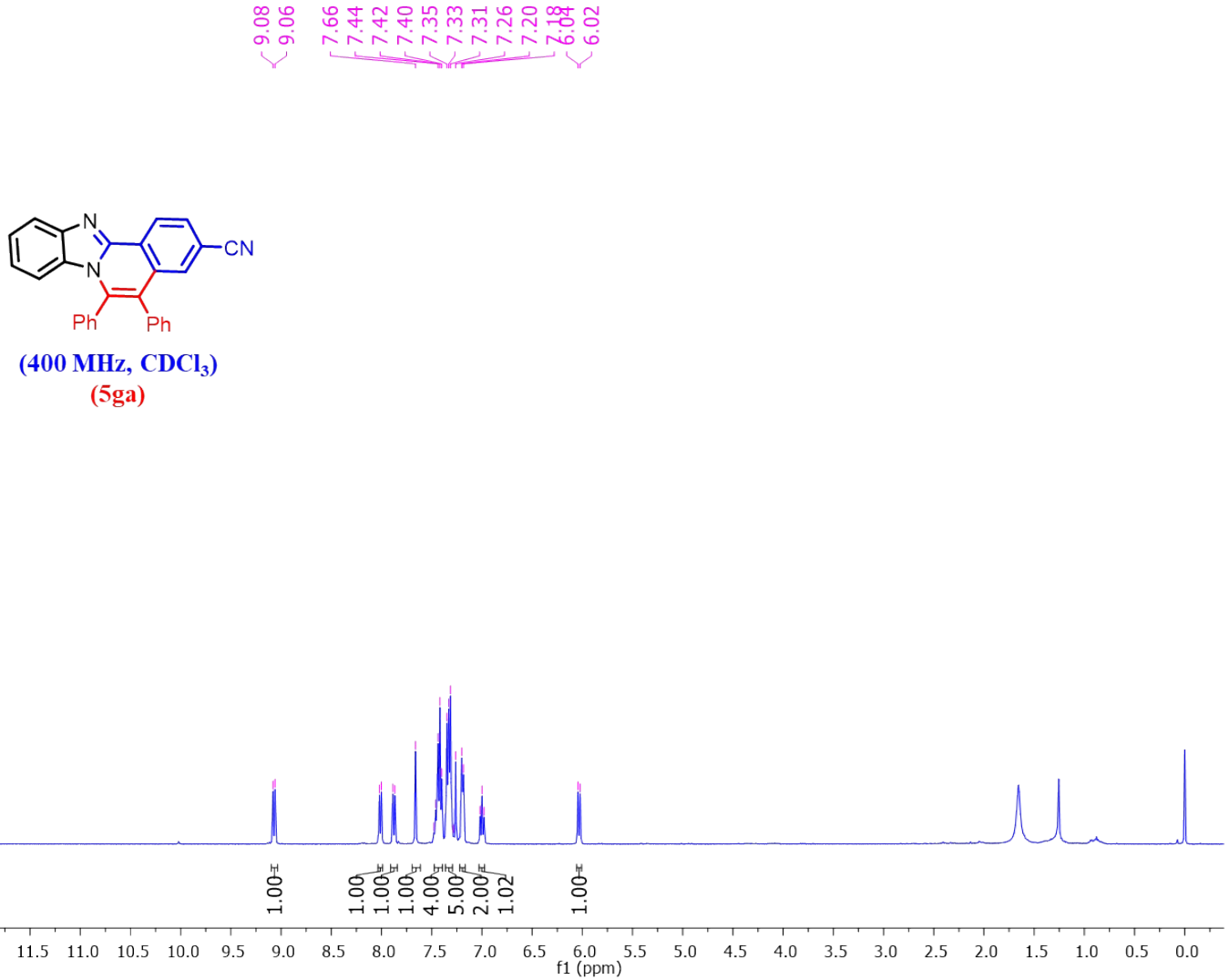


Fig. S29. ^{1}H NMR spectra of 5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile (**5ga**) in $CDCl_3$.

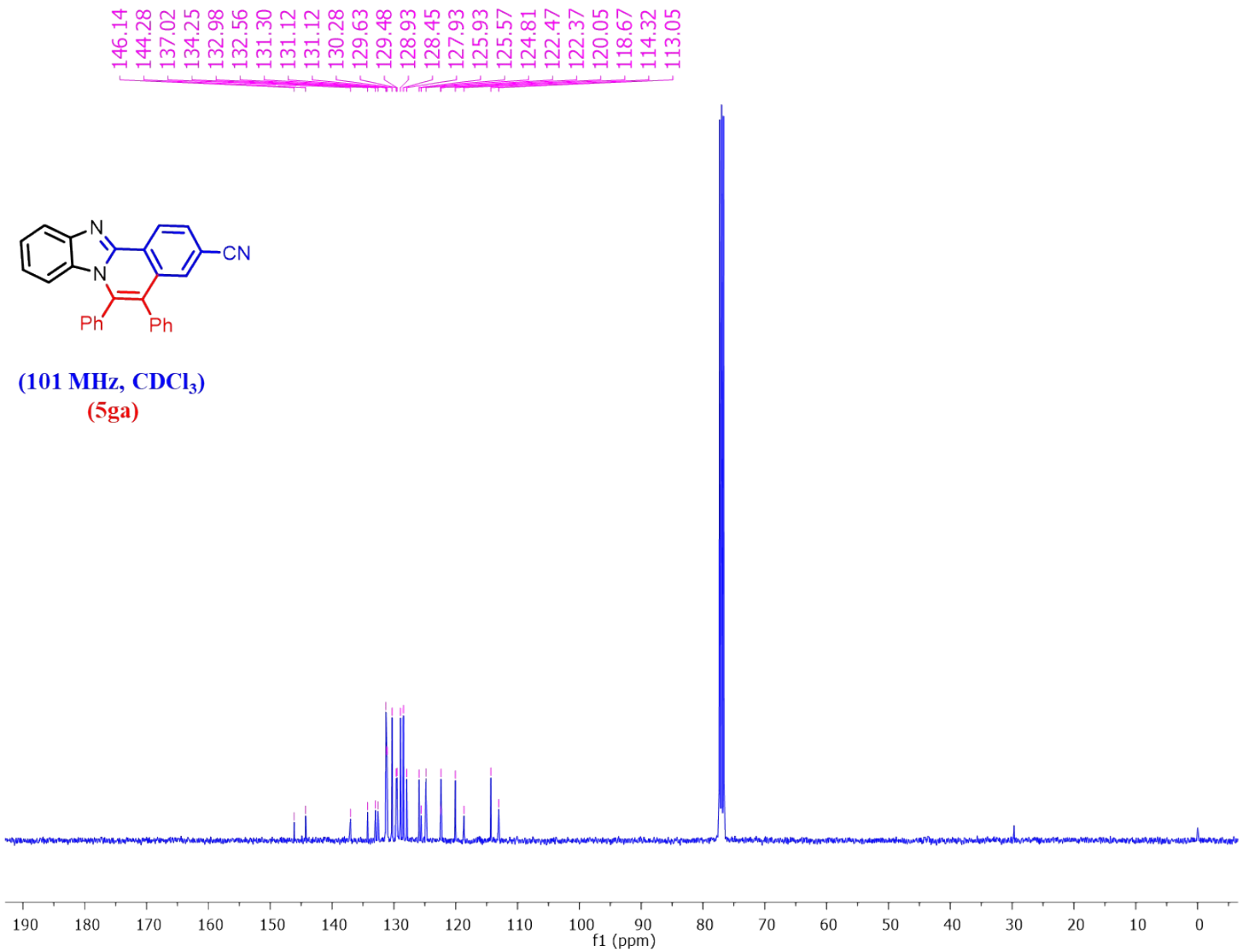


Fig. S30. ^{13}C NMR spectra of 5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile (**5ga**) in $CDCl_3$.

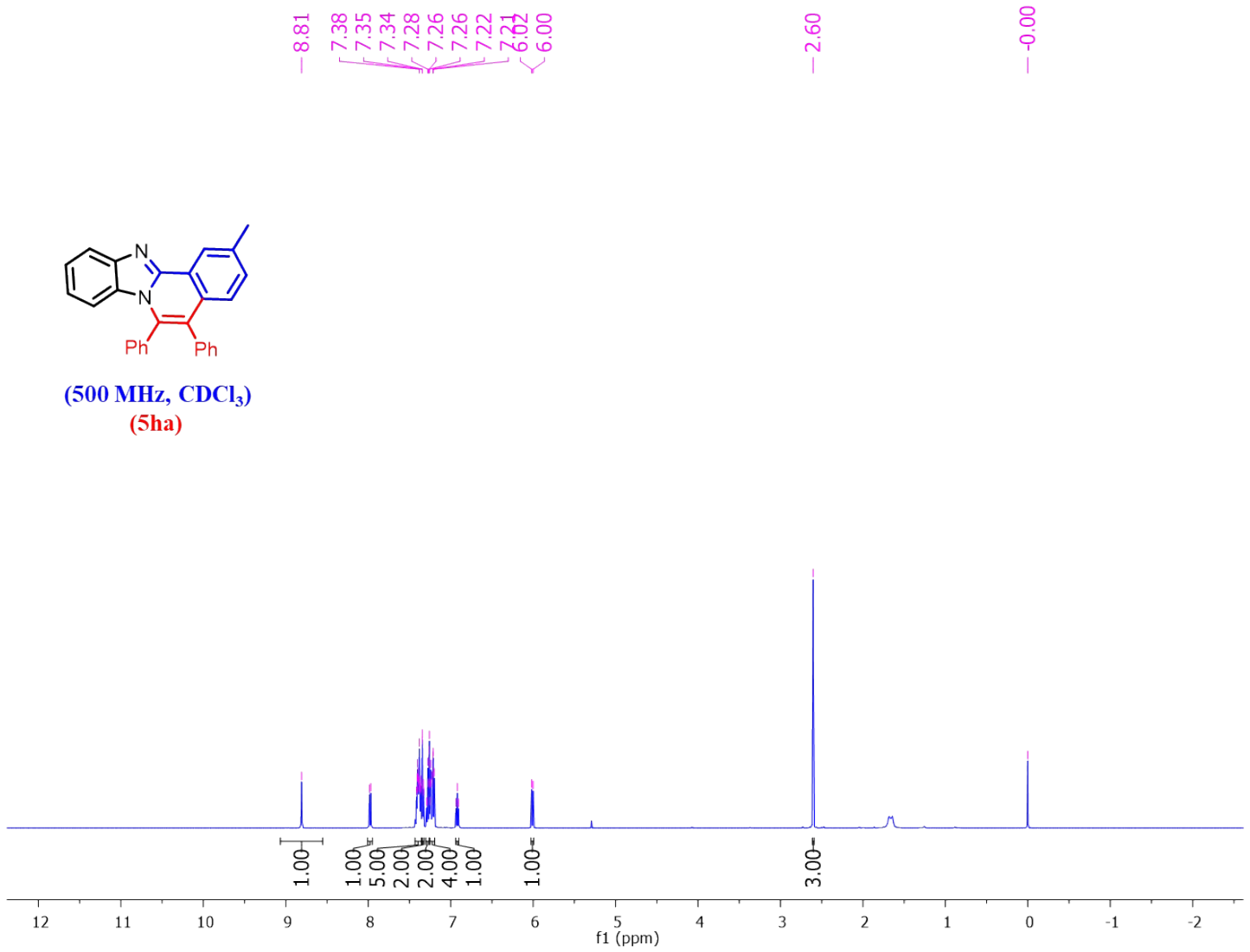


Fig. S31. ^{1}H NMR spectra of 2-methyl-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5ha**) in $CDCl_3$.

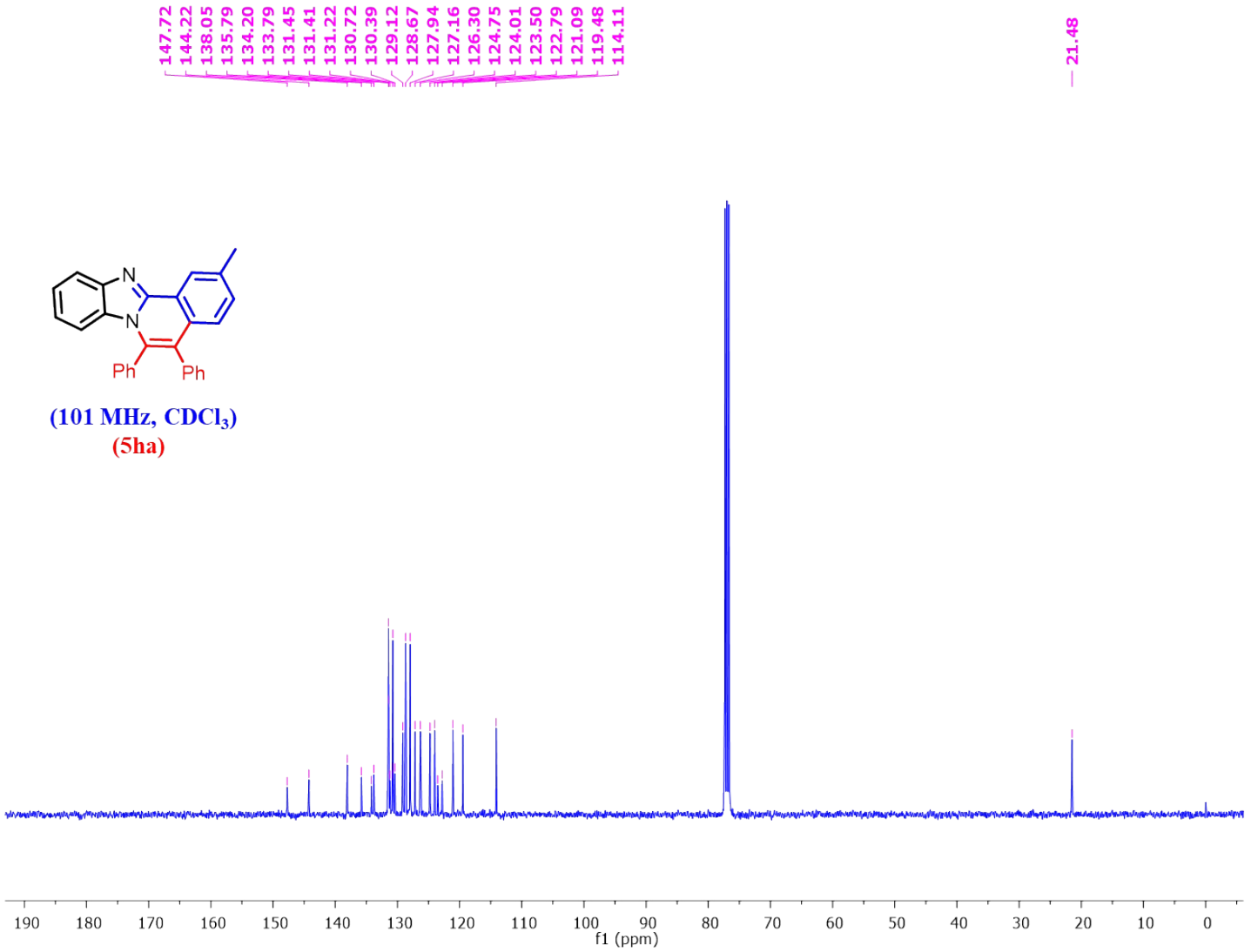


Fig. S32. ^{13}C NMR spectra of 2-methyl-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5ha**) in $CDCl_3$.

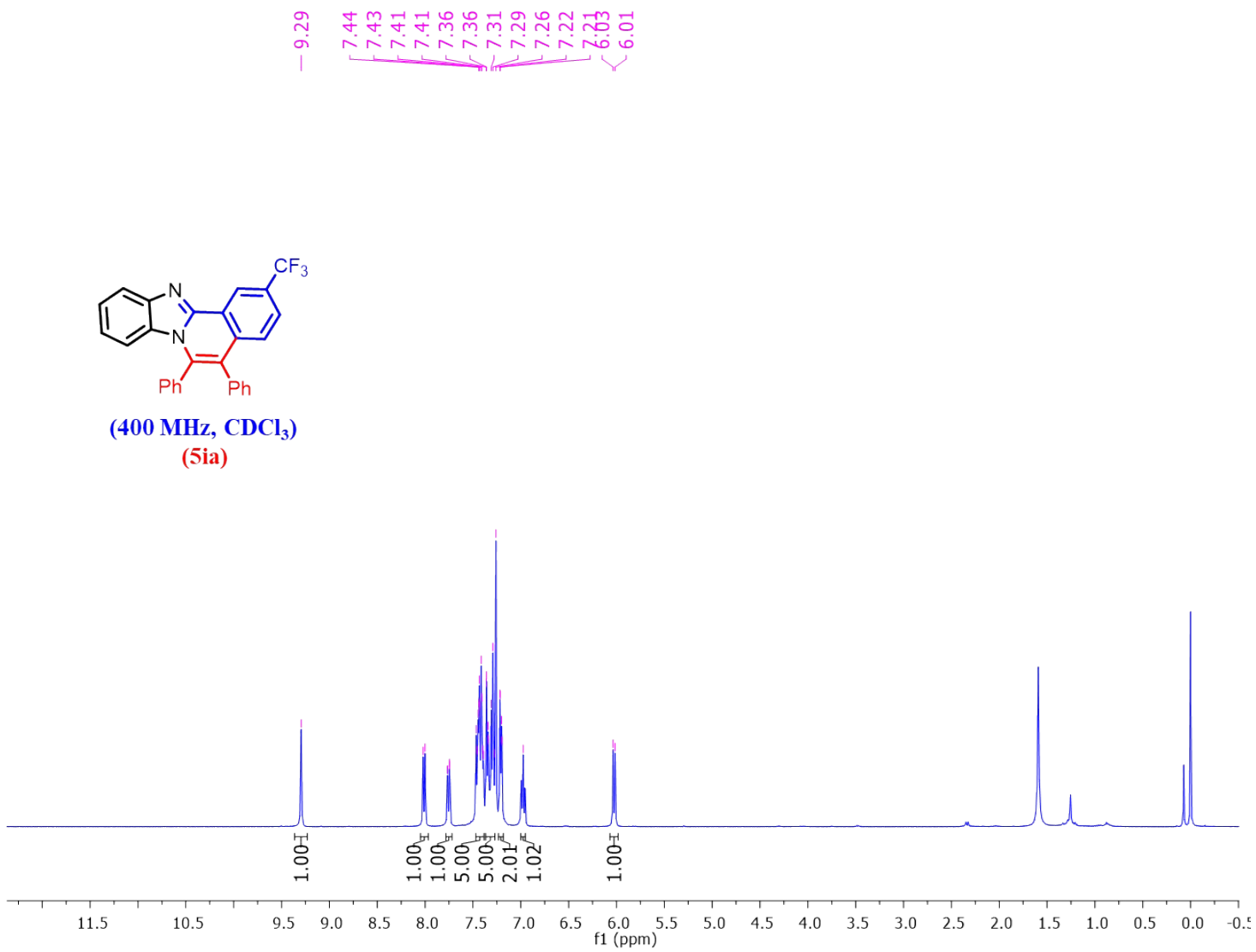


Fig. S33. ^{1}H NMR spectra of 5,6-diphenyl-2-(trifluoromethyl)benzo[4,5]imidazo[2,1-a]isoquinoline (**5ia**) in $CDCl_3$.

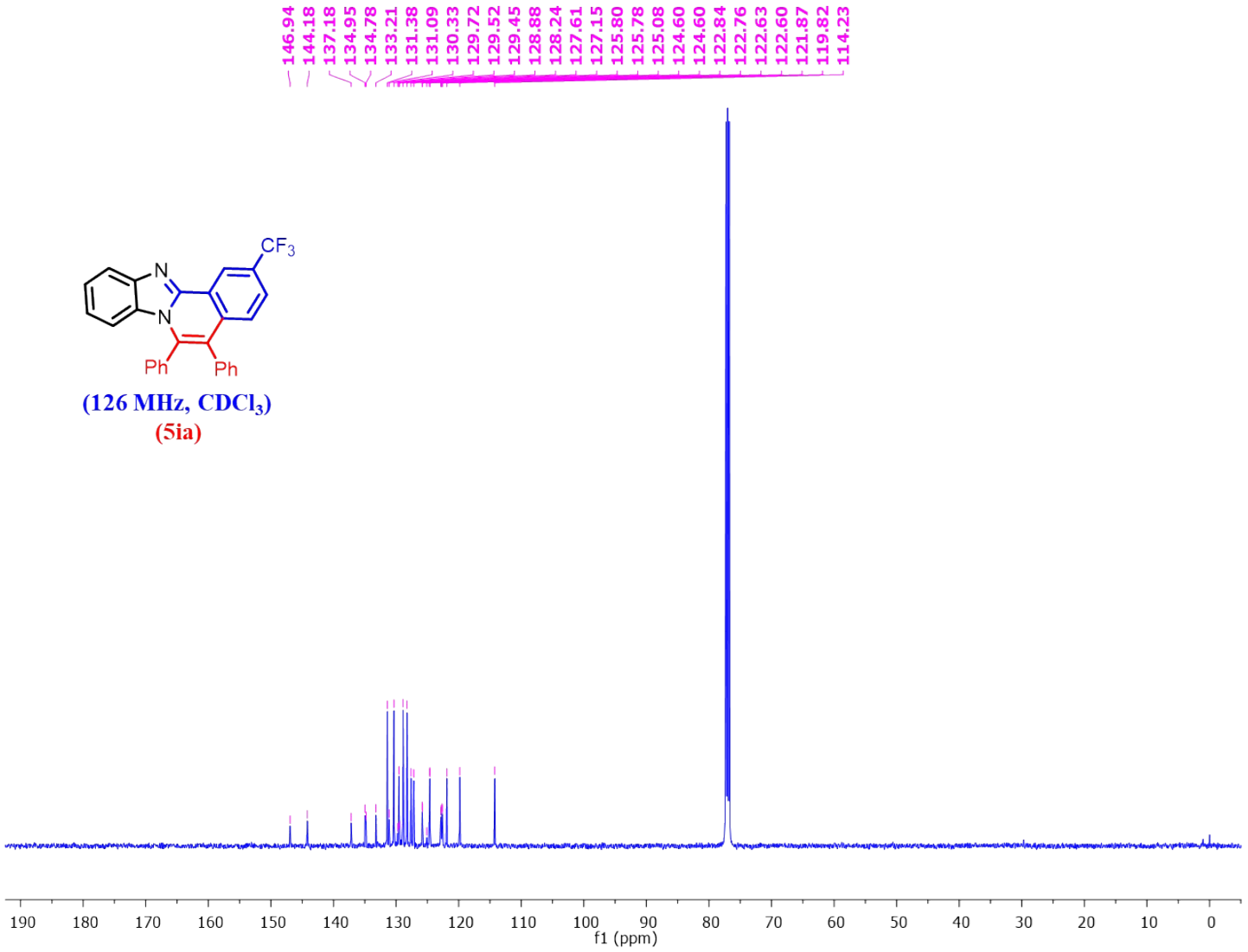


Fig. S34. ^{13}C NMR spectra of 5,6-diphenyl-2-(trifluoromethyl)benzo[4,5]imidazo[2,1-a]isoquinoline (**5ia**) in $CDCl_3$.

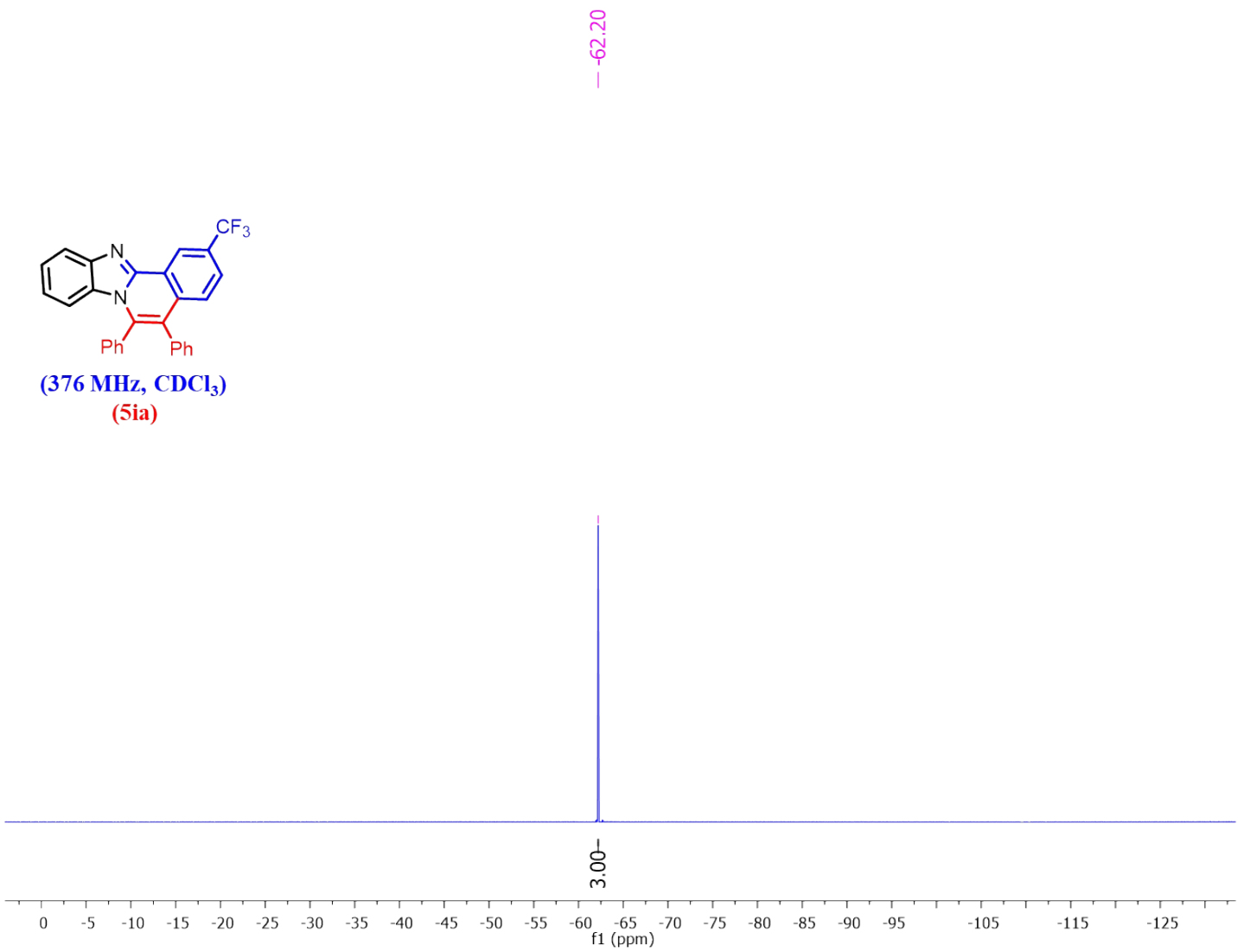


Fig. S35. ^{19}F NMR spectra of 5,6-diphenyl-2-(trifluoromethyl)benzo[4,5]imidazo[2,1-a]isoquinoline (**5ia**) in $CDCl_3$.

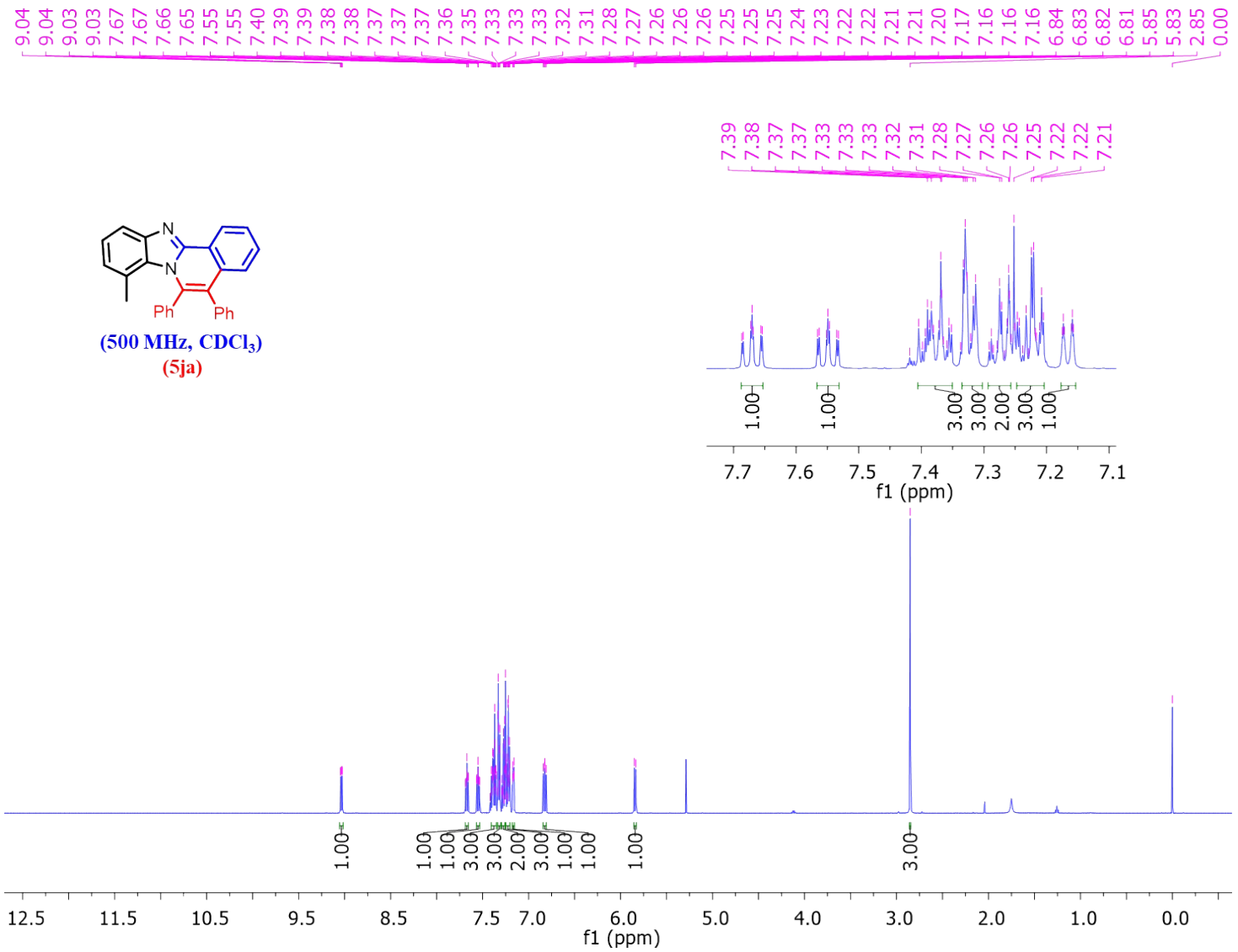


Fig. S36. ^{1}H NMR spectra of 8-methyl-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5ja**) in $CDCl_3$.

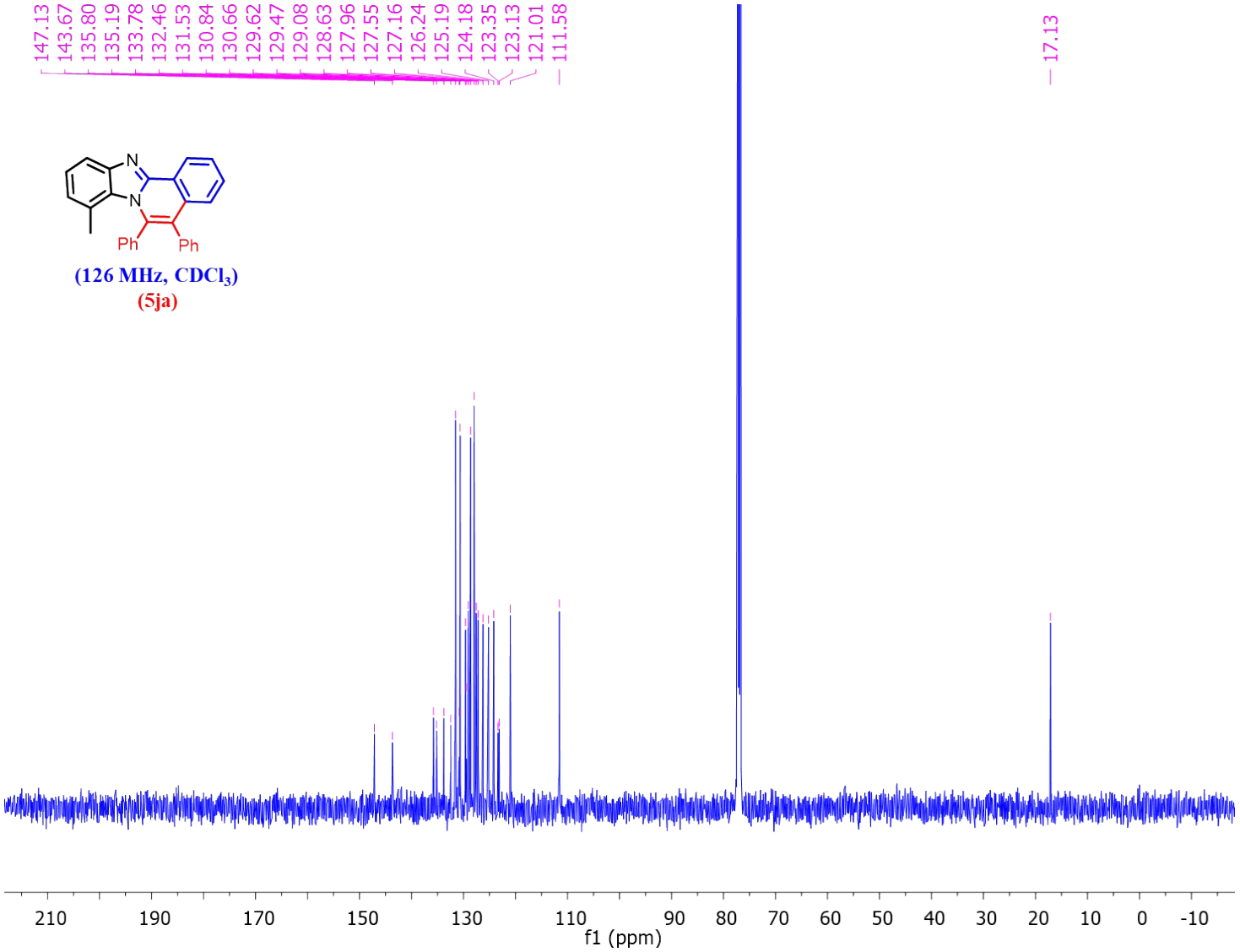


Fig. S37. ^{13}C NMR spectra of 8-methyl-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5ja**) in $CDCl_3$.

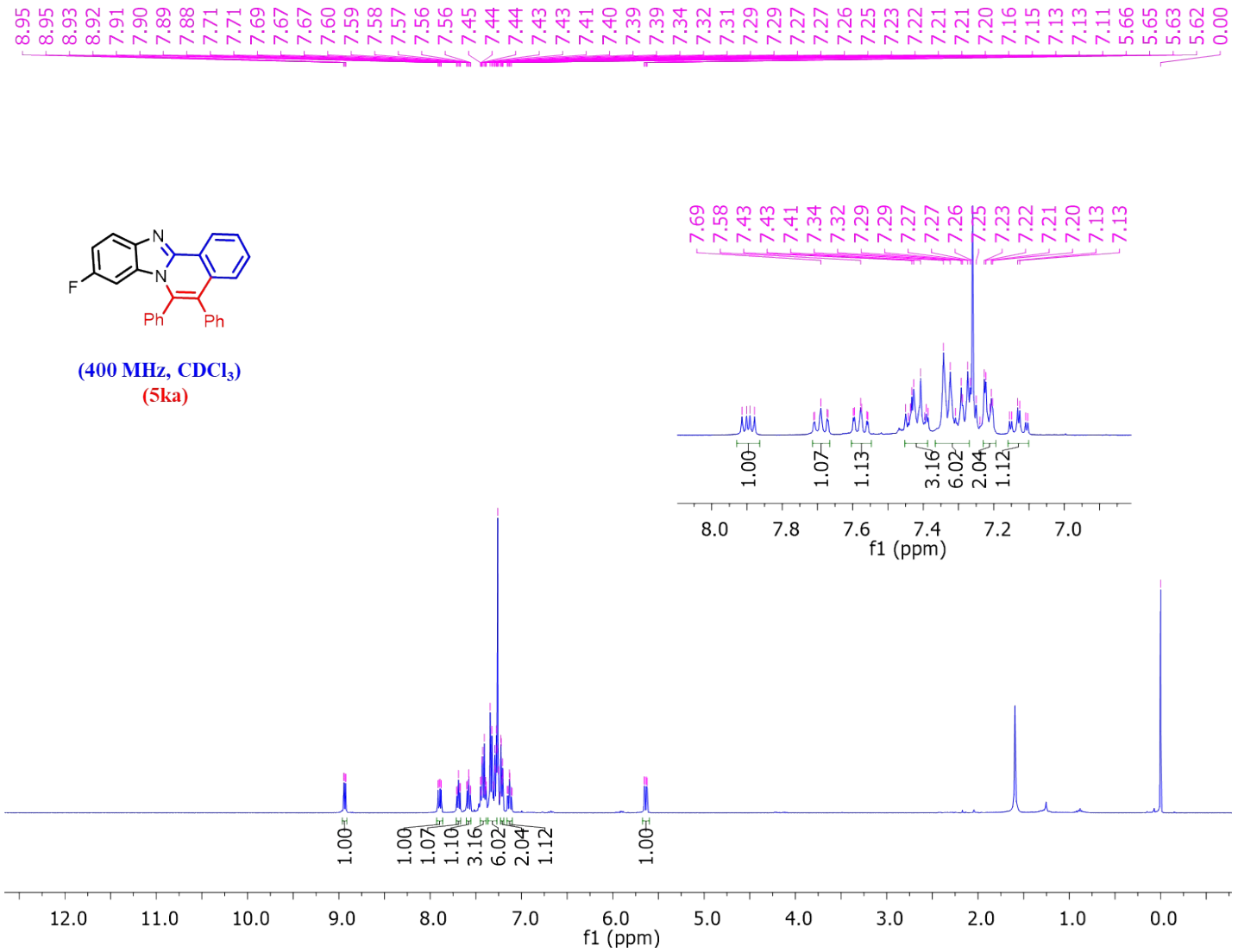


Fig. S38. ^{1}H NMR spectra of 9-fluoro-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5ka**) in $CDCl_3$.

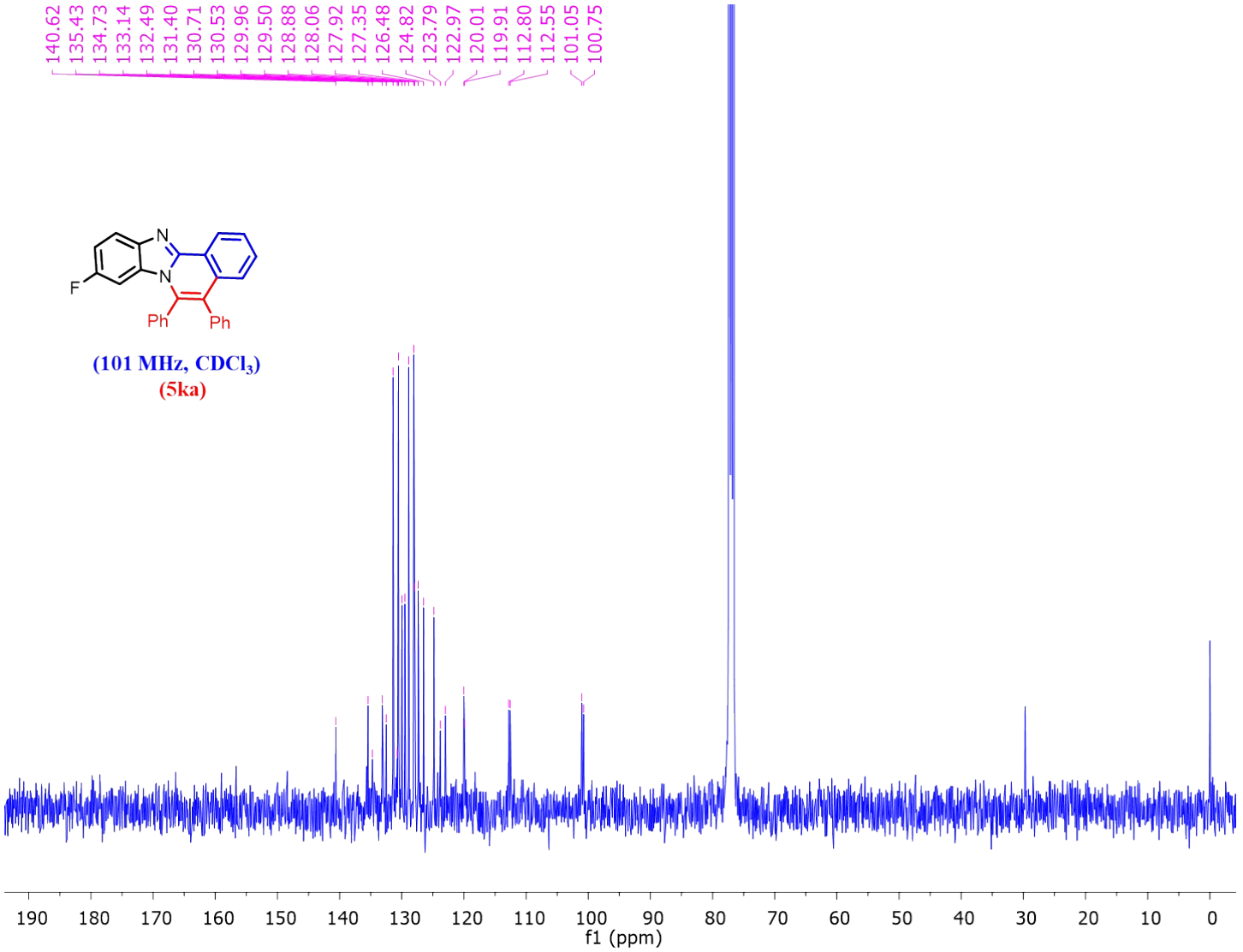


Fig. S39. ^{13}C NMR spectra of 9-fluoro-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5ka**) in $CDCl_3$.

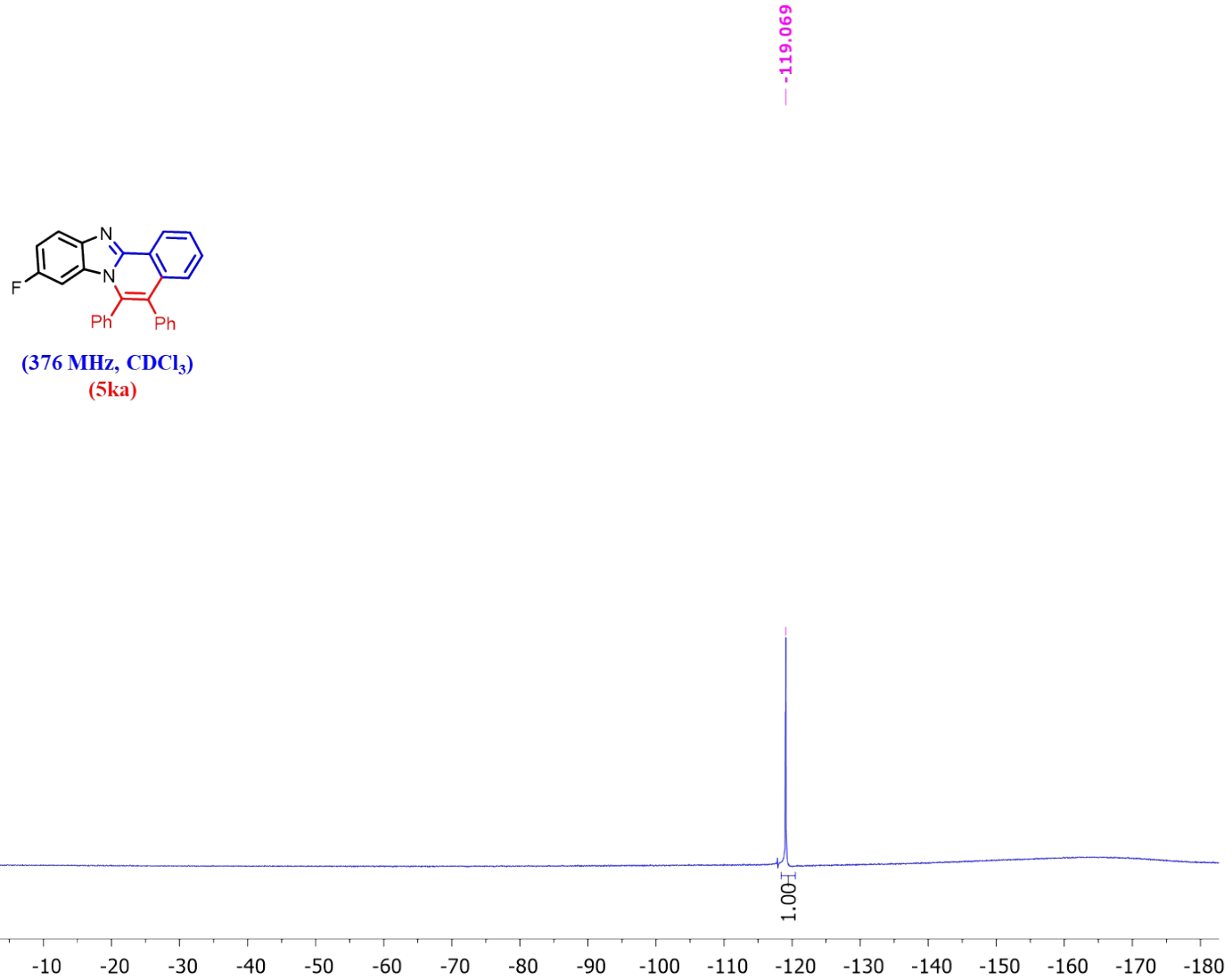


Fig. S40. ^{19}F NMR spectra of 9-fluoro-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5ka**) in $CDCl_3$.

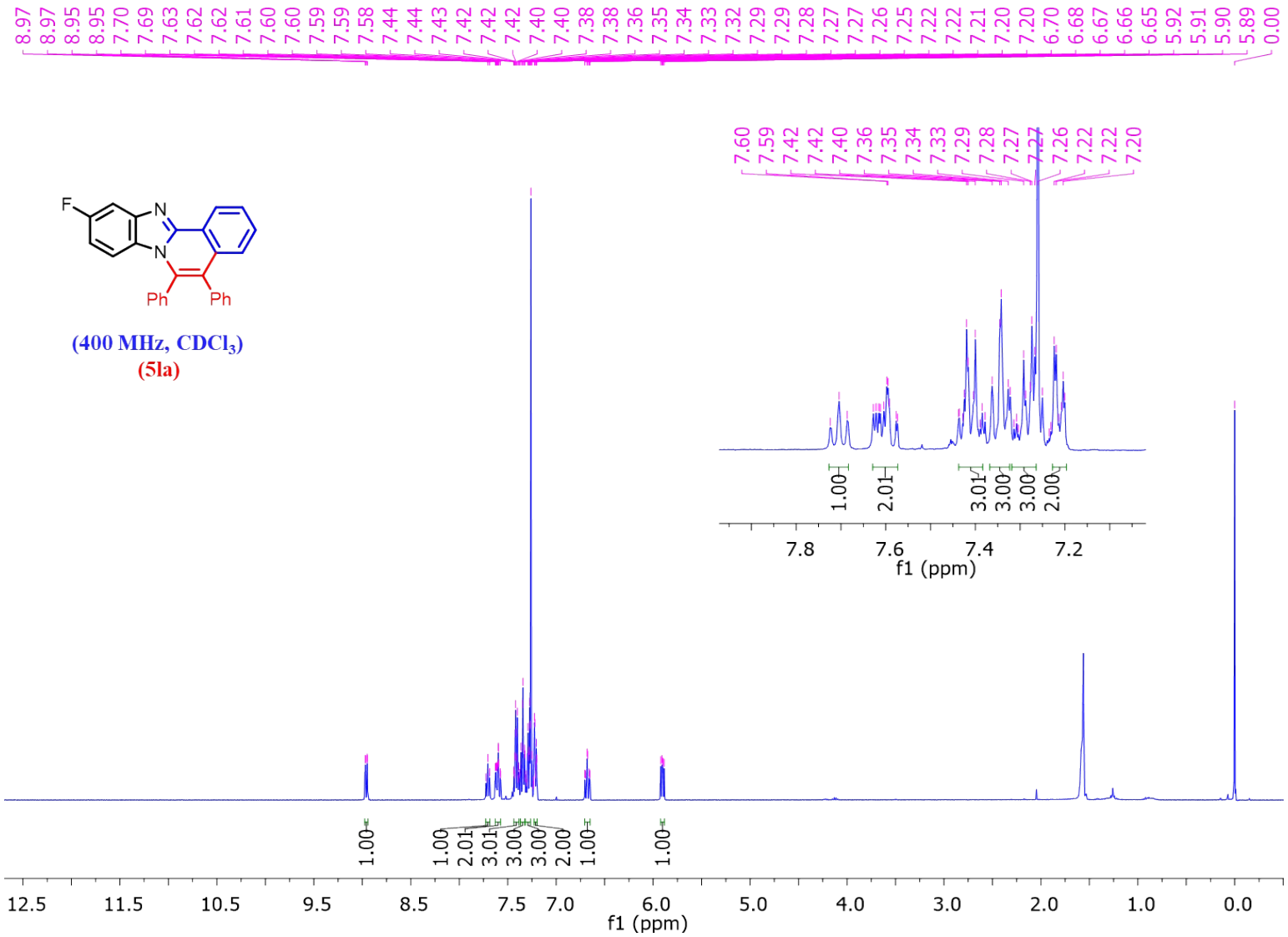


Fig. S41. ^{1}H NMR spectra of 10-fluoro-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5la**) in $CDCl_3$.

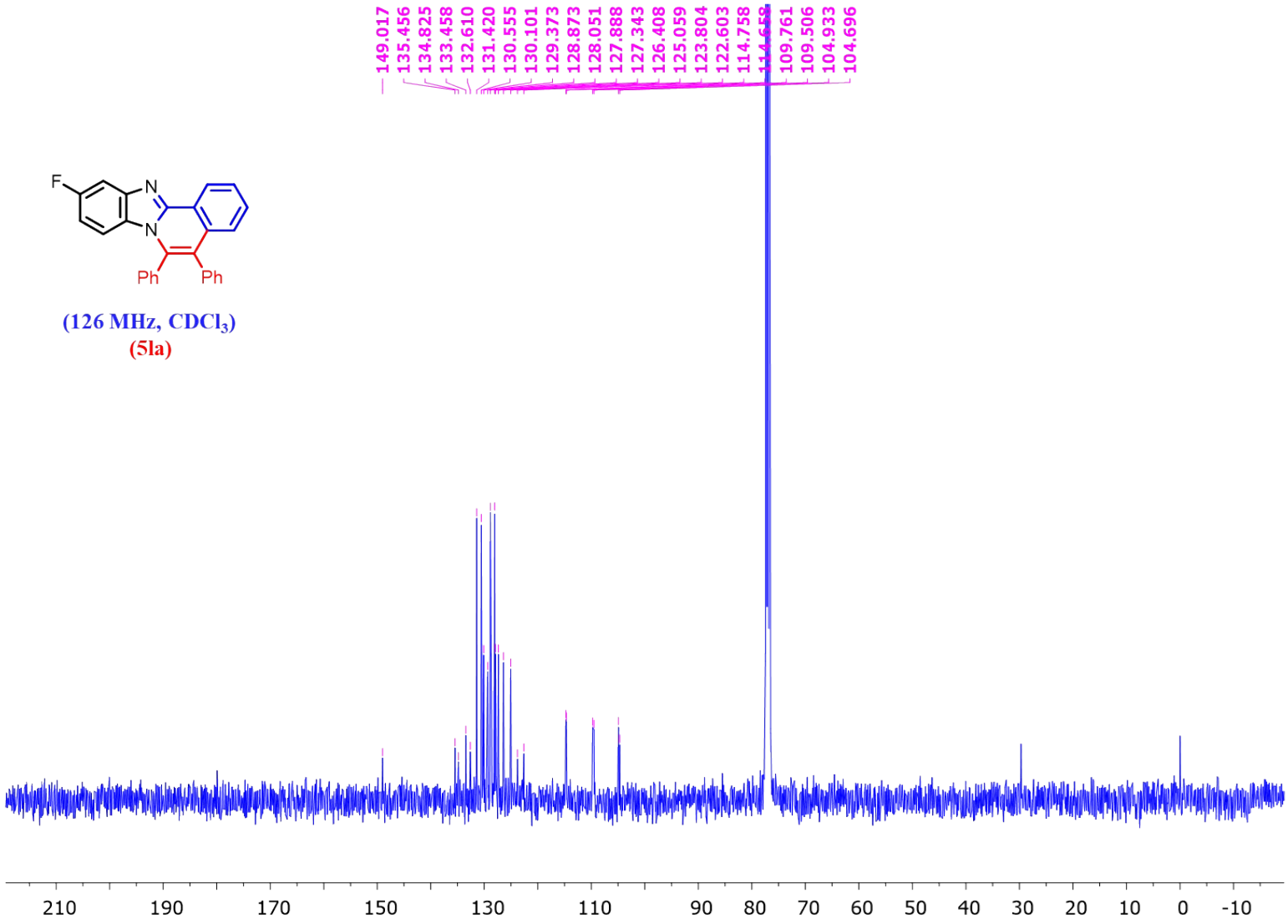


Fig. S42. ^{13}C NMR spectra of 10-fluoro-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5la**) in $CDCl_3$.

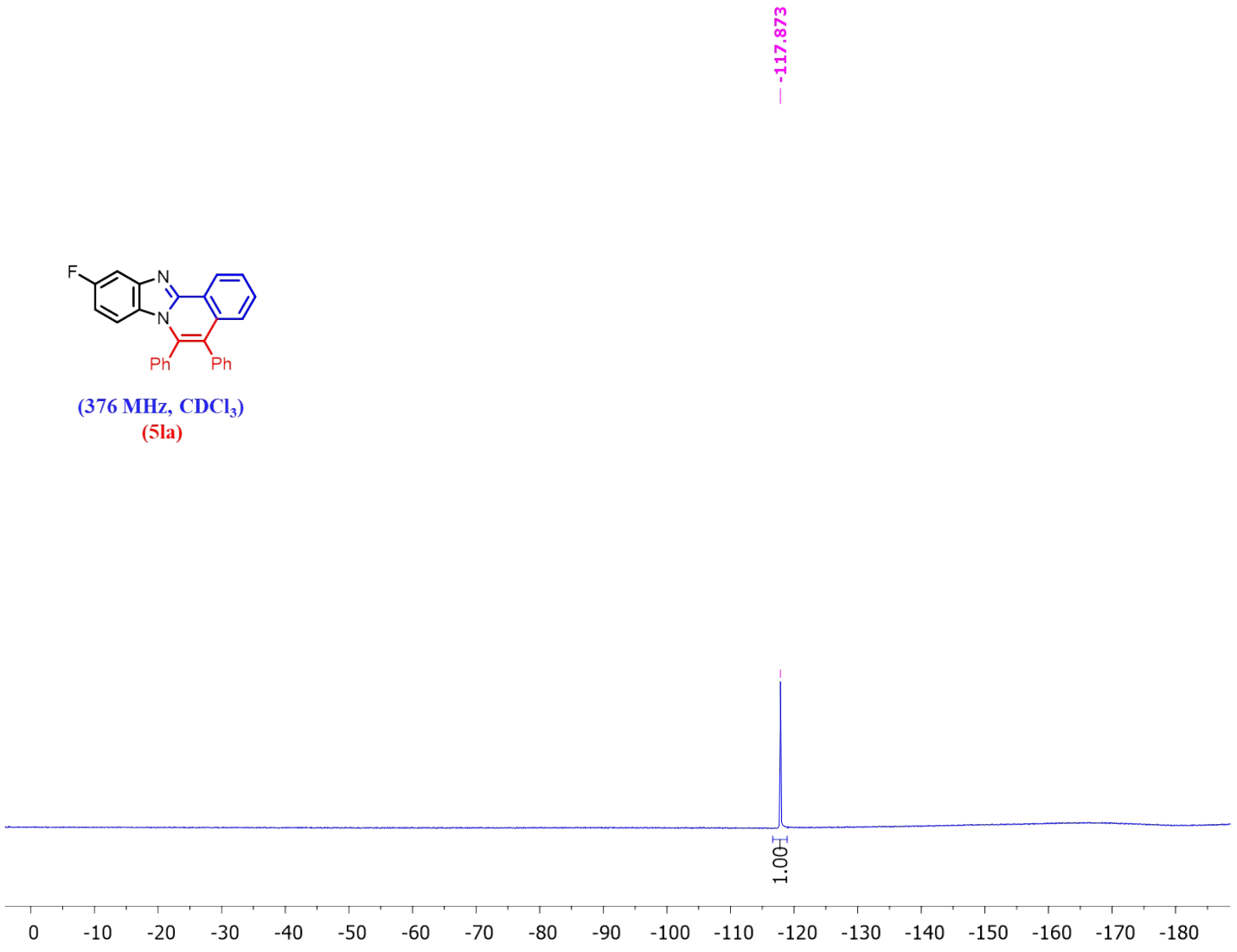


Fig. S43. ^{19}F NMR spectra of 10-fluoro-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5la**) in $CDCl_3$.

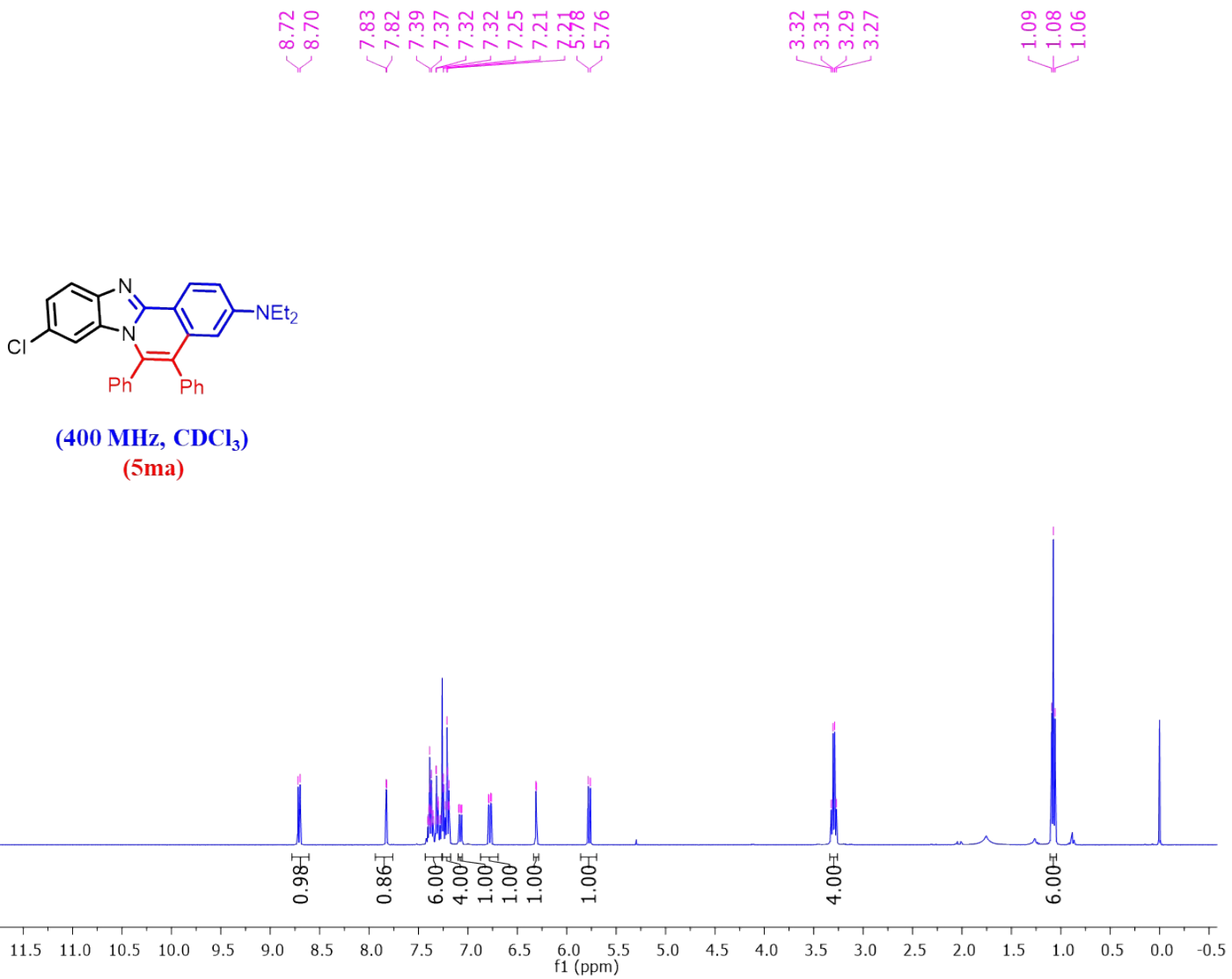


Fig. S44. ^{1}H NMR spectra of 9-chloro-N, N-diethyl-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinolin-3-amine (**5ma**) in $CDCl_3$.

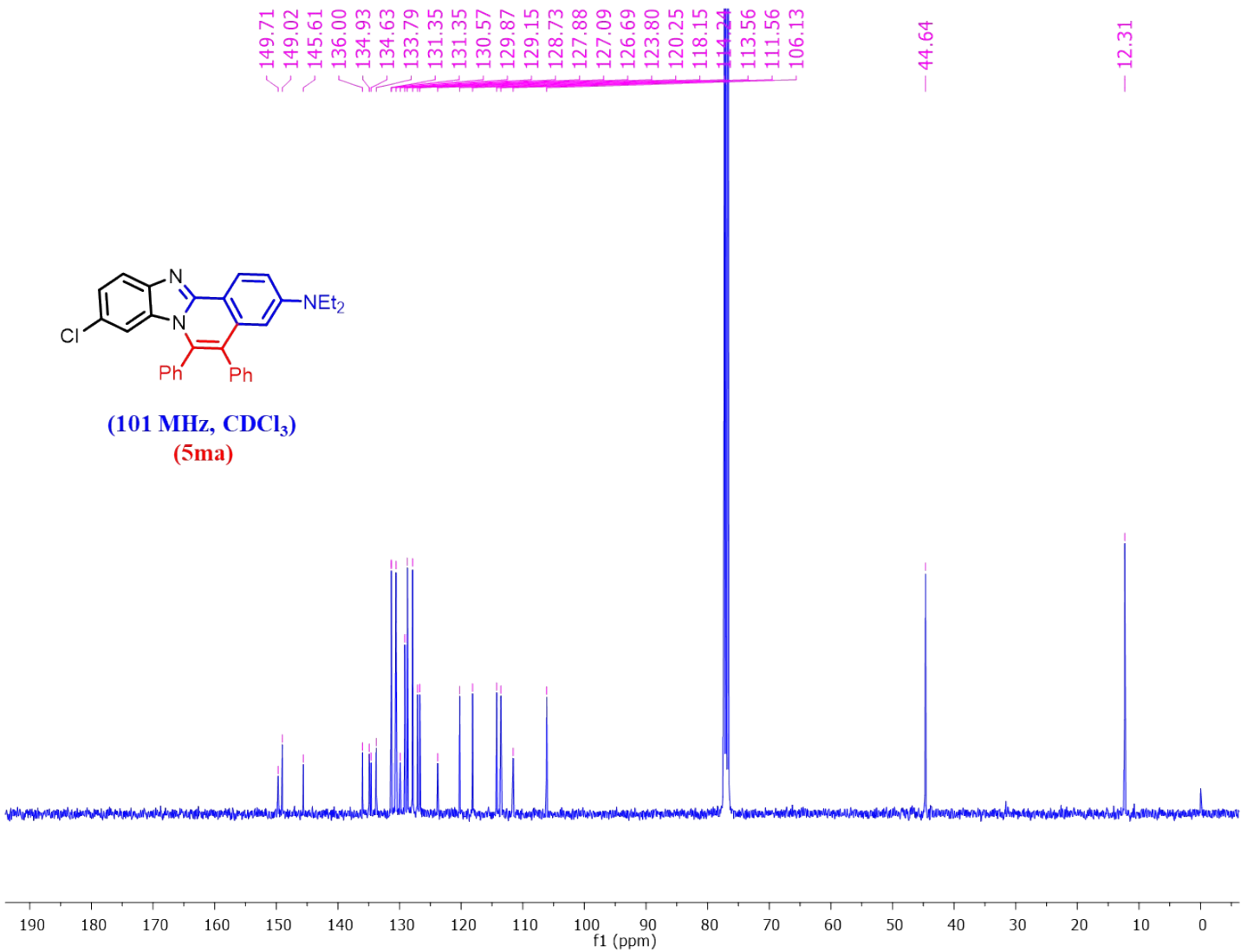


Fig. S45. ^{13}C NMR spectra of 9-chloro-N, N-diethyl-5,6-diphenylbenzo[4,5]imidazo[2,1-a]isoquinolin-3-amine (**5ma**) in $CDCl_3$.

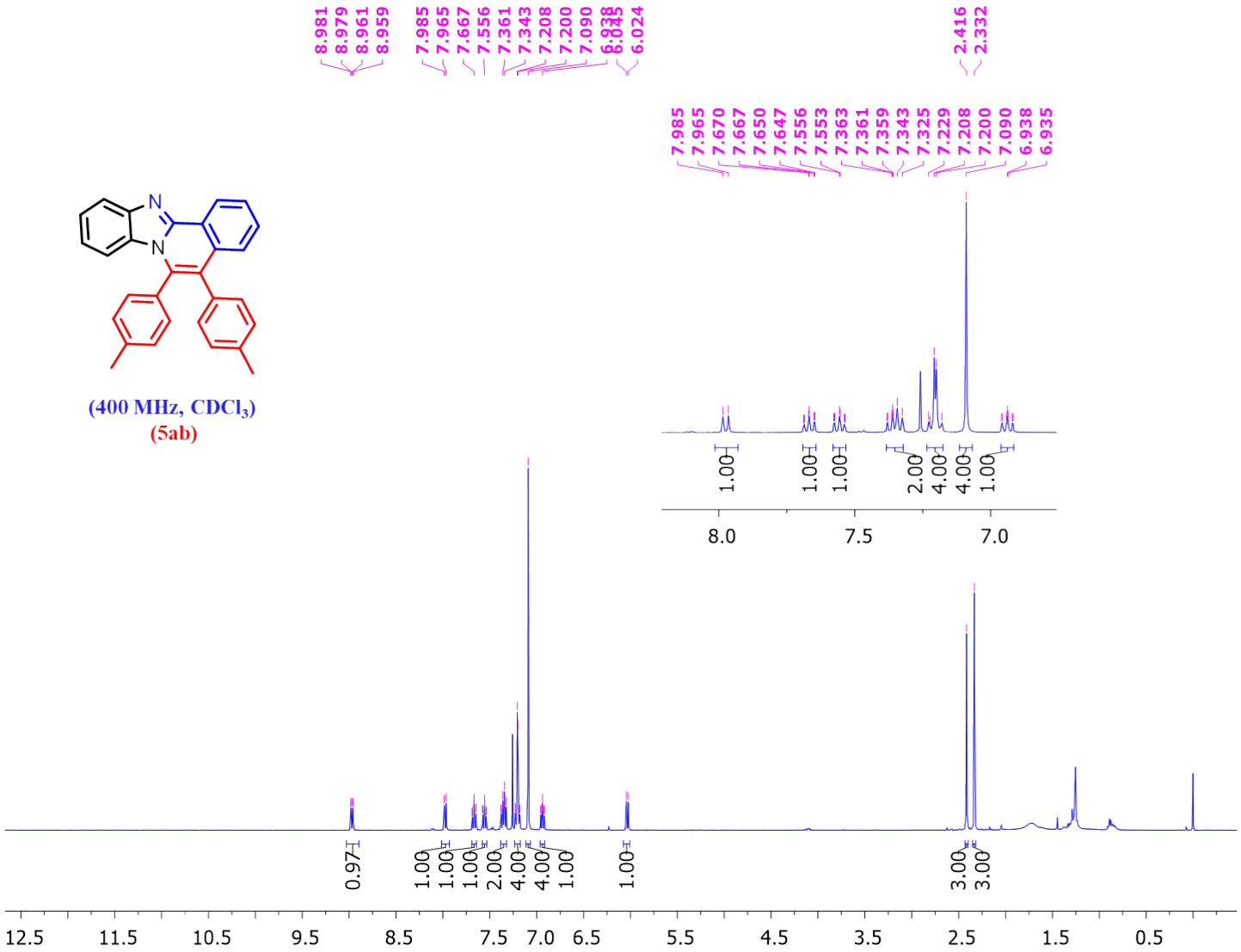


Fig. S46. ^{1}H NMR spectra of 5,6-di-p-tolylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5ab**) in $CDCl_3$.

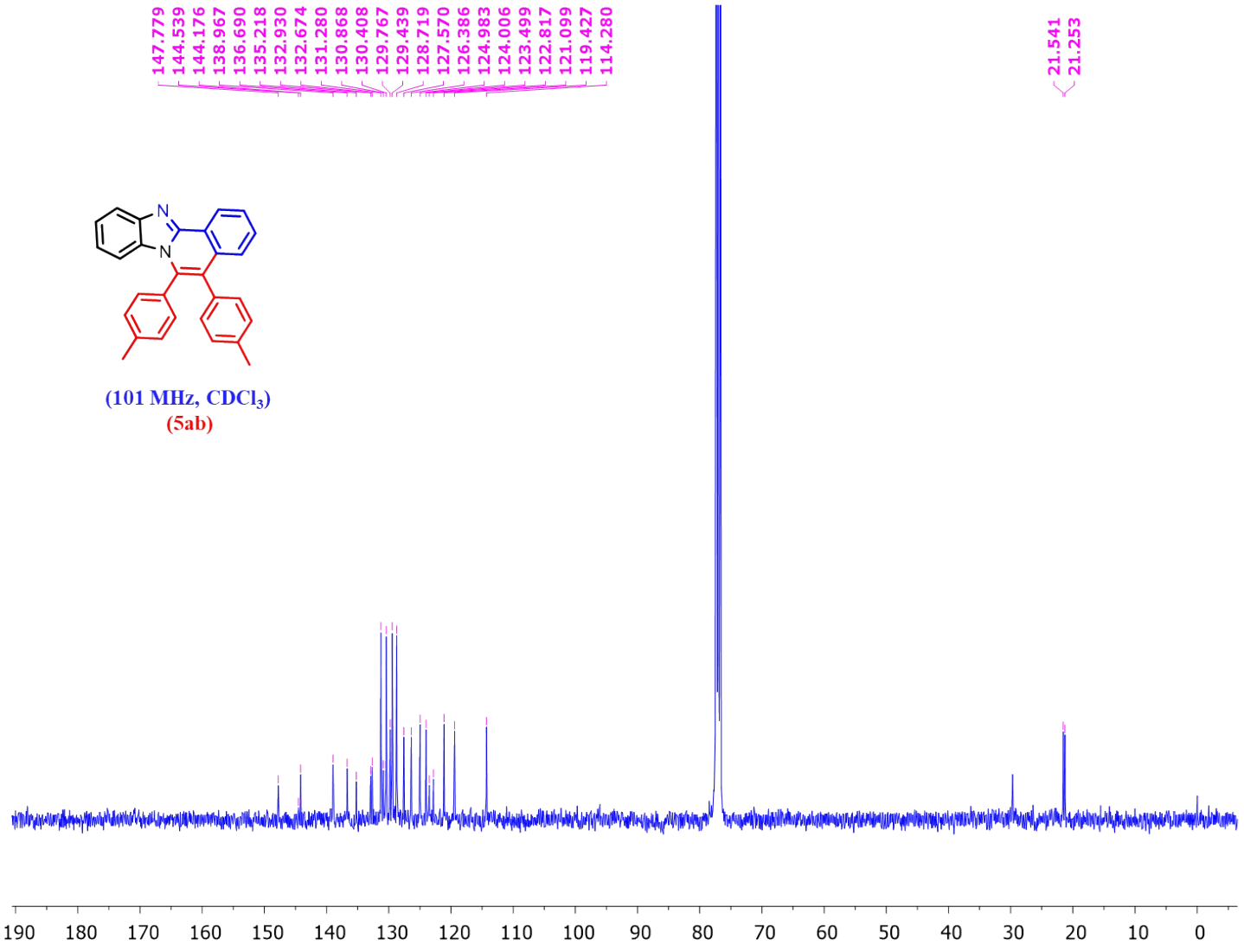


Fig. S47. ^{13}C NMR spectra of 5,6-di-p-tolylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5ab**) in $CDCl_3$.

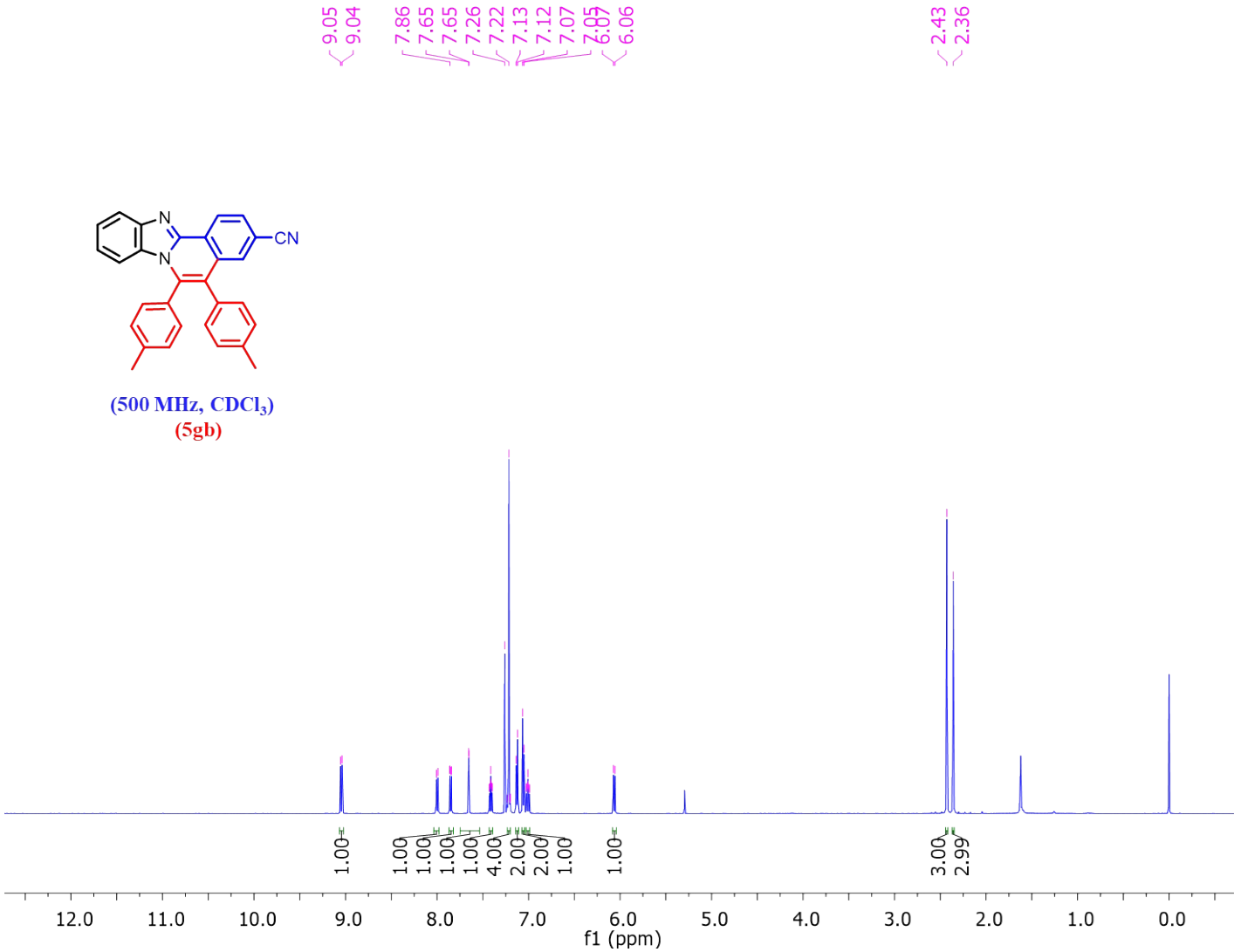


Fig. S48. ^{1}H NMR spectra of 5,6-di-p-tolylbenzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile (**5gb**) in $CDCl_3$.

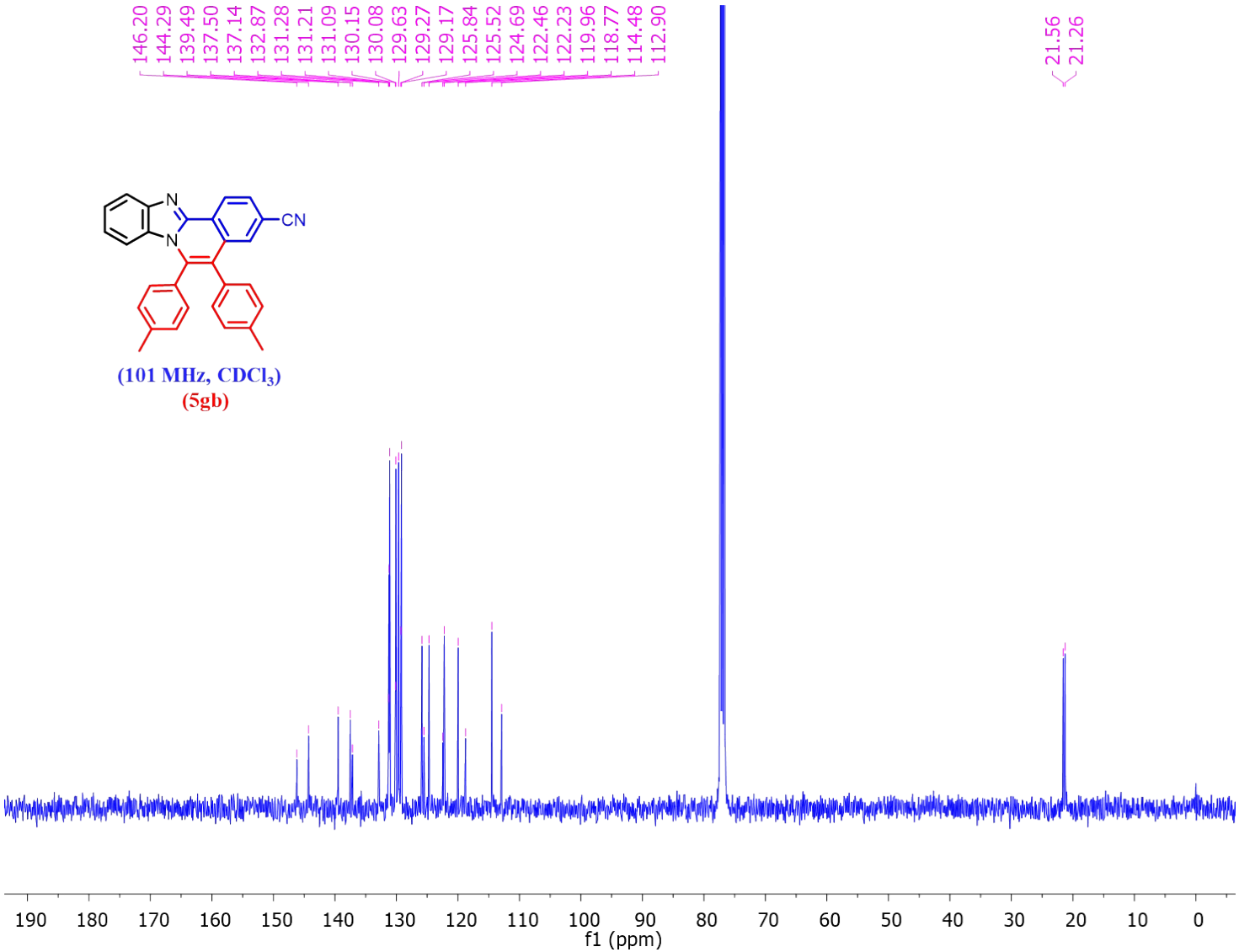


Fig. S49. ^{13}C NMR spectra of 5,6-di-p-tolylbenzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile (**5gb**) in $CDCl_3$.

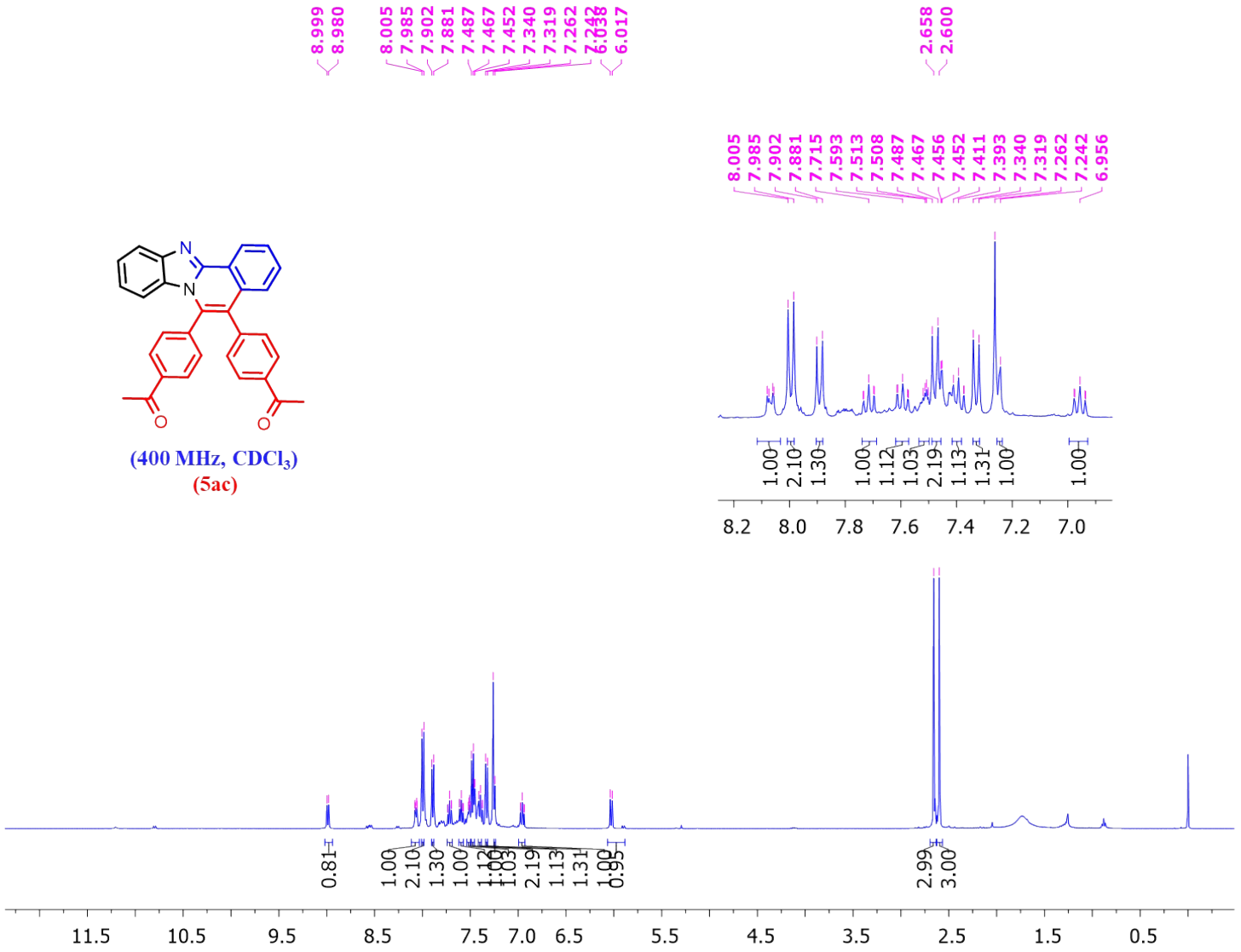


Fig. S50. ^{1}H NMR spectra of 1,1'-(benzo[4,5]imidazo[2,1-a]isoquinoline-5,6-diylbis(4,1-phenylene))bis(ethan-1-one) (**5ac**) in $CDCl_3$.

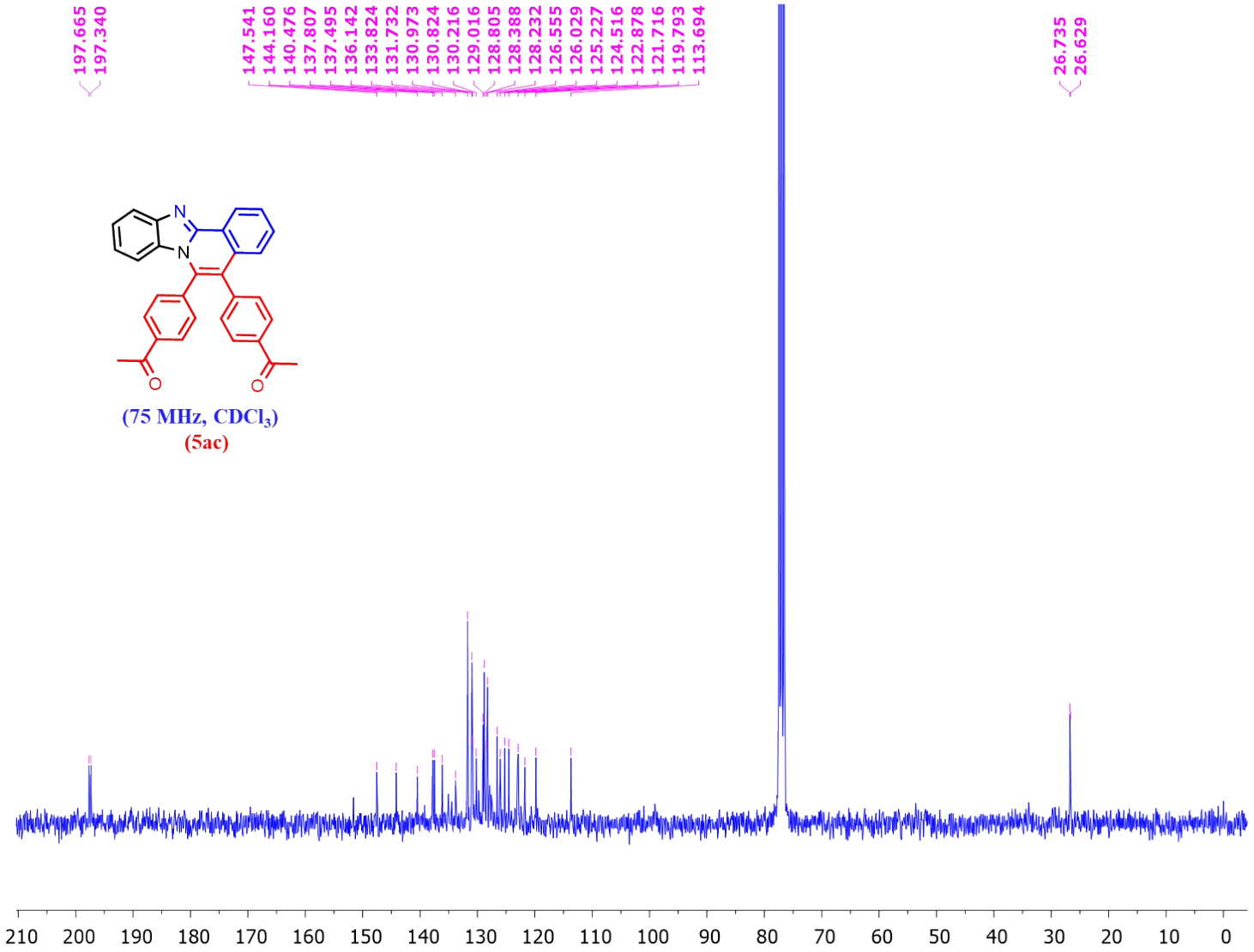


Fig. S51. ^{13}C NMR spectra of 1,1'-(benzo[4,5]imidazo[2,1-a]isoquinoline-5,6-diylbis(4,1-phenylene))bis(ethan-1-one) (**5ac**) in $CDCl_3$.

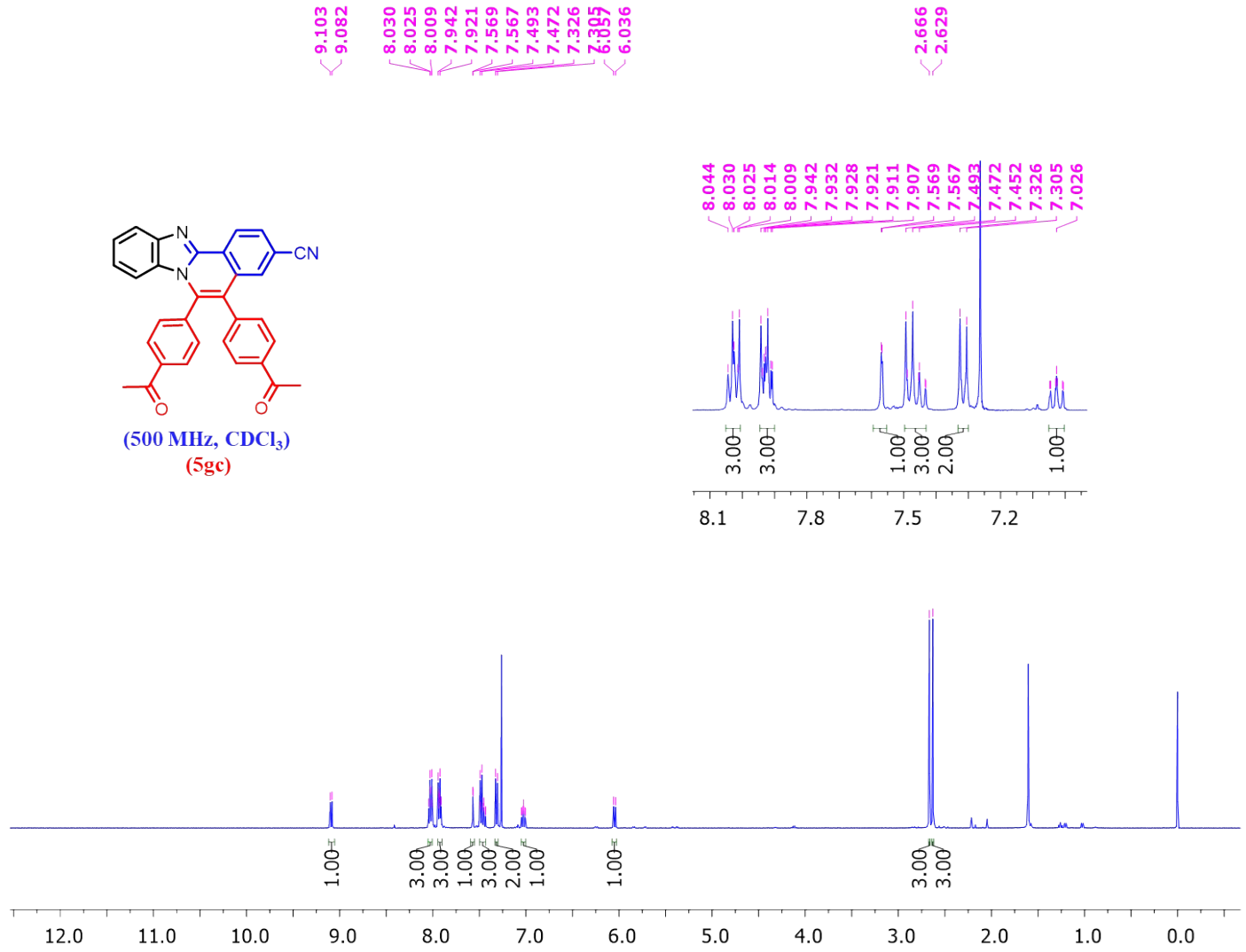


Fig. S52. ^{1}H NMR spectra of 5,6-bis(4-acetylphenyl)benzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile (**5gc**) in $CDCl_3$.

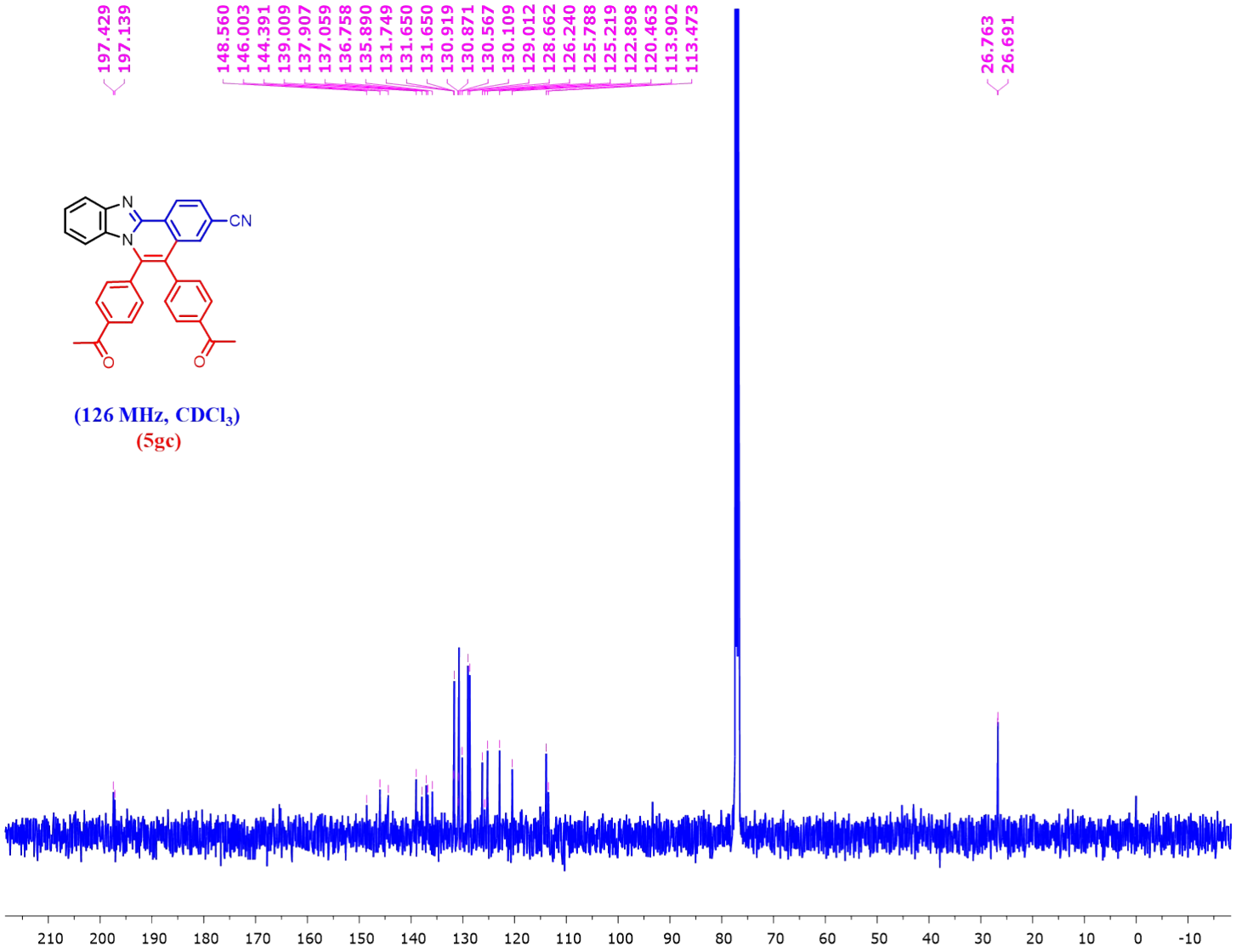


Fig. S53. ^{13}C NMR spectra of 5,6-bis(4-acetylphenyl)benzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile (**5gc**) in $CDCl_3$.

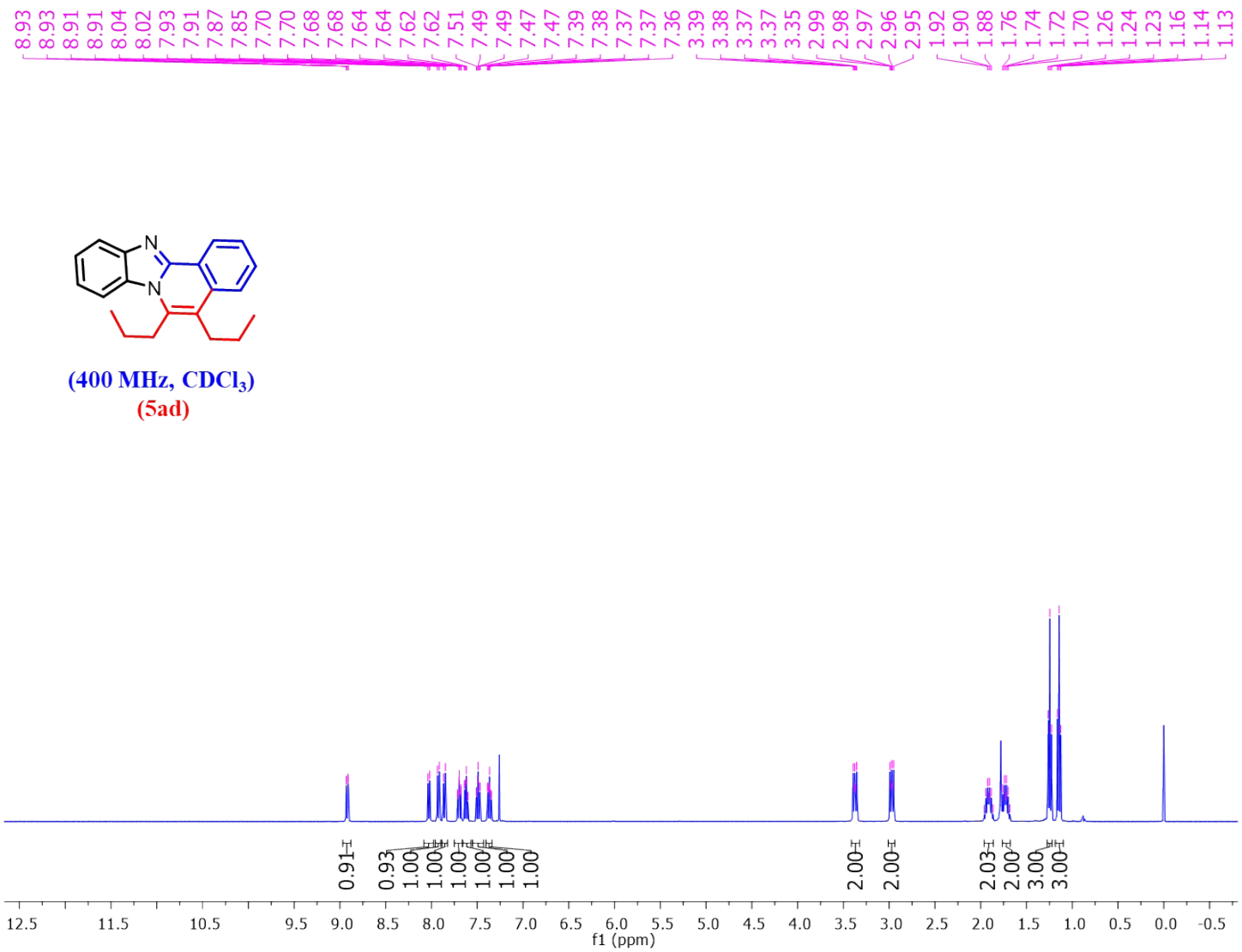


Fig. S54. ^{1}H NMR spectra of 5,6-dipropylbenzo [4,5] imidazo [2,1-a] isoquinoline (**5ad**) in $CDCl_3$.

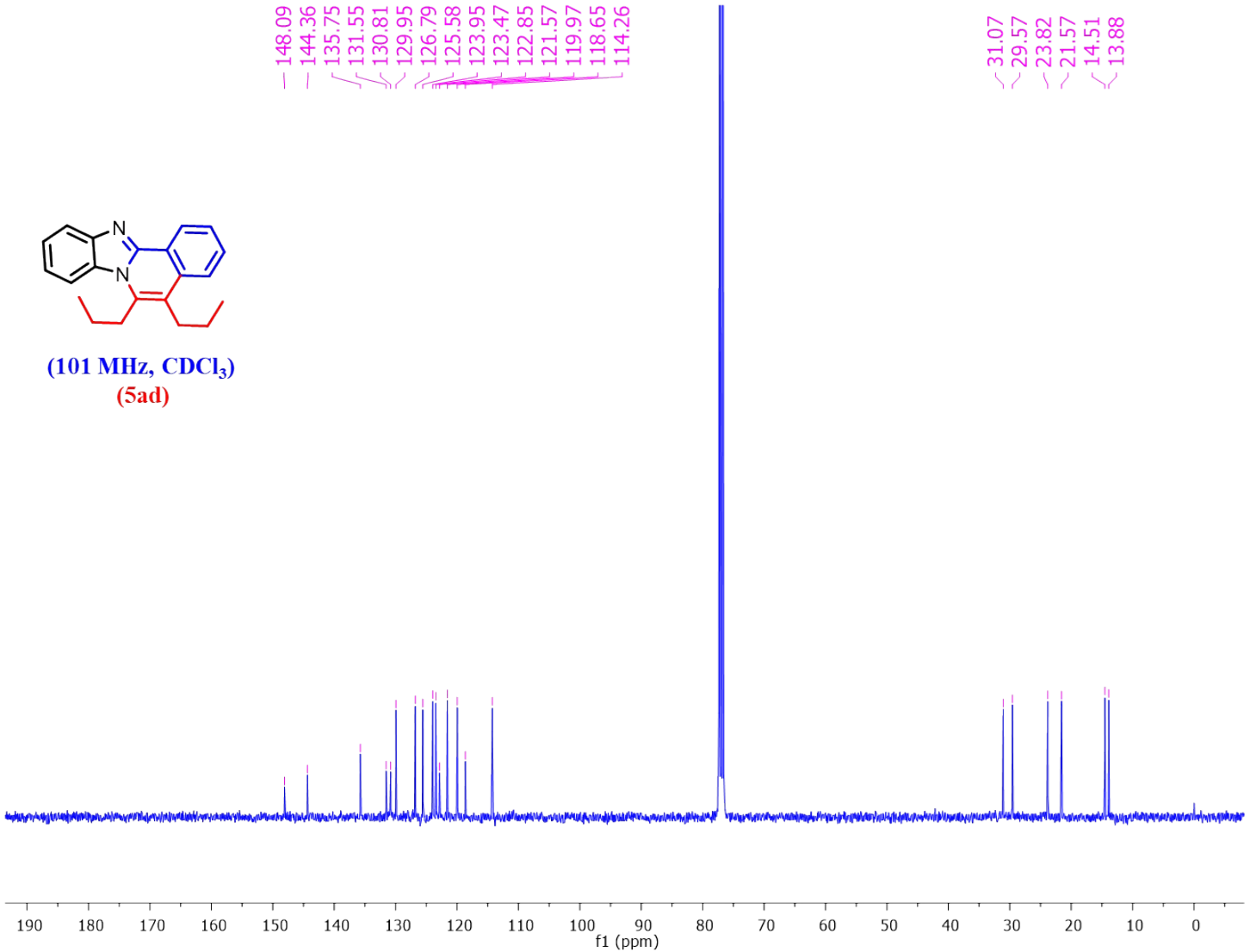


Fig. S55. ^{13}C NMR spectra of 5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5ad**) in $CDCl_3$.

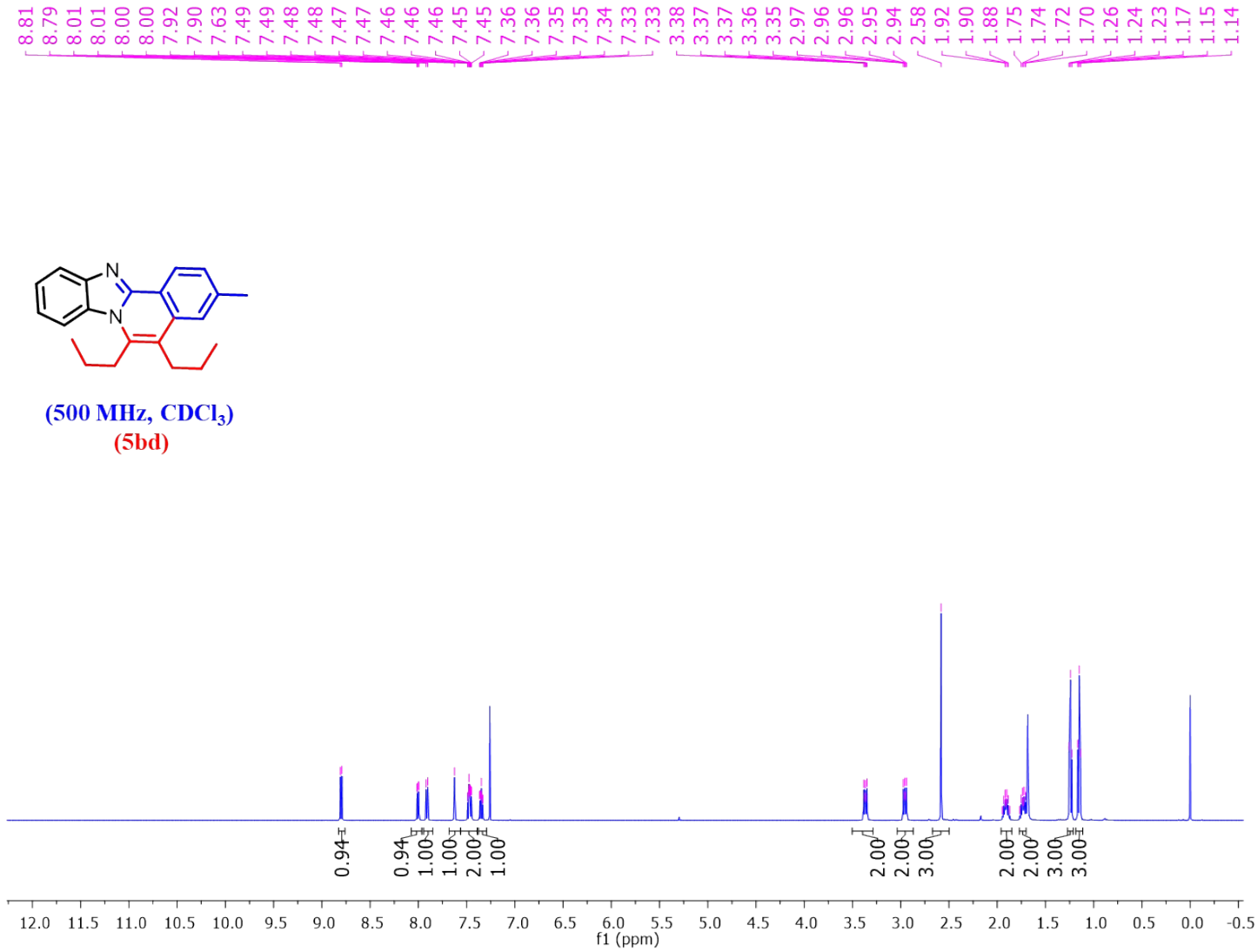


Fig. S56. ^{1}H NMR spectra of 3-methyl-5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5bd**) in $CDCl_3$.

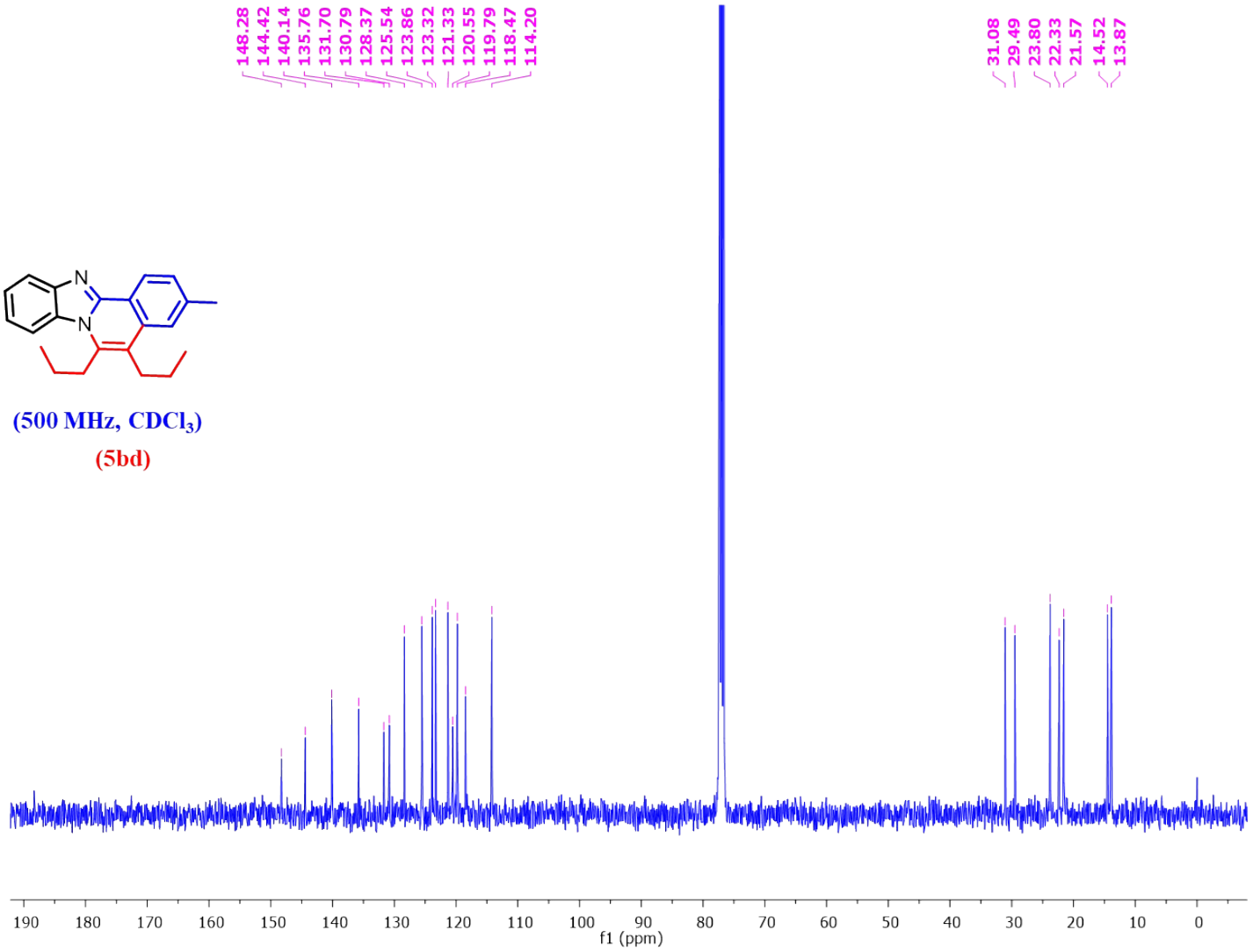


Fig. S57. ^{13}C NMR spectra of 3-methyl-5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5bd**) in $CDCl_3$.

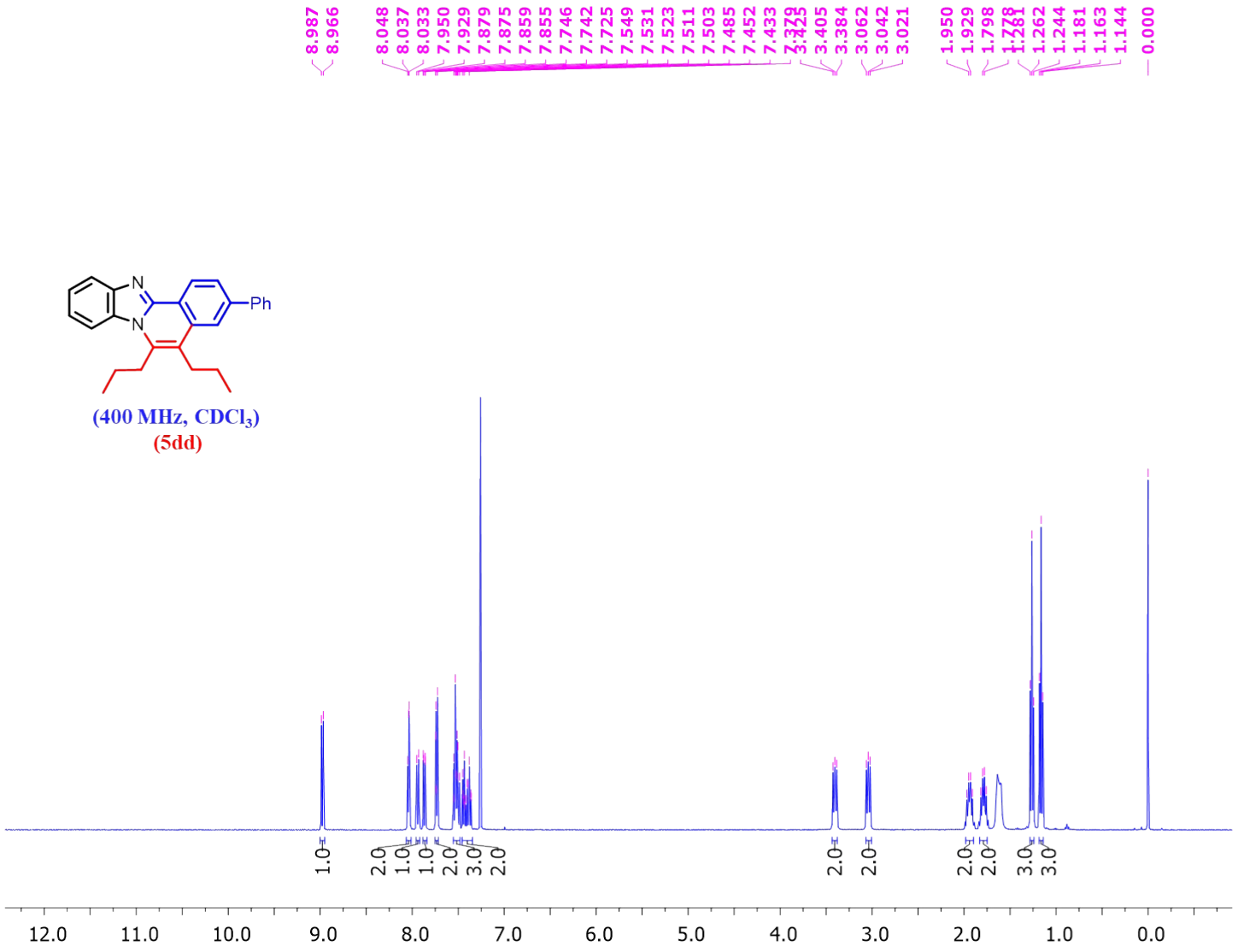


Fig. S58. ^{1}H NMR spectra of 3-phenyl-5,6-dipropylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5dd**) in $CDCl_3$.

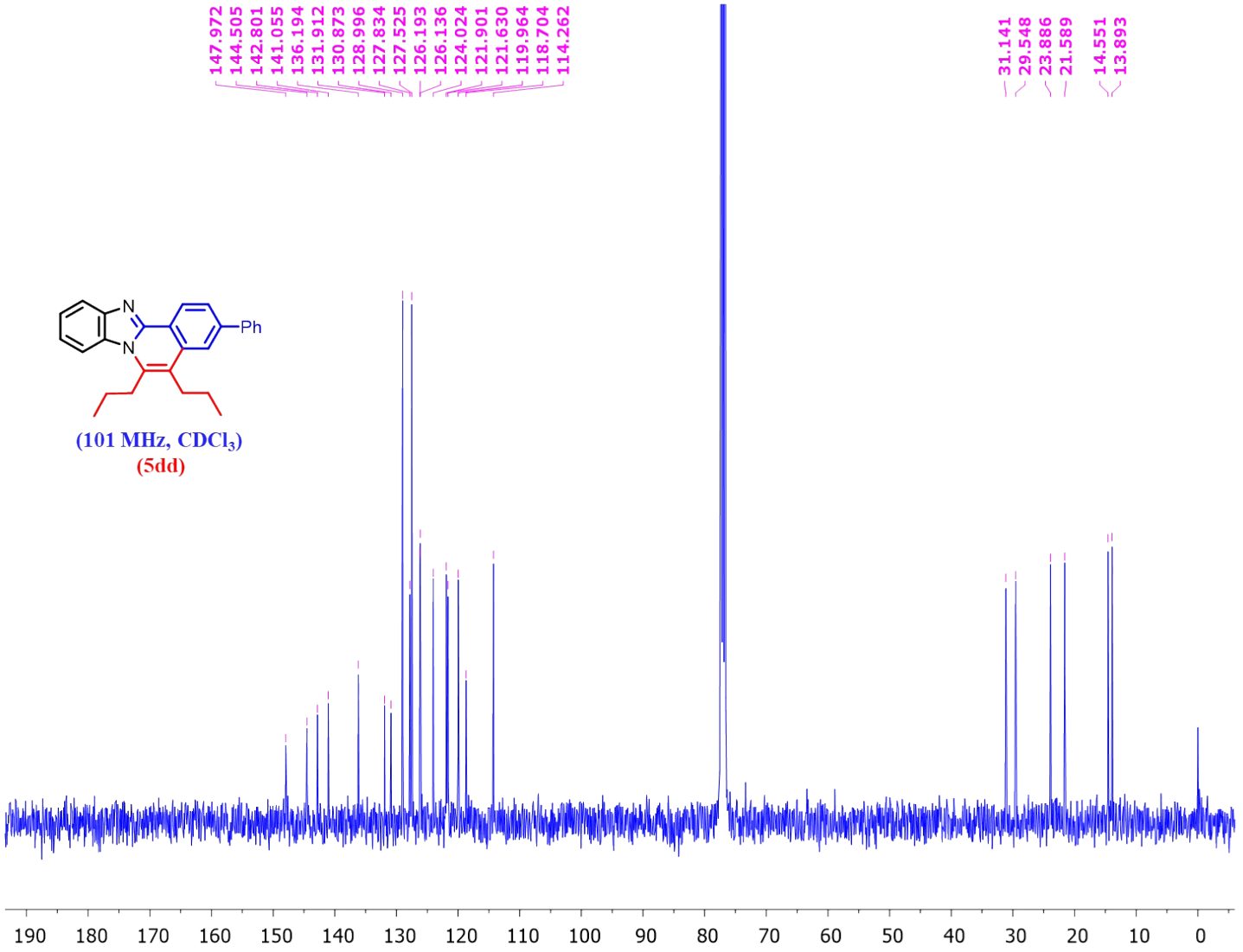


Fig. S59. ^{13}C NMR spectra of 3-phenyl-5,6-dipropylbenzo[4,5]imidazo[2,1-a]isoquinoline (**5dd**) in $CDCl_3$.

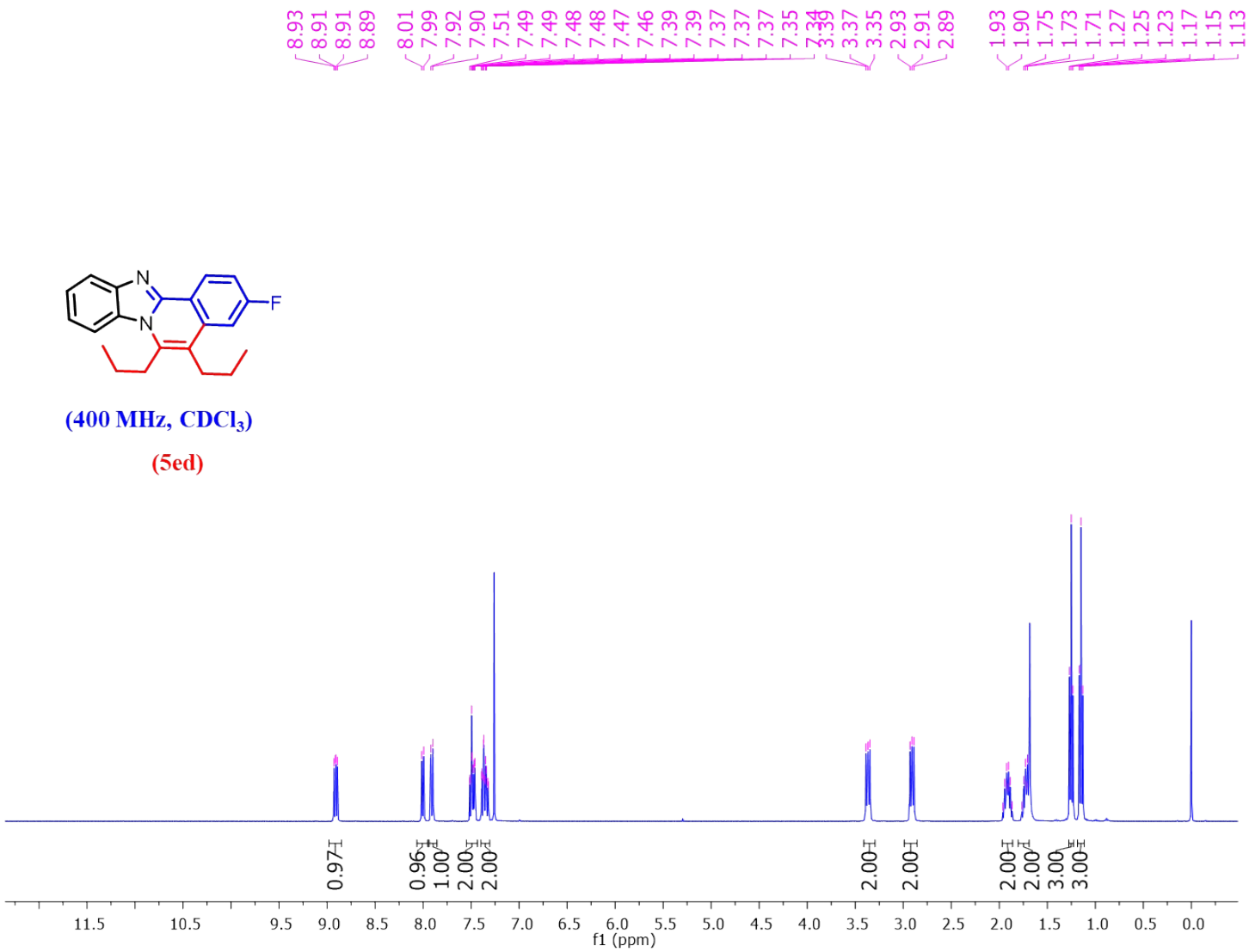


Fig. S60. ^{1}H NMR spectra of 3-fluoro-5,6-dipropylbenzo [4,5] imidazo [2,1-a] isoquinoline (**5ed**) in $CDCl_3$.

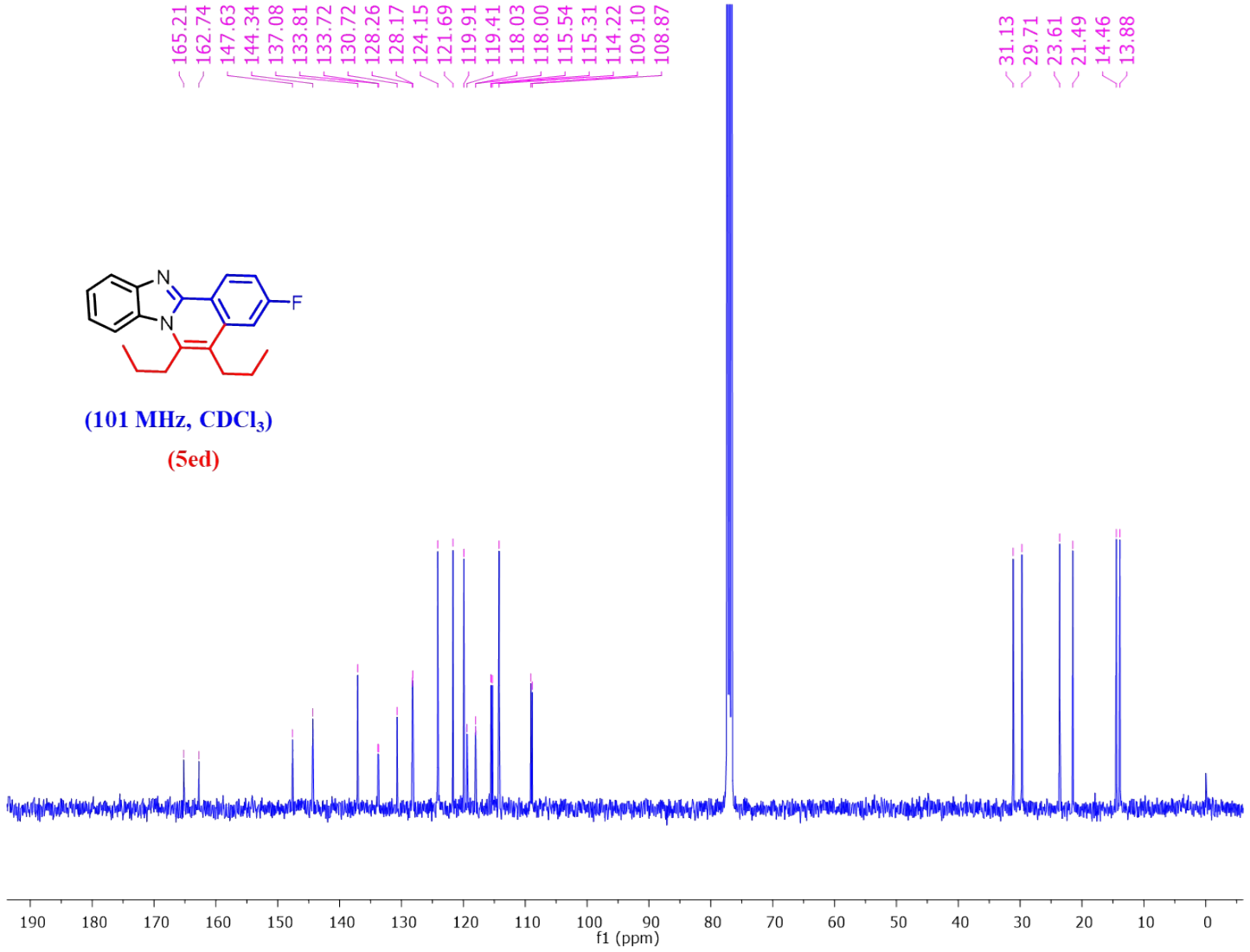


Fig. S61. ^{13}C NMR spectra of 3-fluoro-5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5ed**) in $CDCl_3$.

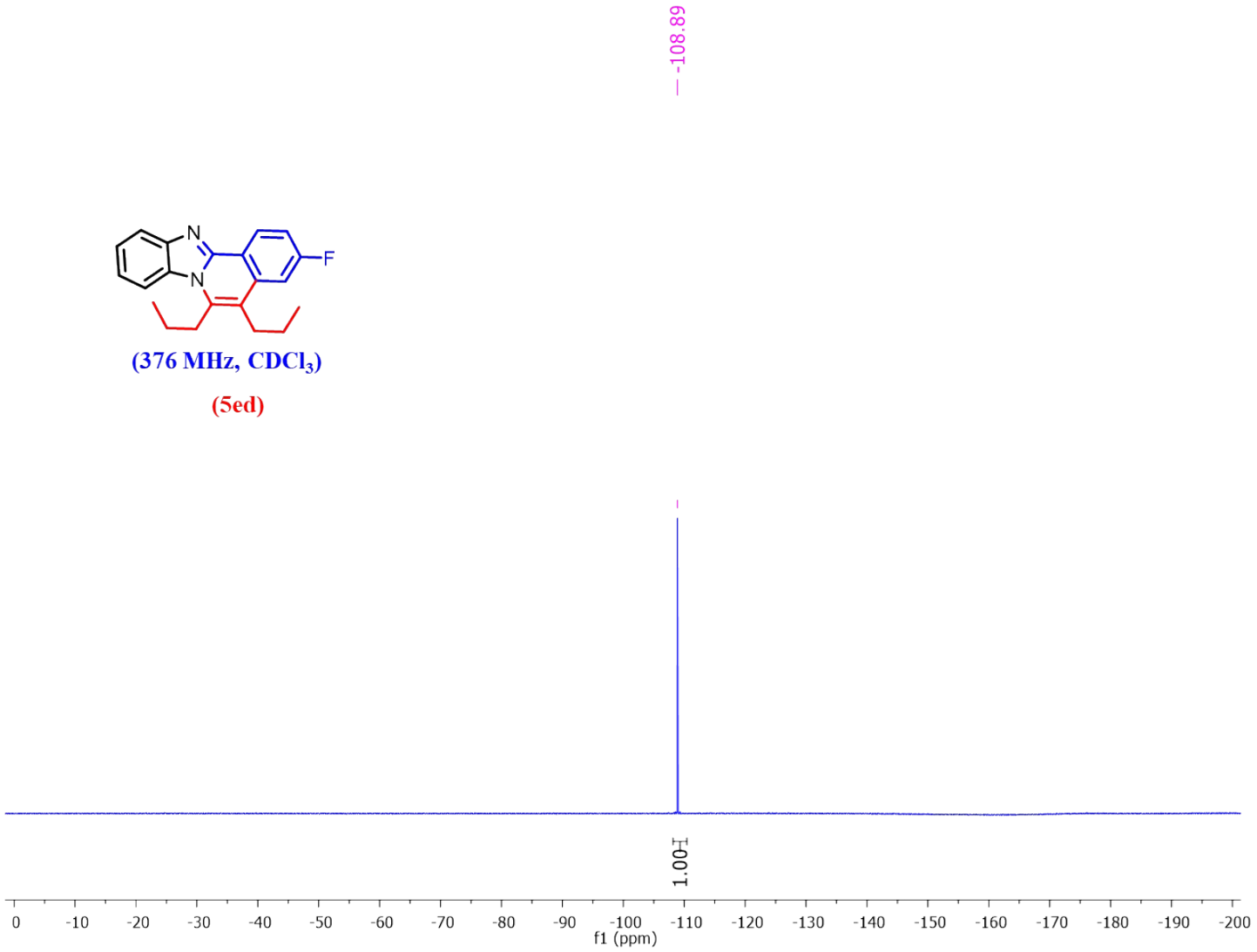


Fig. S62. IR spectra of 3-fluoro-5,6-dipropylbenzo [4,5] imidazo [2,1-a] isoquinoline (**5ed**) in $CDCl_3$.

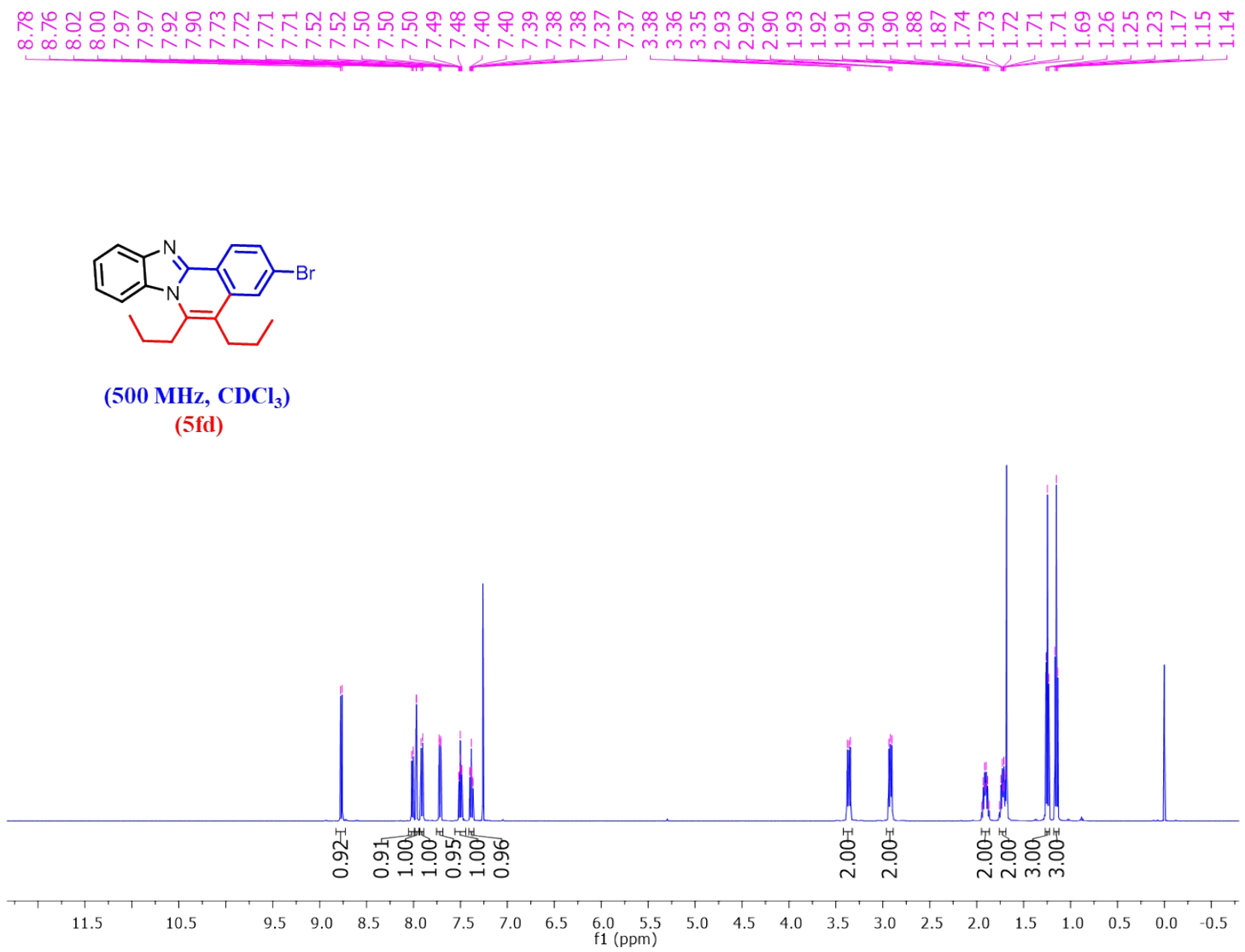


Fig. S63. ^{1}H NMR spectra of 3-bromo-5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5fd**) in $CDCl_3$.

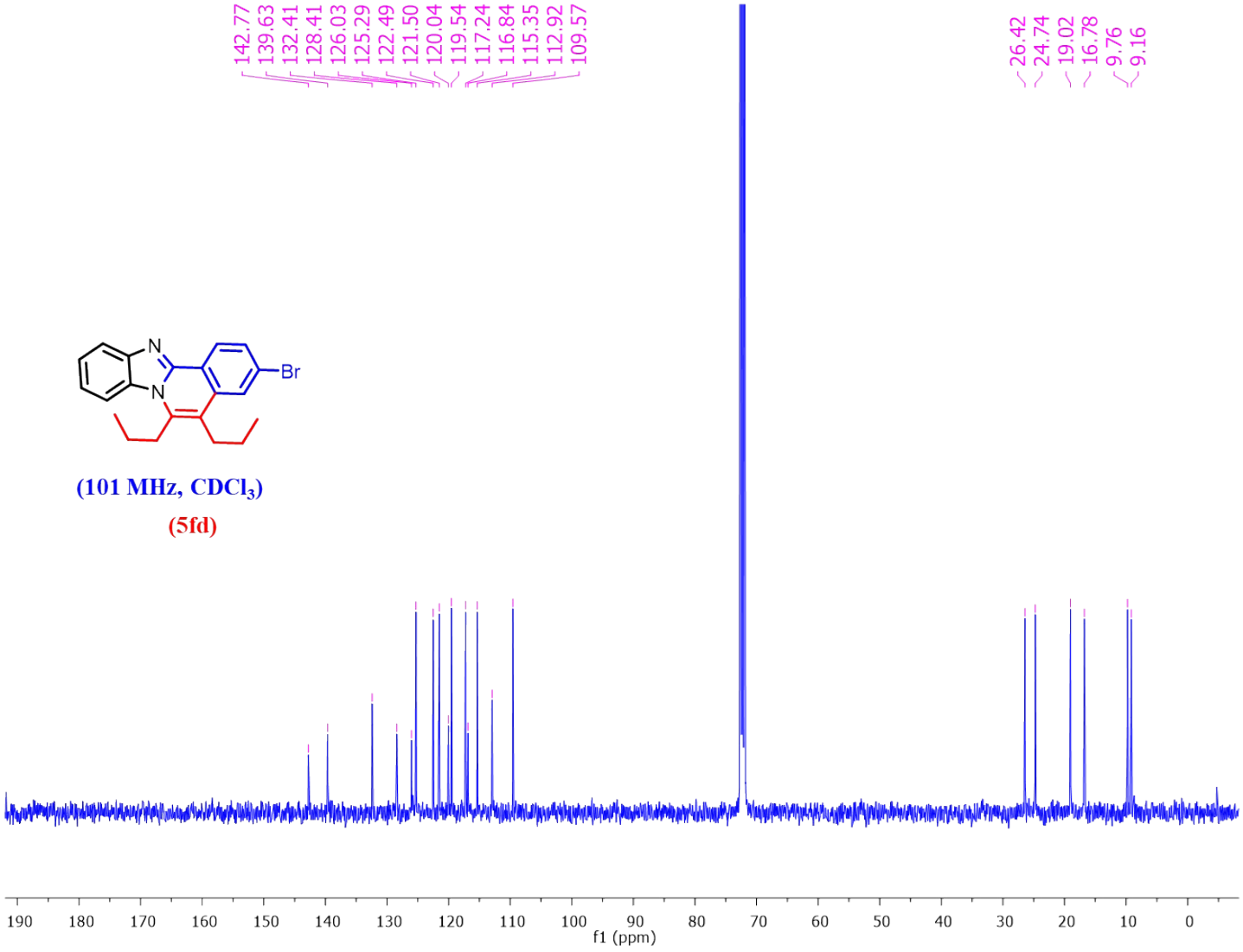


Fig. S64. ^{13}C NMR spectra of 3-bromo-5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5fd**) in $CDCl_3$.

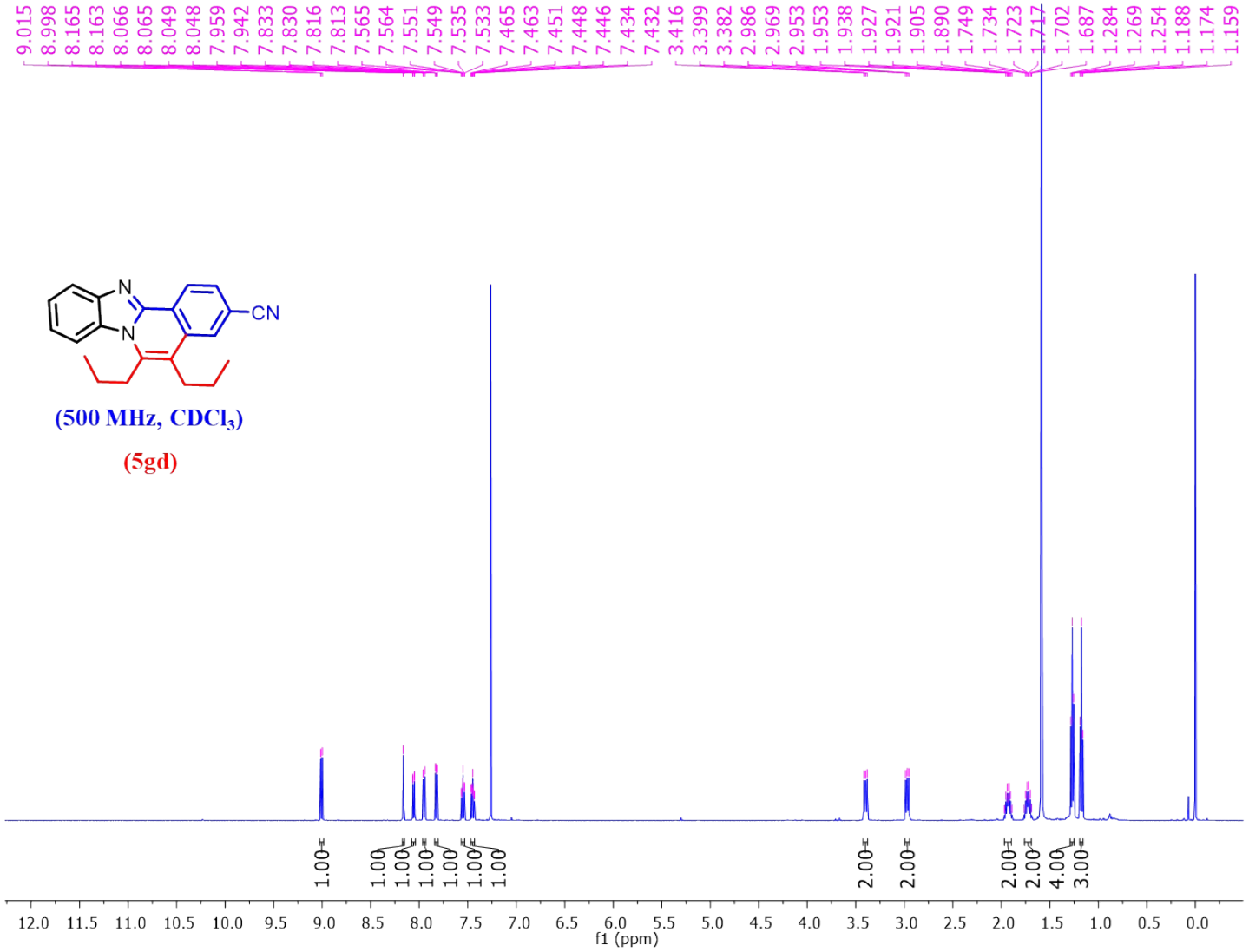


Fig. S65. ^{1}H NMR spectra of 5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline-3-carbonitrile (**5gd**) in $CDCl_3$.

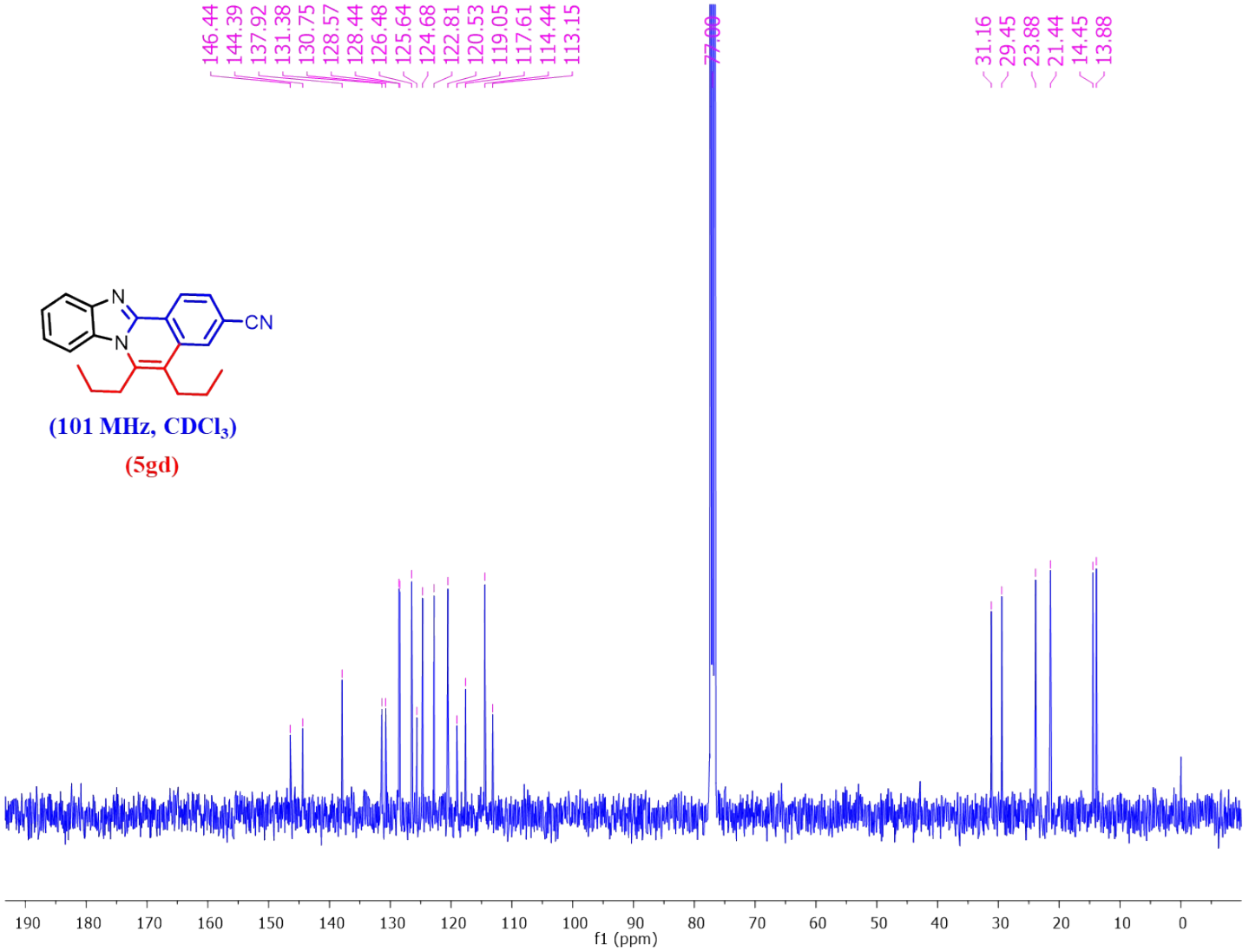


Fig. S66. ^{13}C NMR spectra of 5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline-3-carbonitrile (**5gd**) in $CDCl_3$.

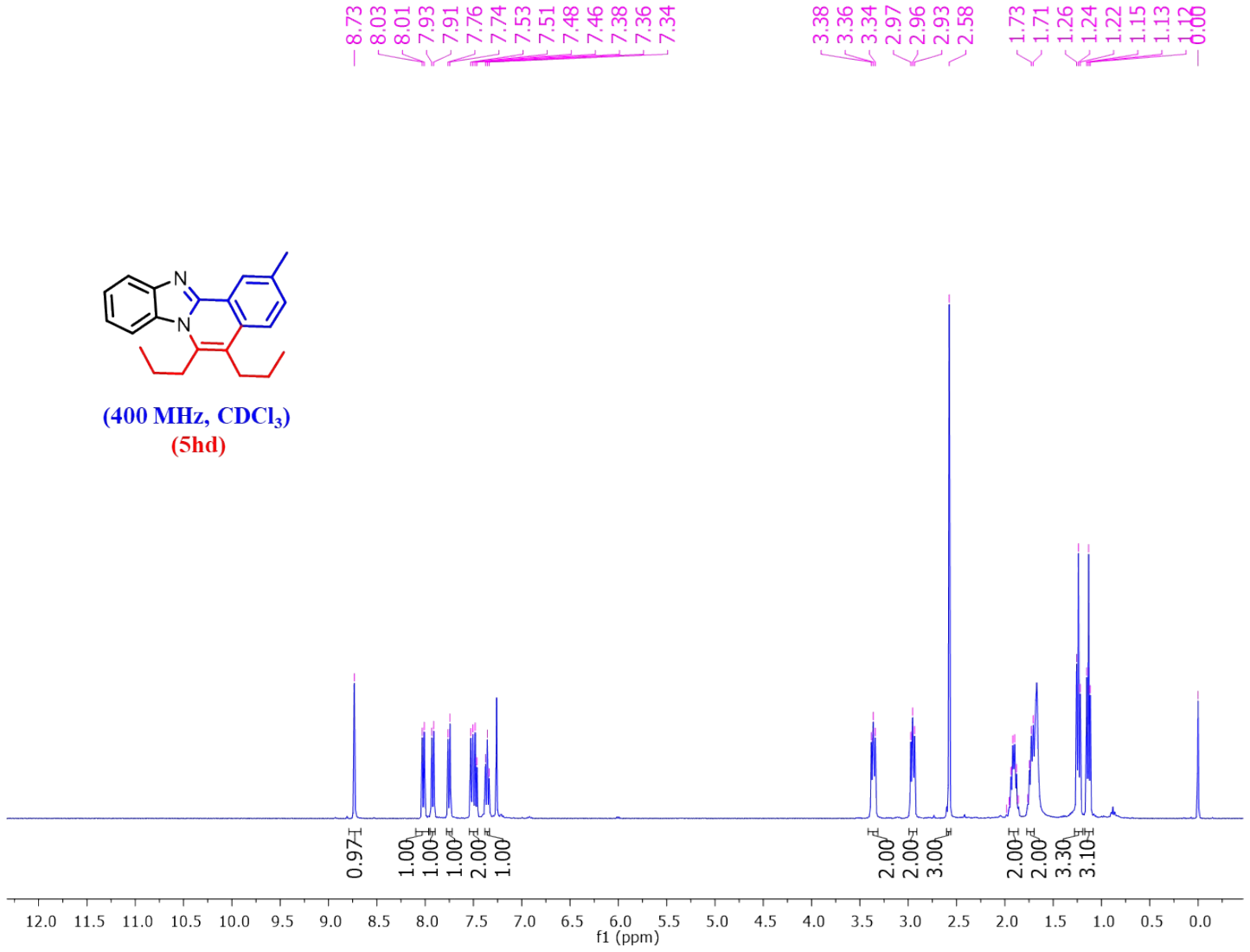


Fig. S67. ^{1}H NMR spectra of 2-methyl-5,6-dipropylbenzo [4,5] imidazo [2,1-a] isoquinoline (**5hd**) in $CDCl_3$.

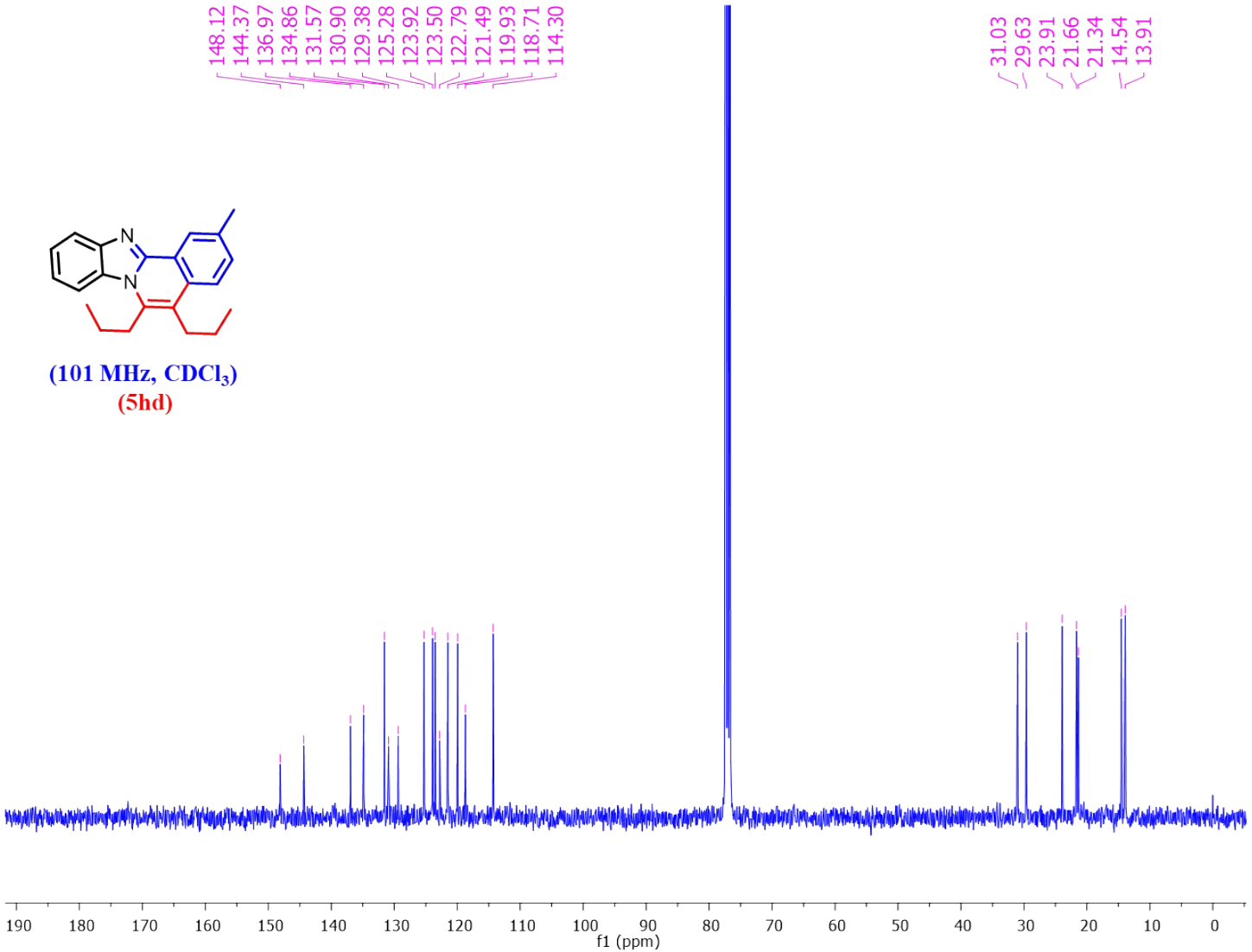


Fig. S68. ^{13}C NMR spectra of 2-methyl-5,6-dipropylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5hd**) in $CDCl_3$.

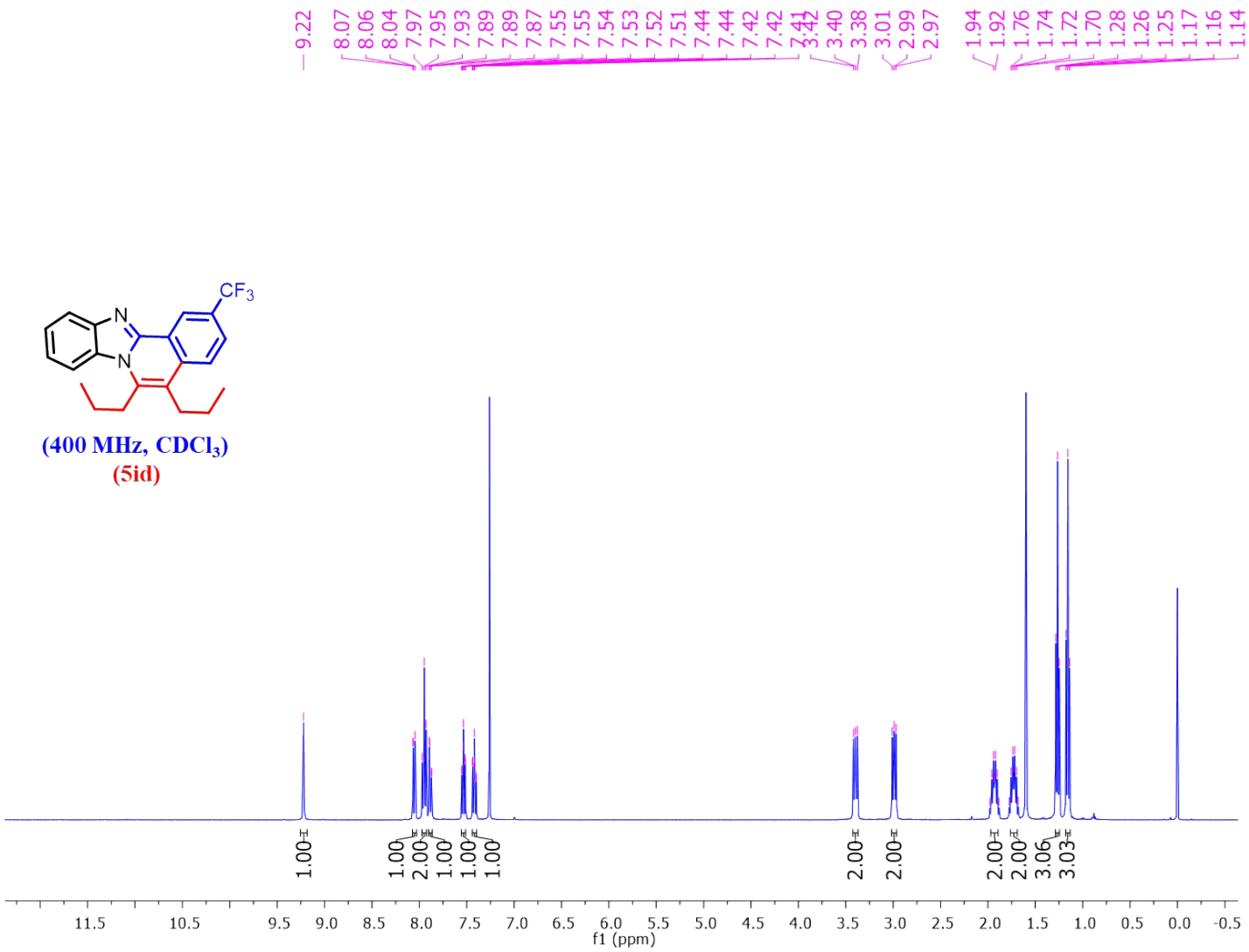


Fig. S69. ^{1}H NMR spectra of 5,6-dipropyl-2-(trifluoromethyl) benzo [4,5] imidazo[2,1-a] isoquinoline (**5id**) in $CDCl_3$.

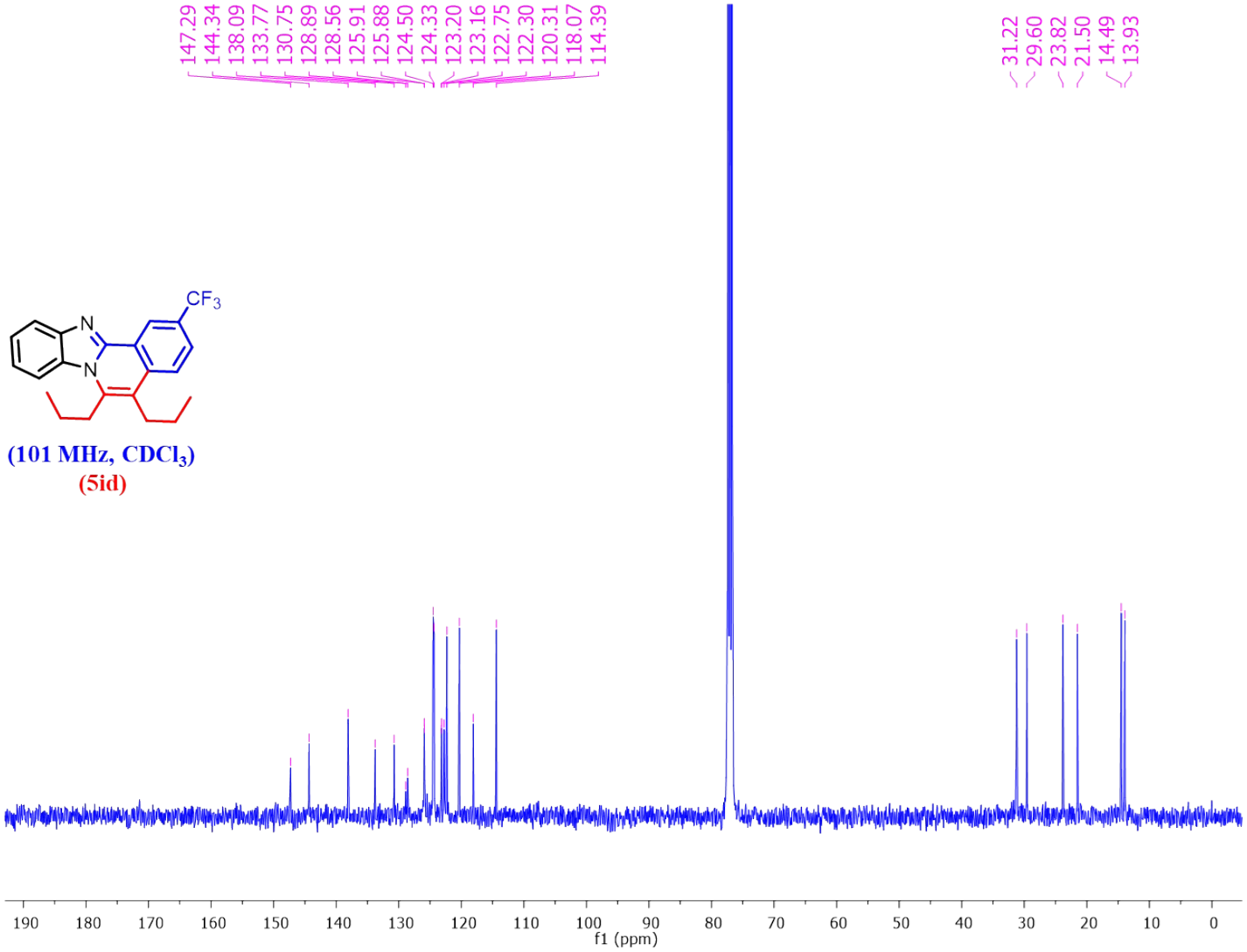


Fig. S70. ^{13}C NMR spectra of 5,6-dipropyl-2-(trifluoromethyl) benzo [4,5] imidazo[2,1-a] isoquinoline (**5id**) in $CDCl_3$.

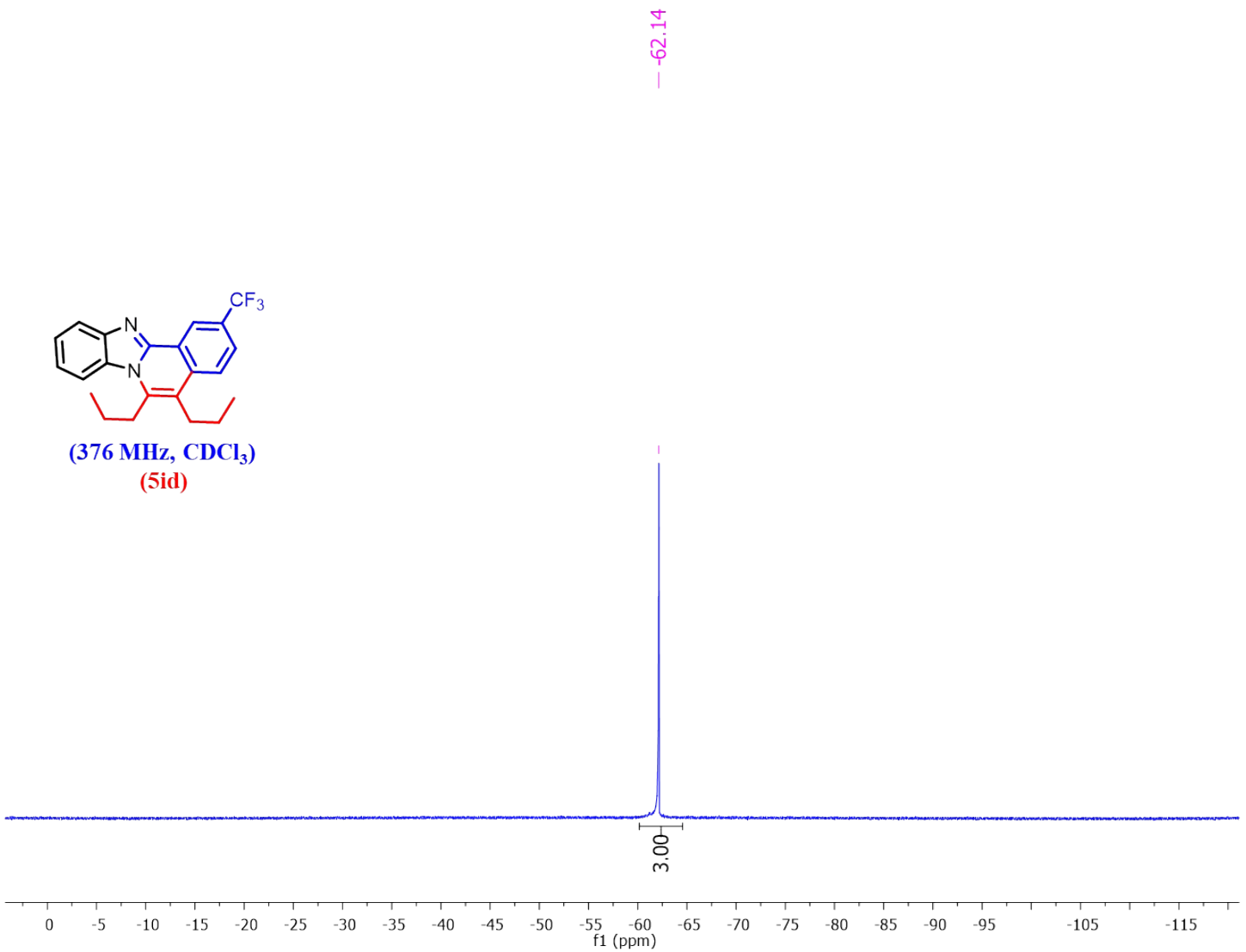


Fig. S71. ^{19}F NMR spectra of 5,6-dipropyl-2-(trifluoromethyl) benzo [4,5] imidazo [2,1-a] isoquinoline (**5id**) in $CDCl_3$.

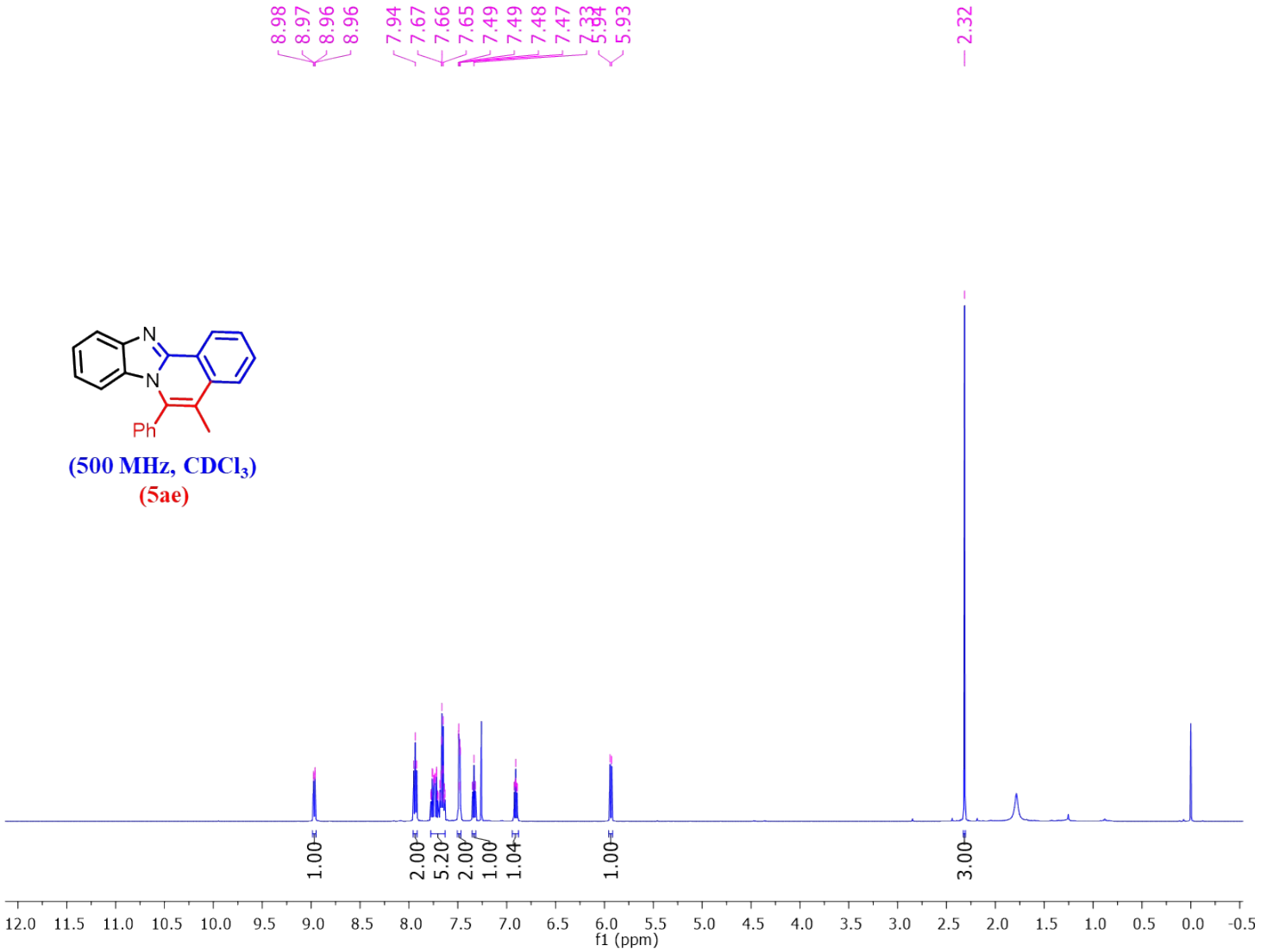


Fig. S72. ^{1}H NMR spectra of 5-methyl-6-phenylbenzo [4,5] imidazo [2,1-a] isoquinoline (**5ae**) in $CDCl_3$.

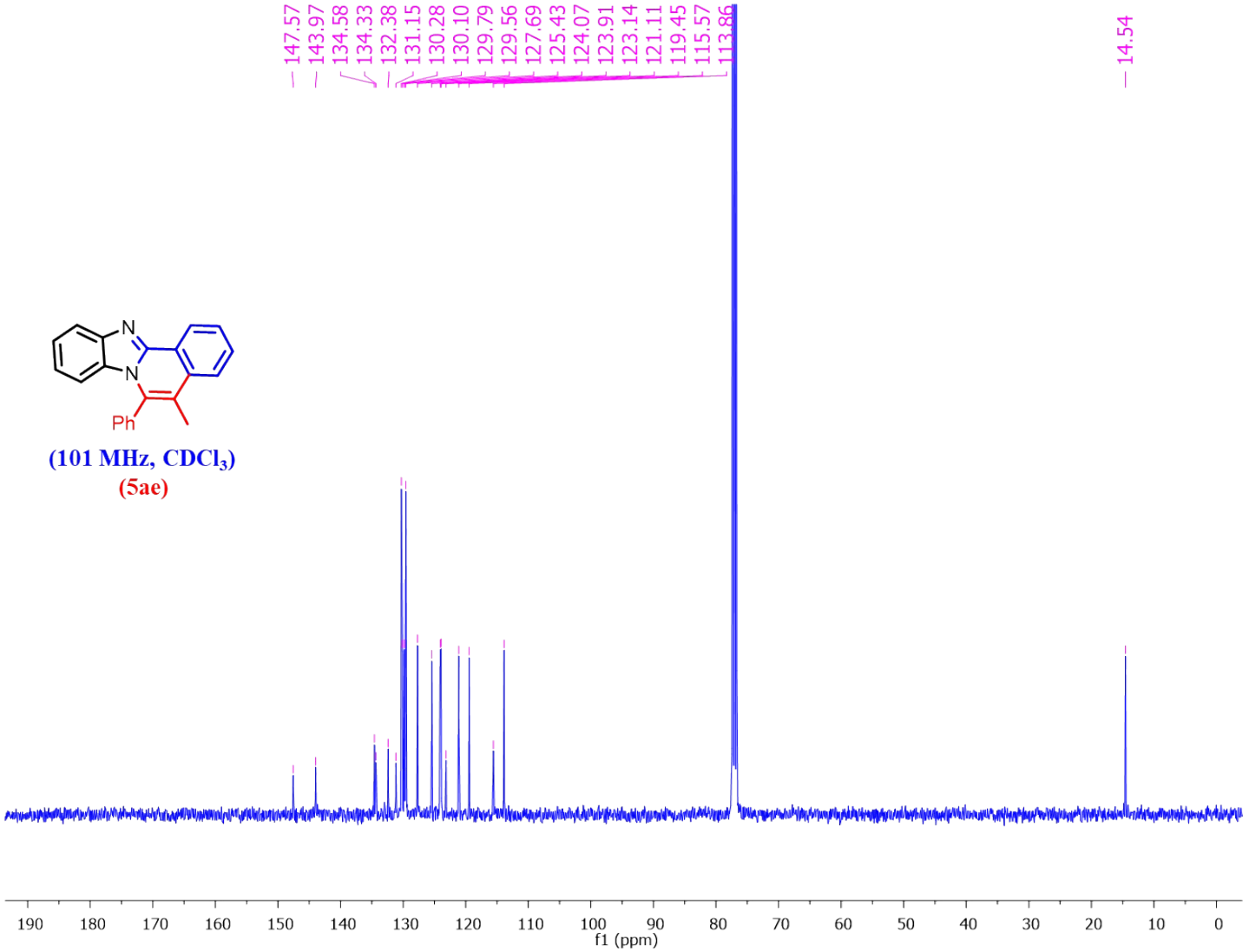


Fig. S73. ^{13}C NMR spectra of 5-methyl-6-phenylbenzo [4,5] imidazo [2,1-a] isoquinoline (**5ae**) in $CDCl_3$.

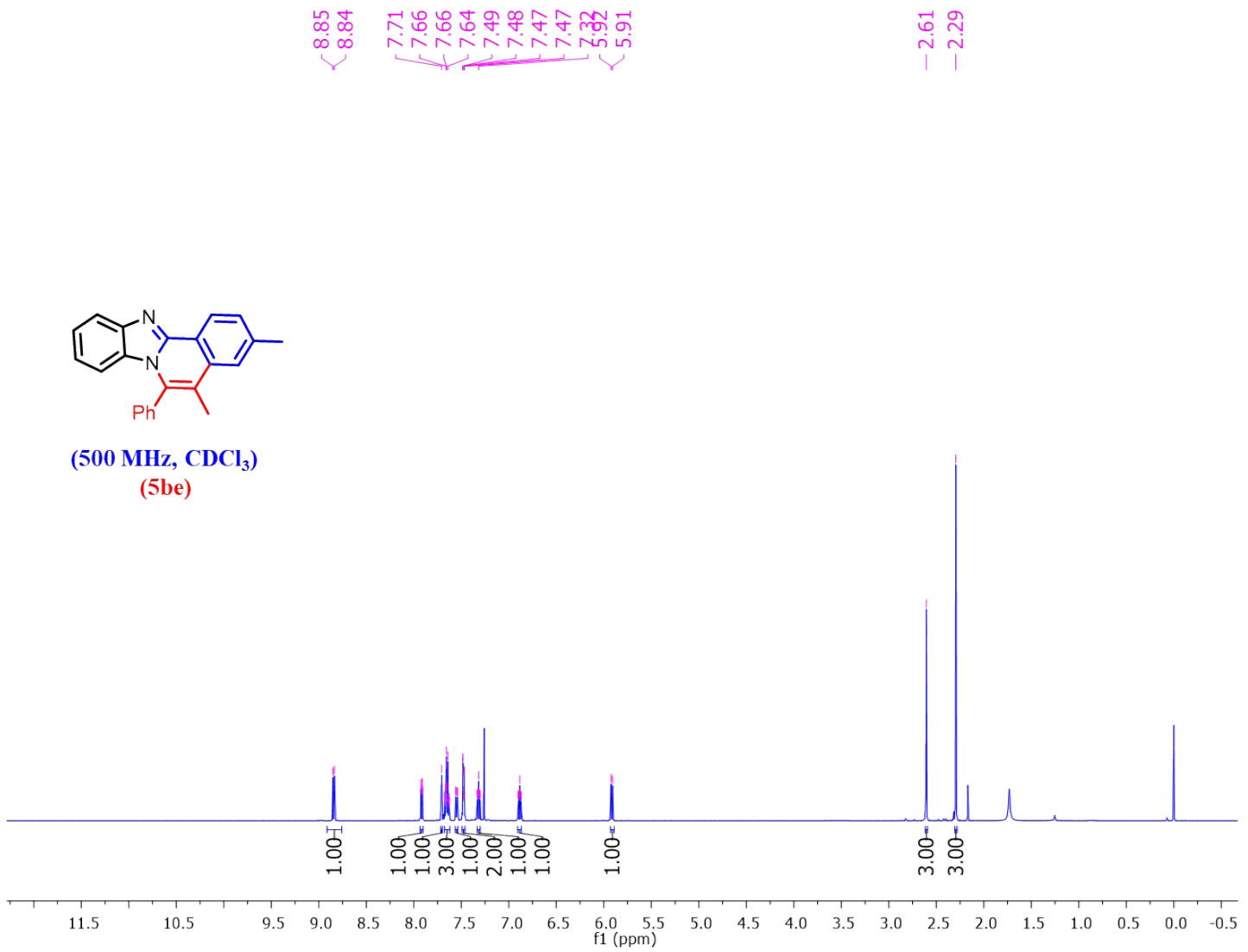


Fig. S74. ^{1}H NMR spectra of 3,5-dimethyl-6-phenylbenzo [4,5] imidazo [2,1-a] isoquinoline (**5be**) in $CDCl_3$.

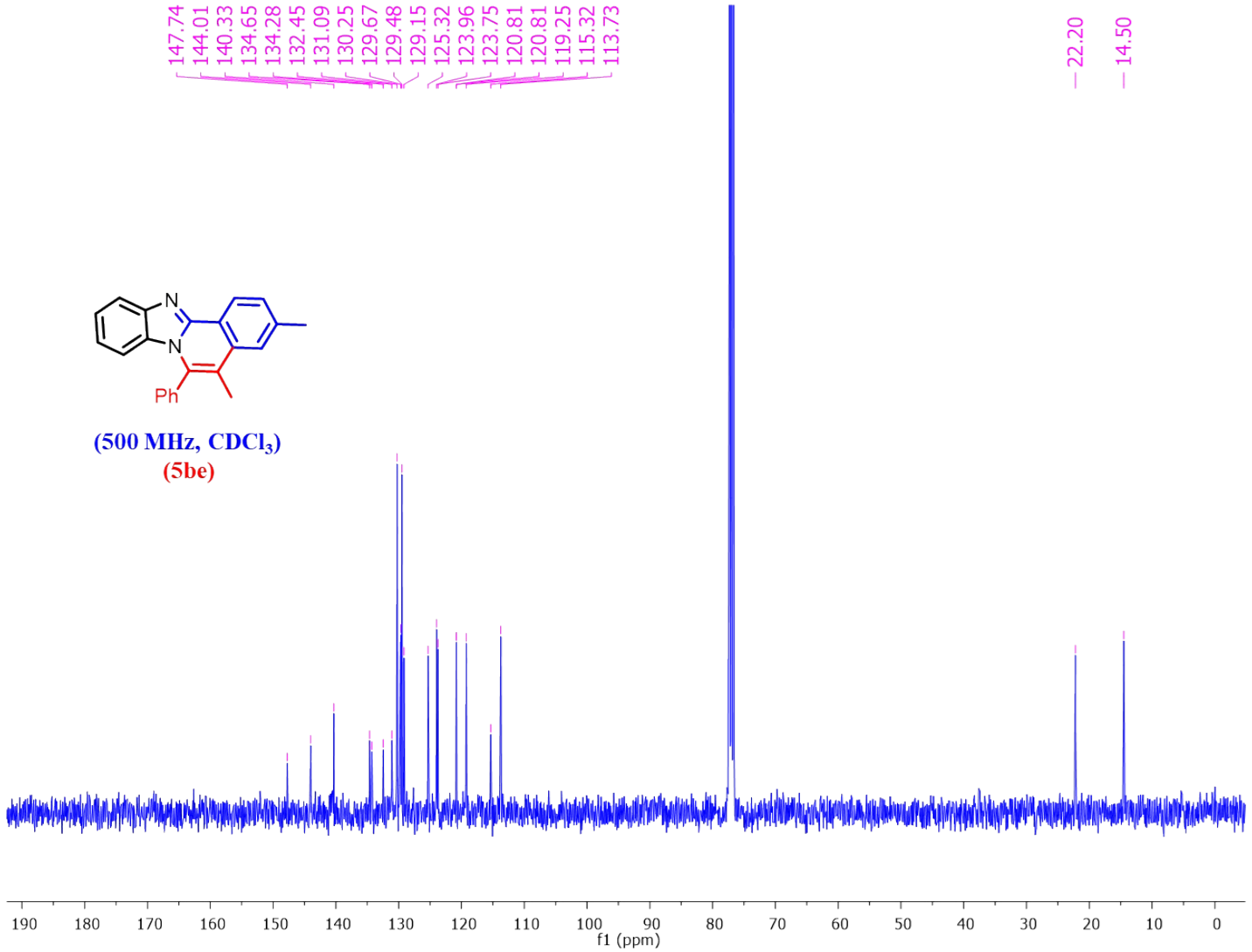


Fig. S75. ^{13}C NMR spectra of 3,5-dimethyl-6-phenylbenzo [4,5] imidazo [2,1-a] isoquinoline (**5be**) in $CDCl_3$.

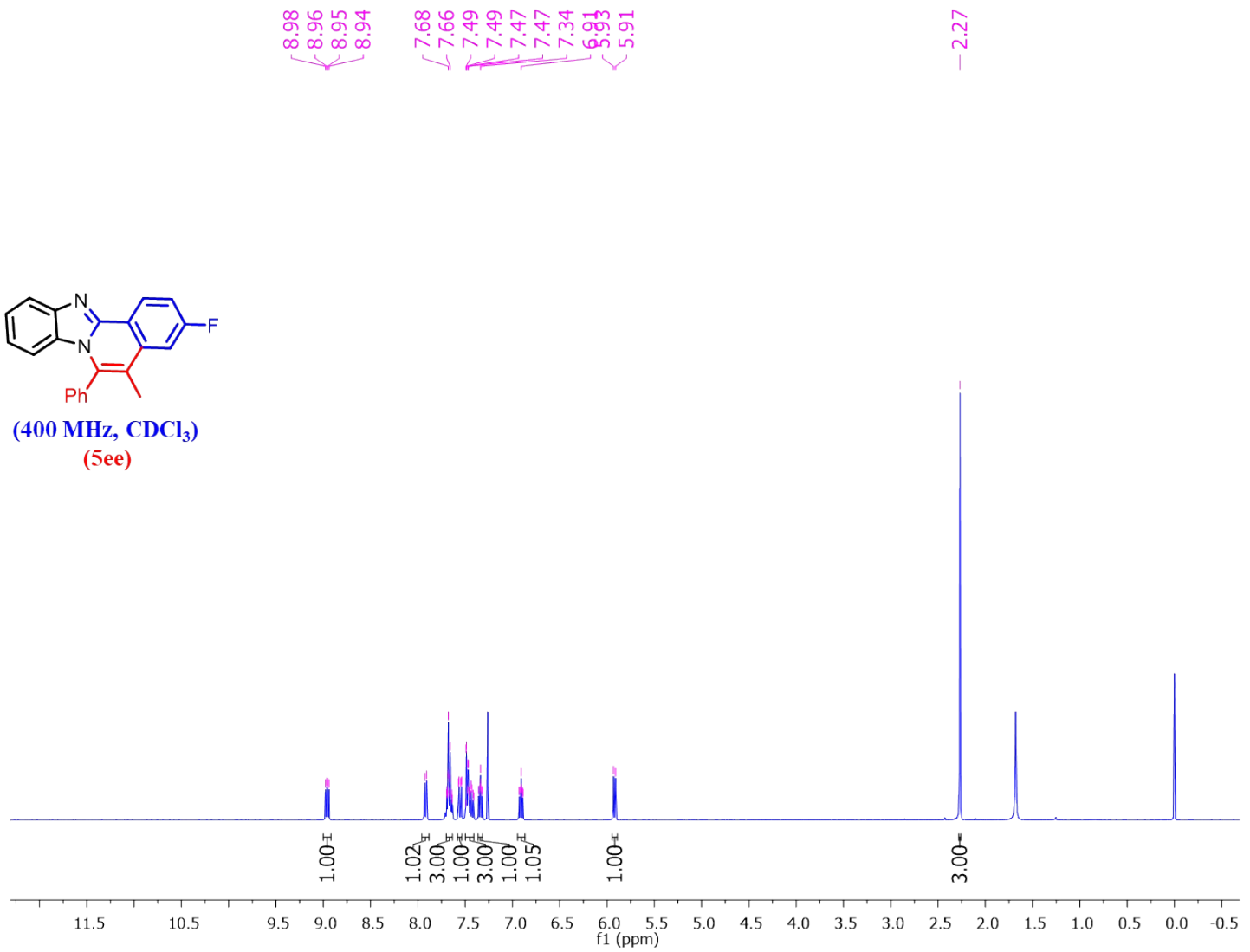


Fig. S.76 ^{1}H NMR spectra of 3-fluoro-5-methyl-6-phenylbenzo [4,5] imidazo [2,1-a] isoquinoline (**5ee**) in $CDCl_3$.

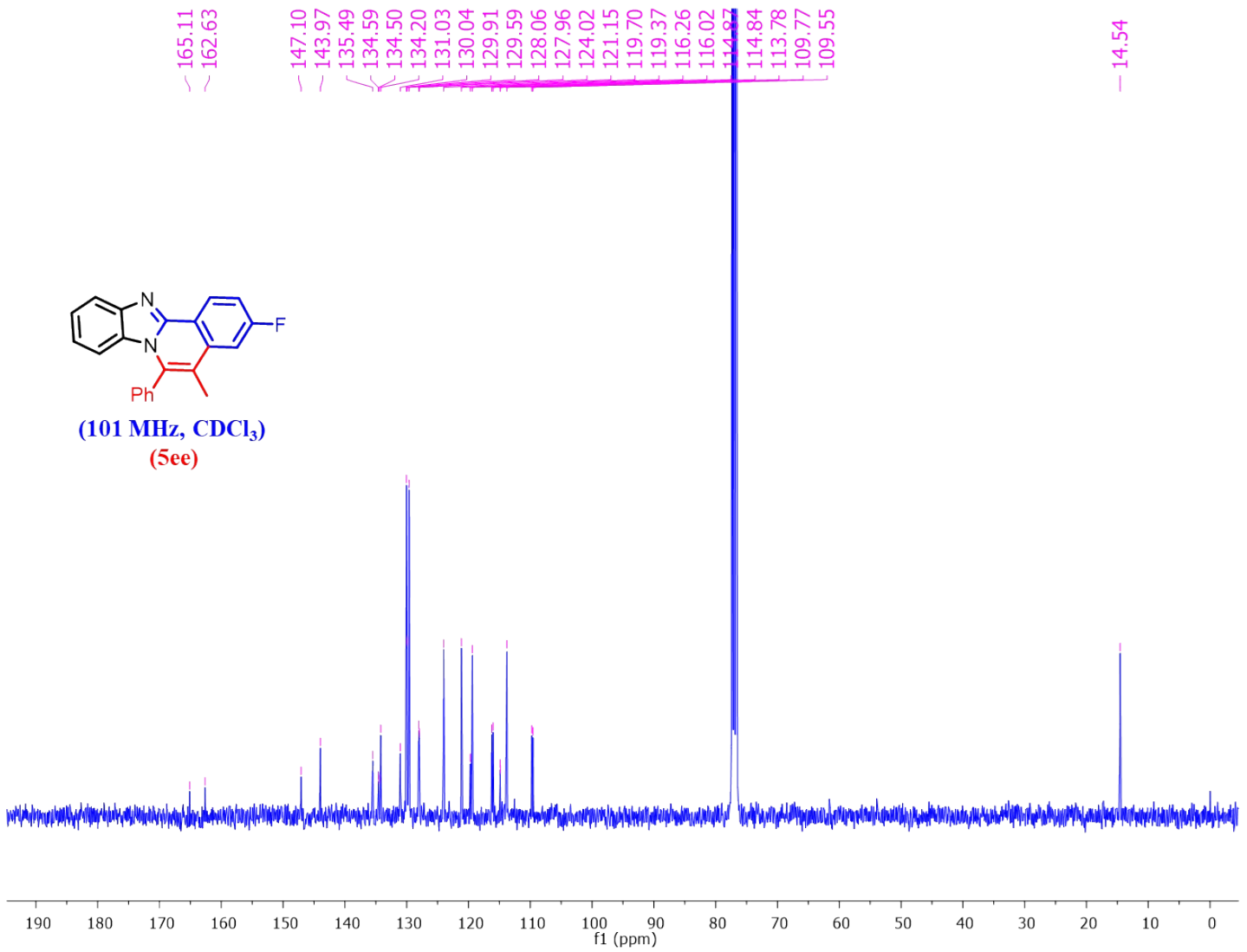


Fig. S77. ^{13}C NMR spectra of 3-fluoro-5-methyl-6-phenylbenzo [4,5] imidazo[2,1-a] isoquinoline (**5ee**) in $CDCl_3$.

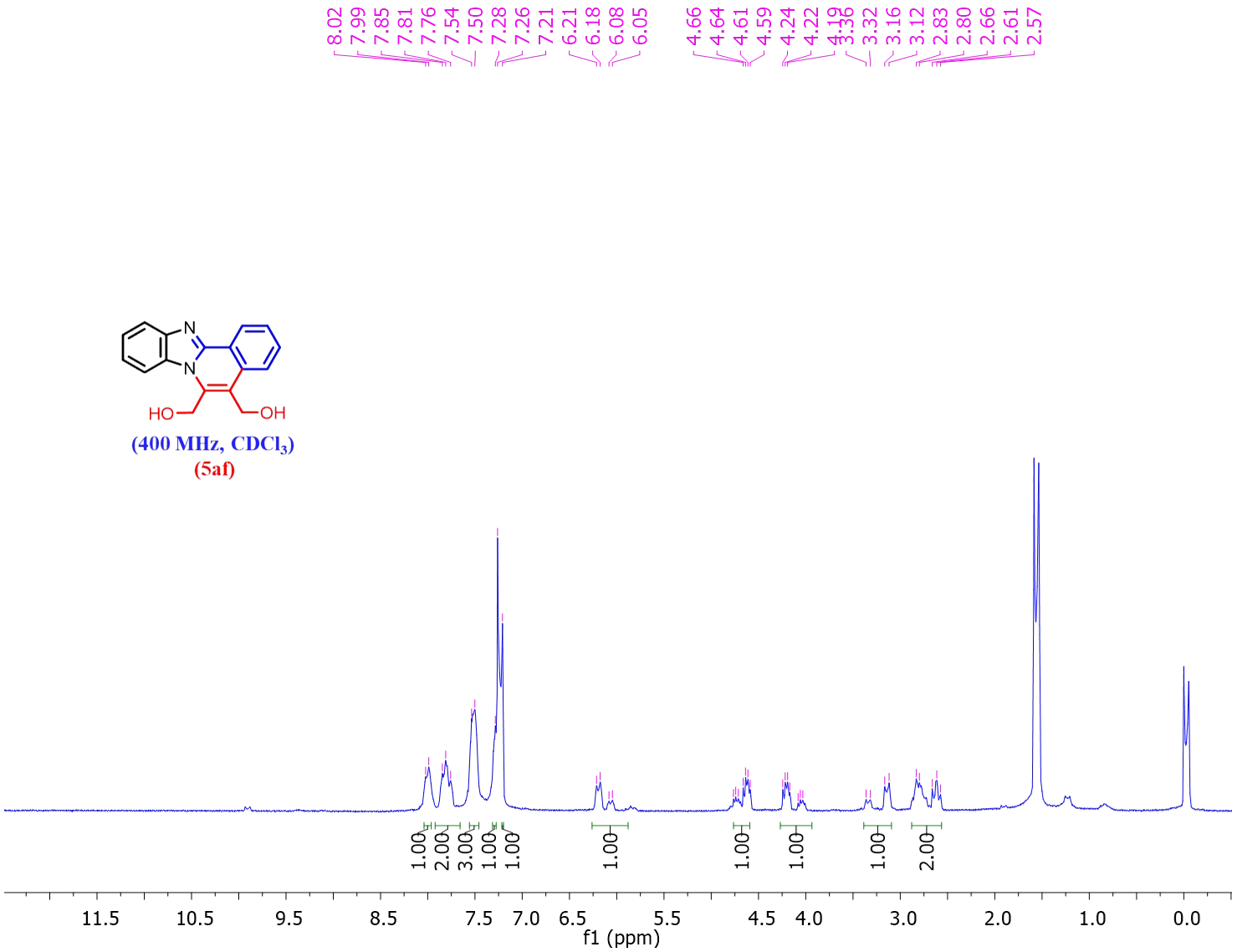


Fig. S78. ^{1}H NMR spectra of benzo[4,5]imidazo[2,1-a]isoquinoline-5,6-diyldimethanol (**5af**) in $CDCl_3$.

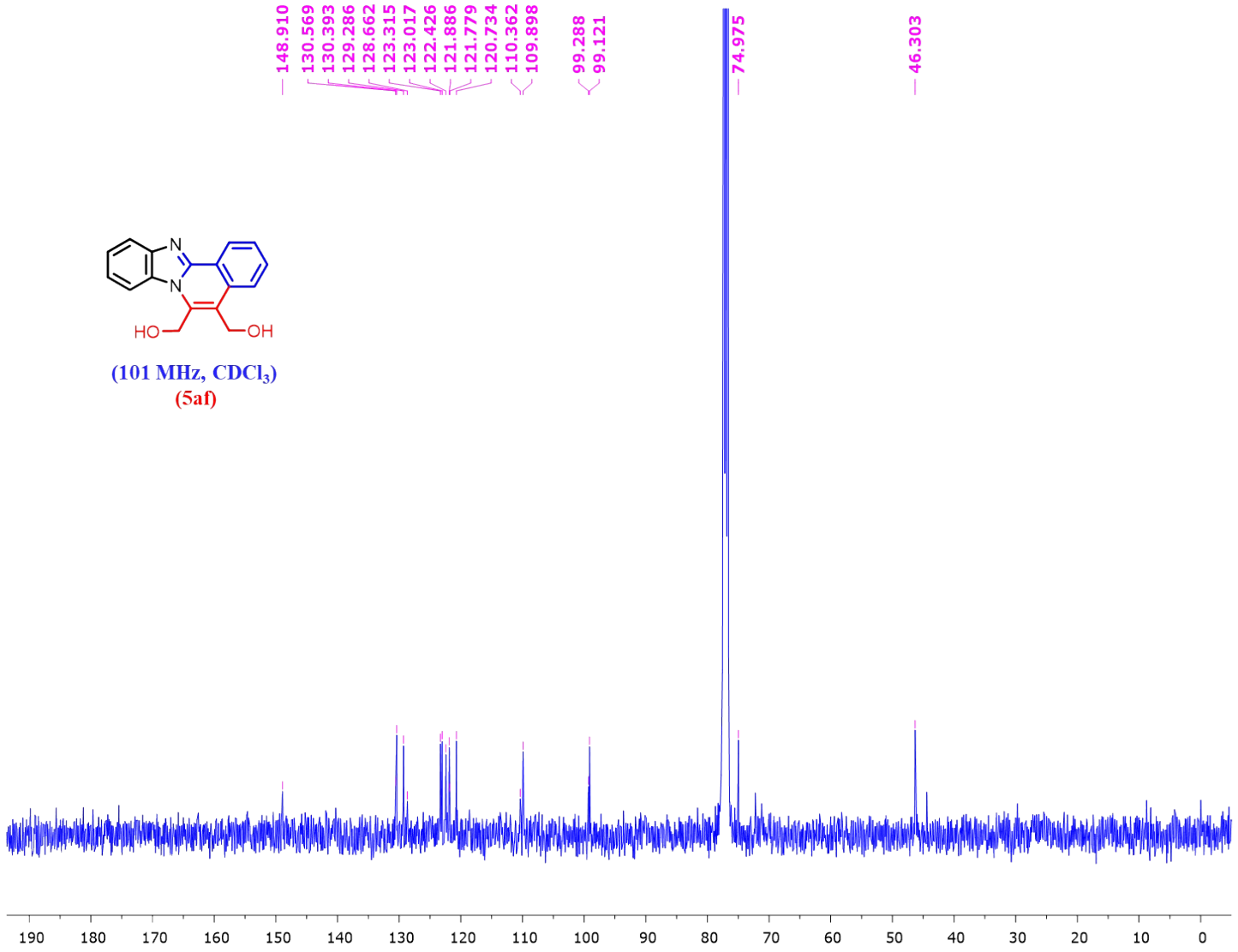


Fig. S79. ^{13}C NMR spectra of benzo[4,5]imidazo[2,1-a]isoquinoline-5,6-diyldimethanol (**5af**) in $CDCl_3$.

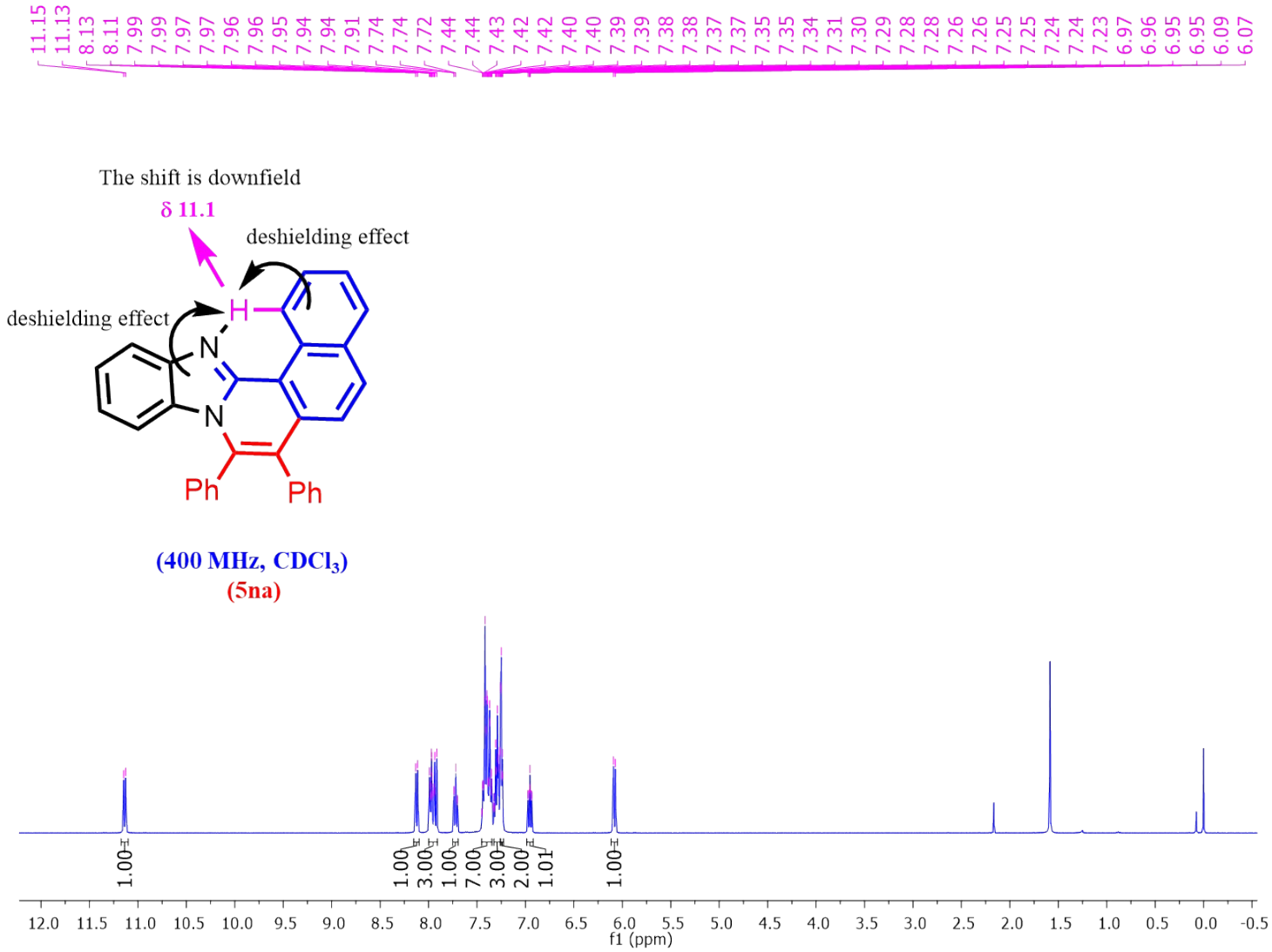


Fig. S80. ^{1}H NMR spectra of 7,8-diphenylbenzo[h]benzo [4,5] imidazo[2,1-a] isoquinoline (**5na**) in $CDCl_3$.

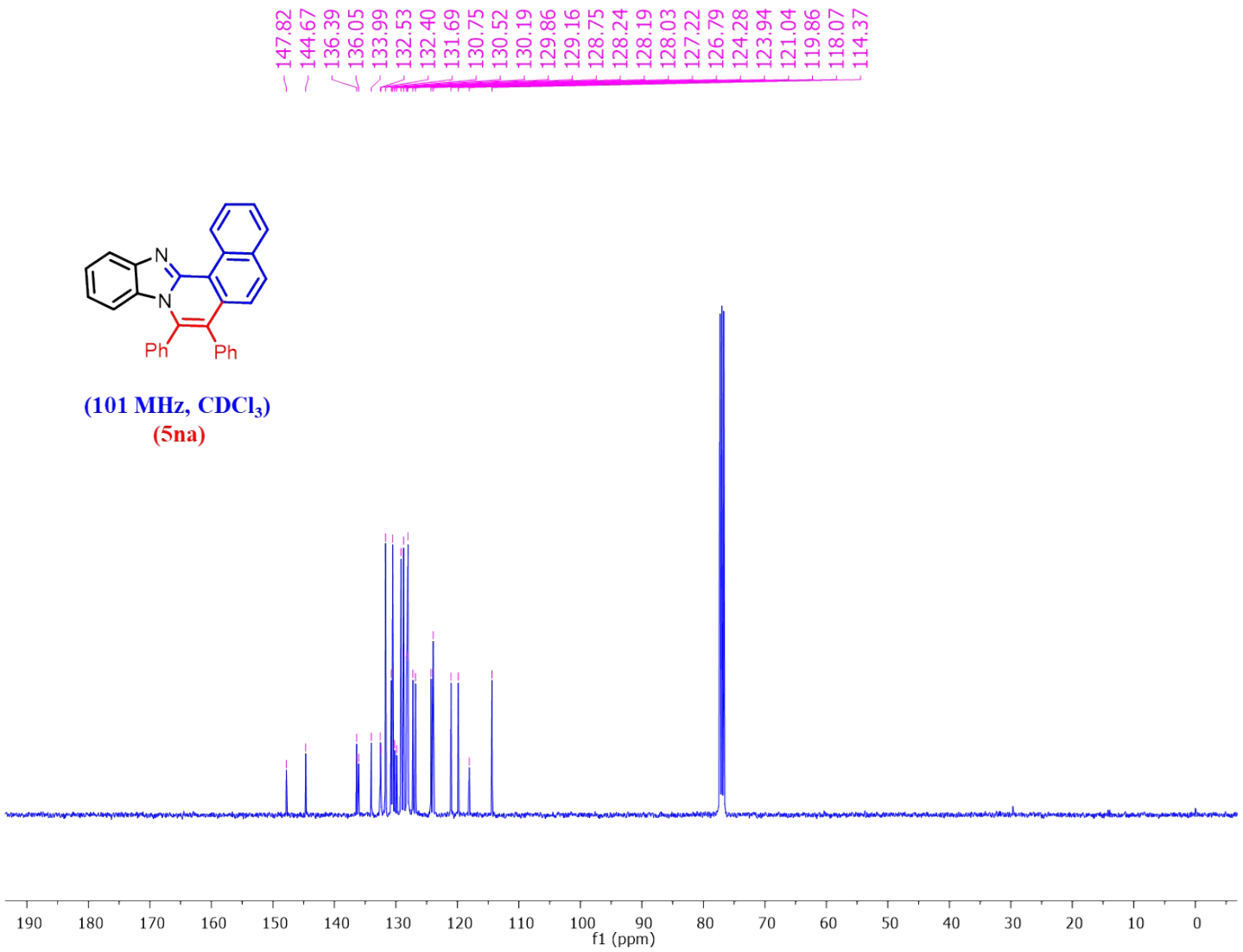


Fig. S81. ^{13}C NMR spectra of 7,8-diphenylbenzo[h] benzo [4,5] imidazo [2,1-a] isoquinoline (**5na**) in $CDCl_3$.

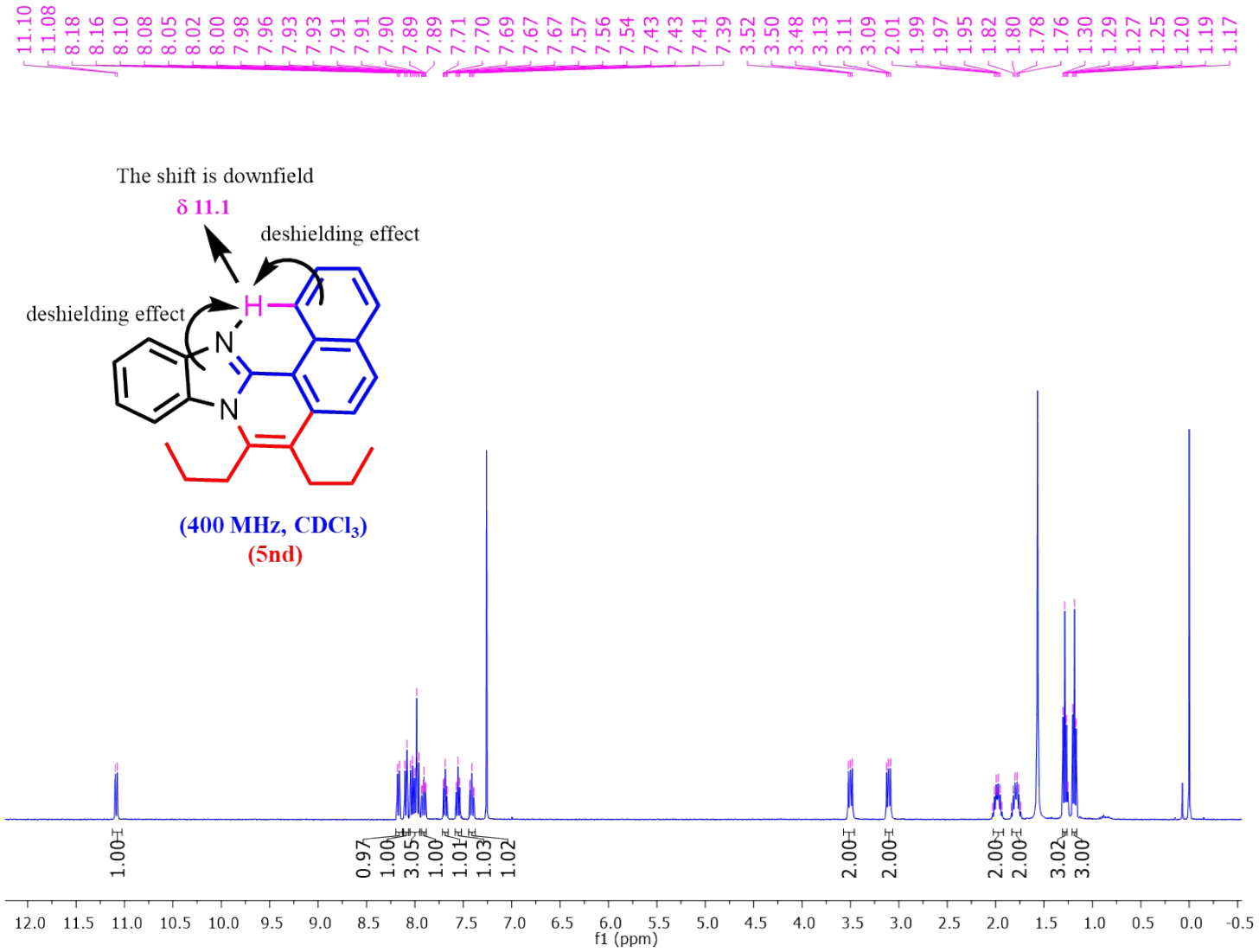


Fig. S82. ^{1}H NMR spectra of 7,8-dipropylbenzo[h]benzo [4,5] imidazo[2,1-a] isoquinoline (**5nd**) in $CDCl_3$.

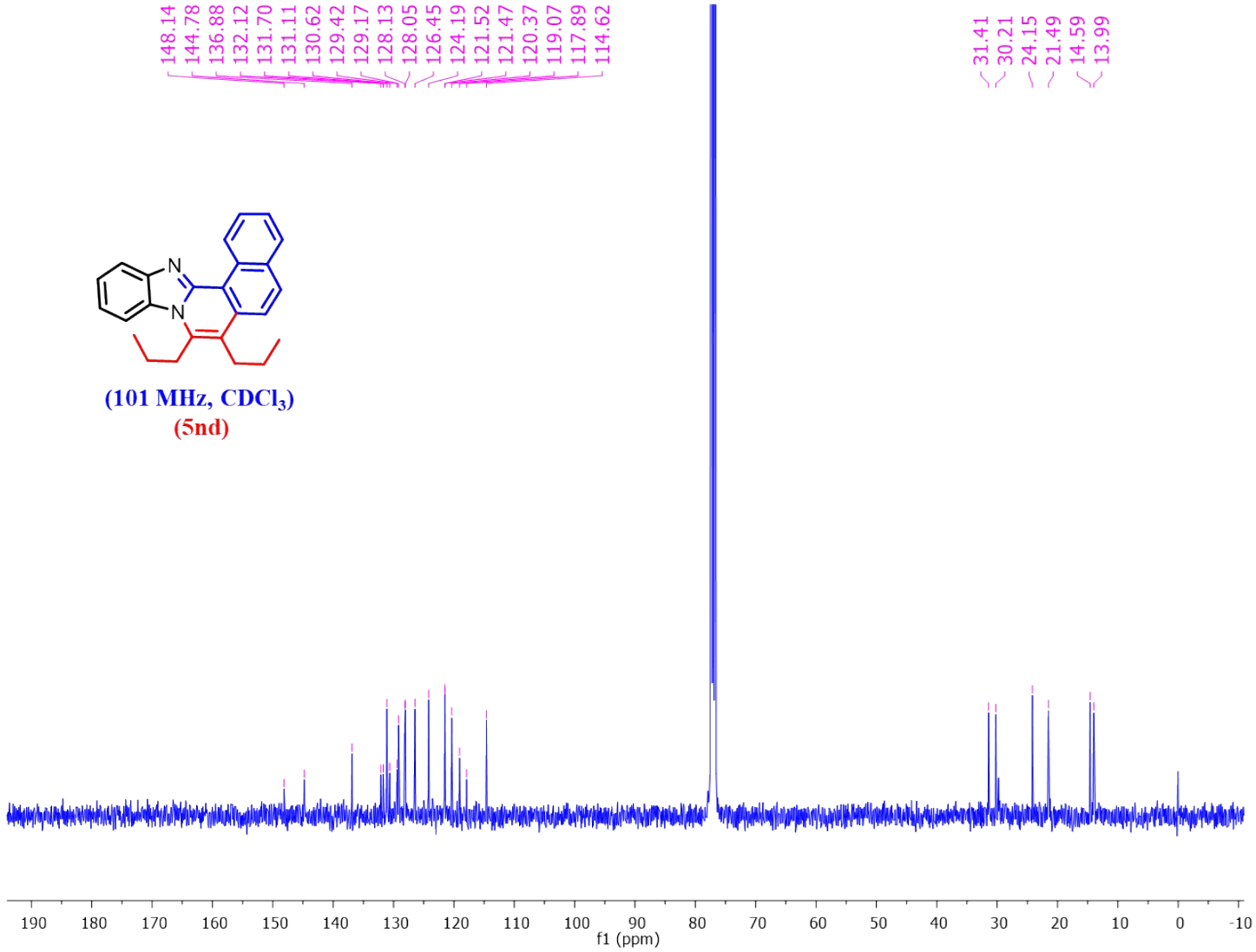


Fig. S83. ^{13}C NMR spectra of 7,8-dipropylbenzo[h]benzo [4,5] imidazo[2,1-a] isoquinoline (**5nd**) in $CDCl_3$.

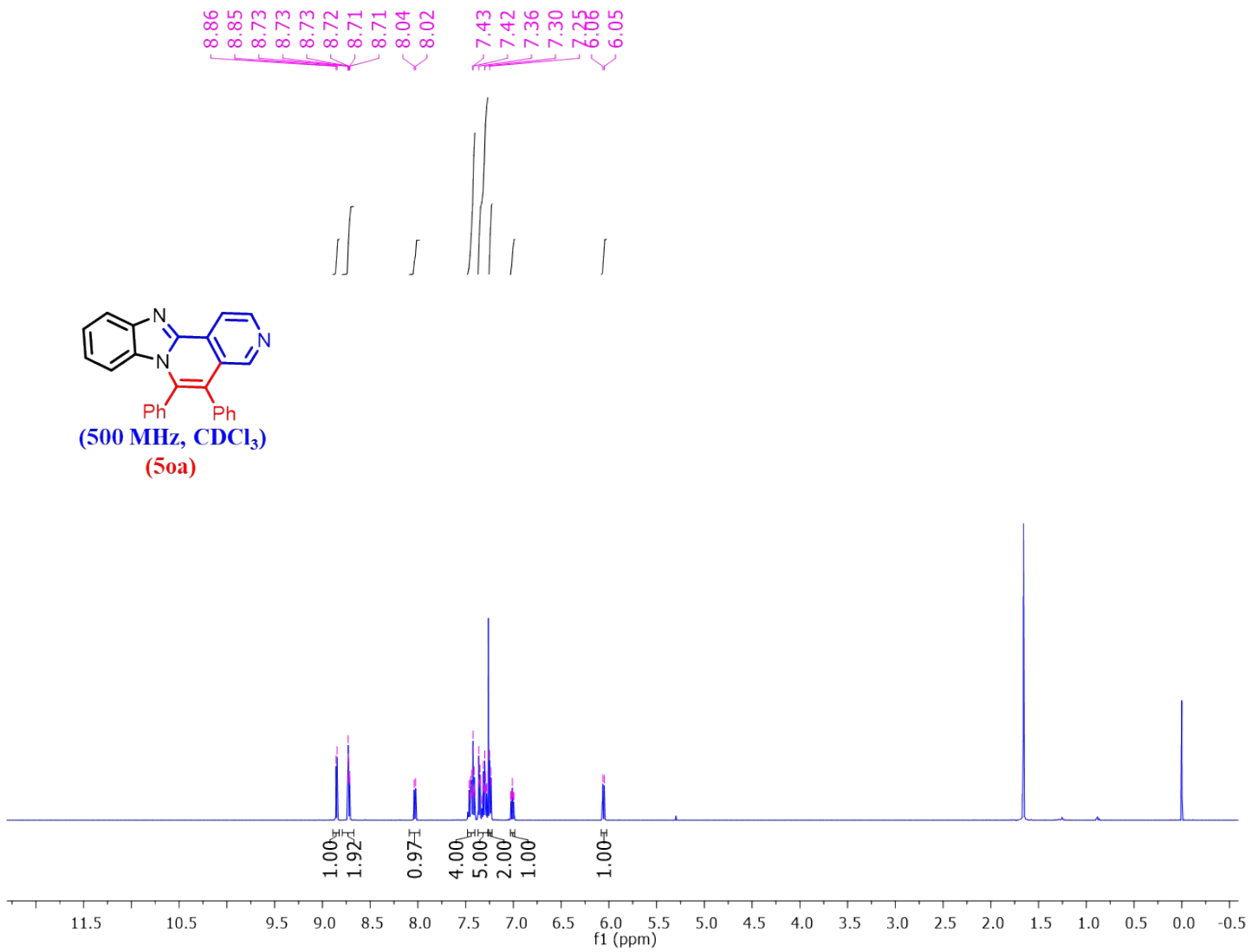


Fig. S84. ^{1}H NMR spectra of 5,6-diphenylbenzo [4,5] imidazo[2,1-a] [2,6] naphthyridine (**5oa**) in $CDCl_3$.

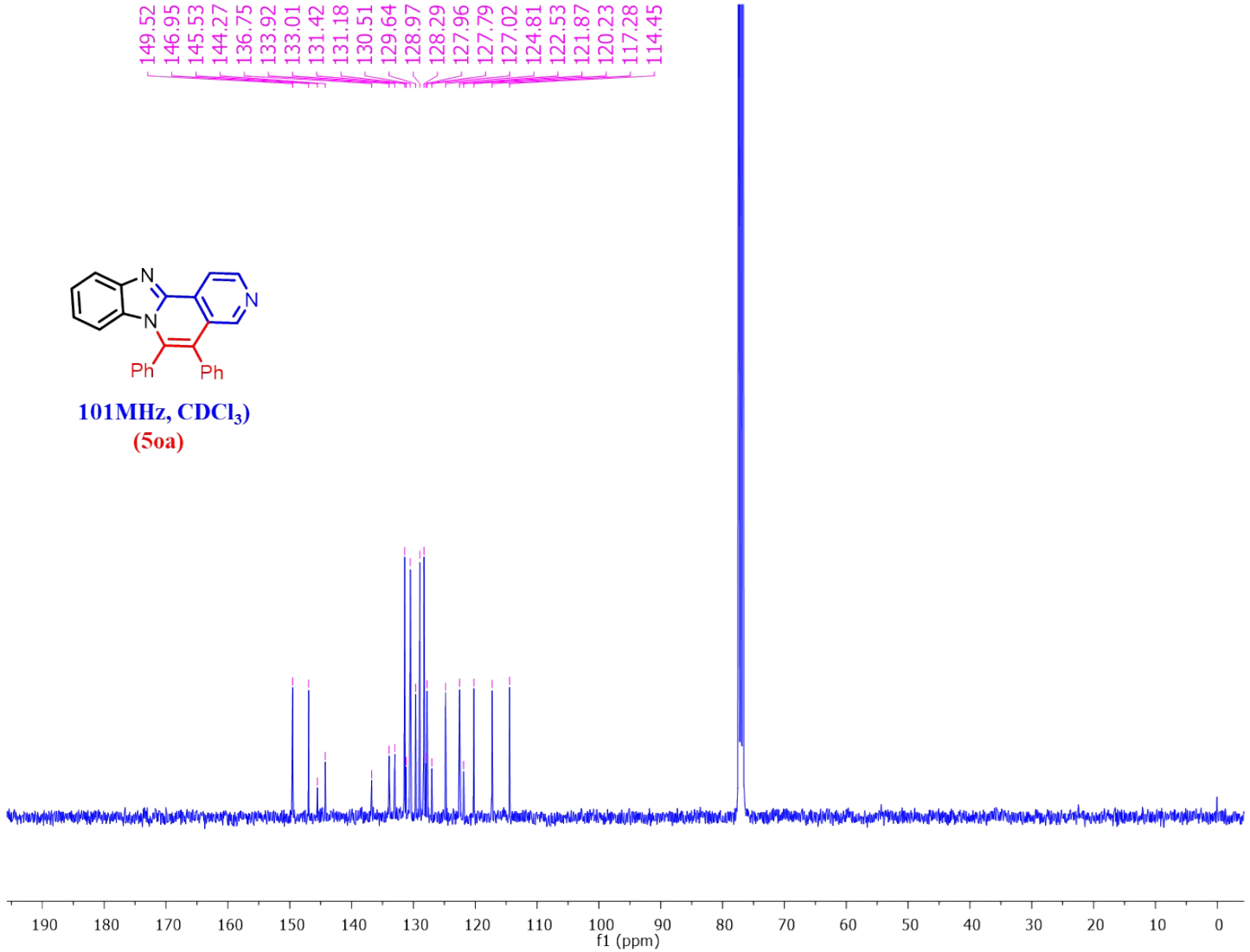


Fig. S85. ^{13}C NMR spectra of 5,6-diphenylbenzo [4,5] imidazo[2,1-a] [2,6] naphthyridine (**5oa**) in $CDCl_3$.

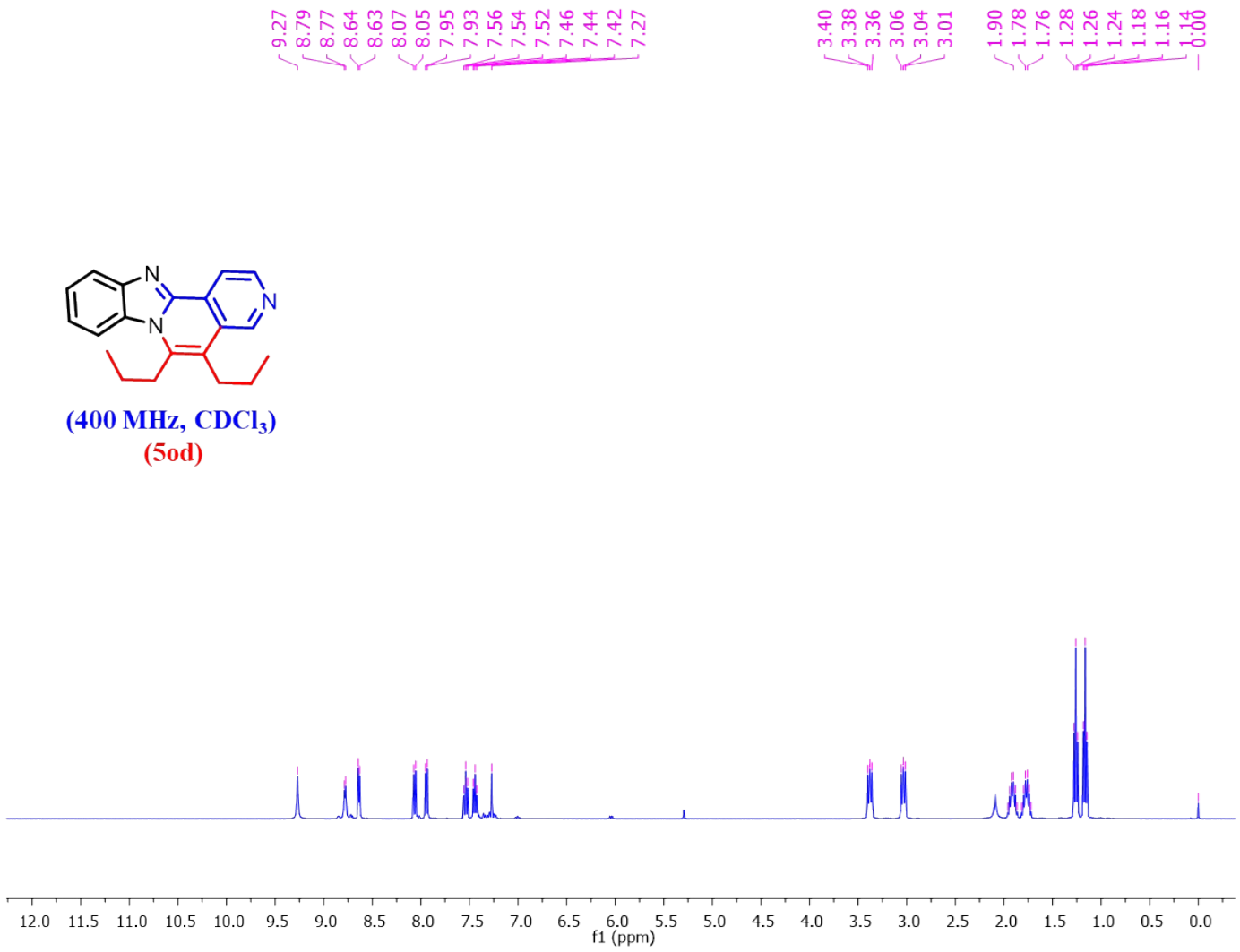


Fig. S86. ^{1}H NMR spectra of 5,6-dipropylbenzo [4,5] imidazo[2,1-a] [2,6] naphthyridine (**5od**) in $CDCl_3$.

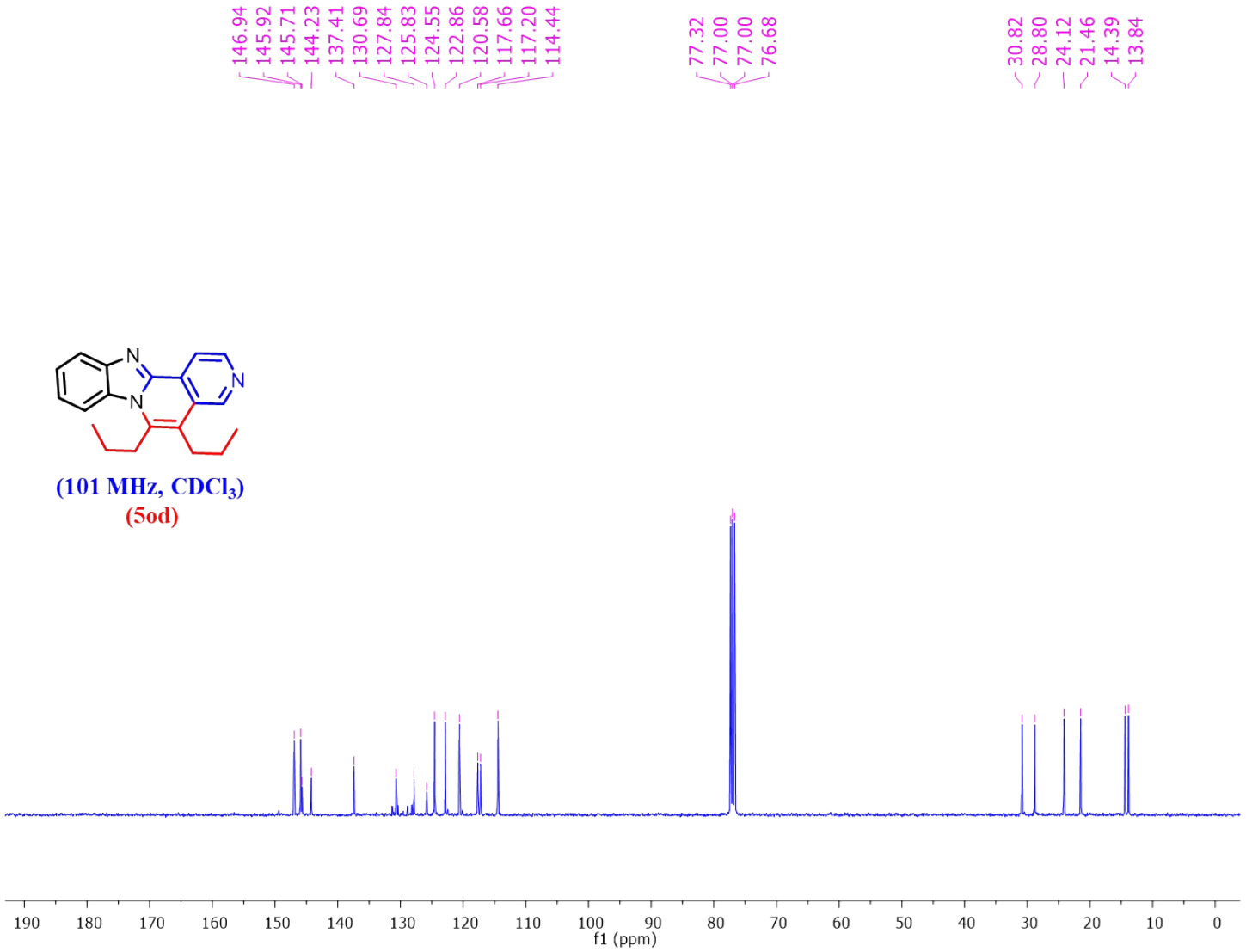


Fig. S87. ^{13}C NMR spectra of 5,6-dipropylbenzo [4,5] imidazo [2,1-a] [2,6] naphthyridine (**5od**) in $CDCl_3$.

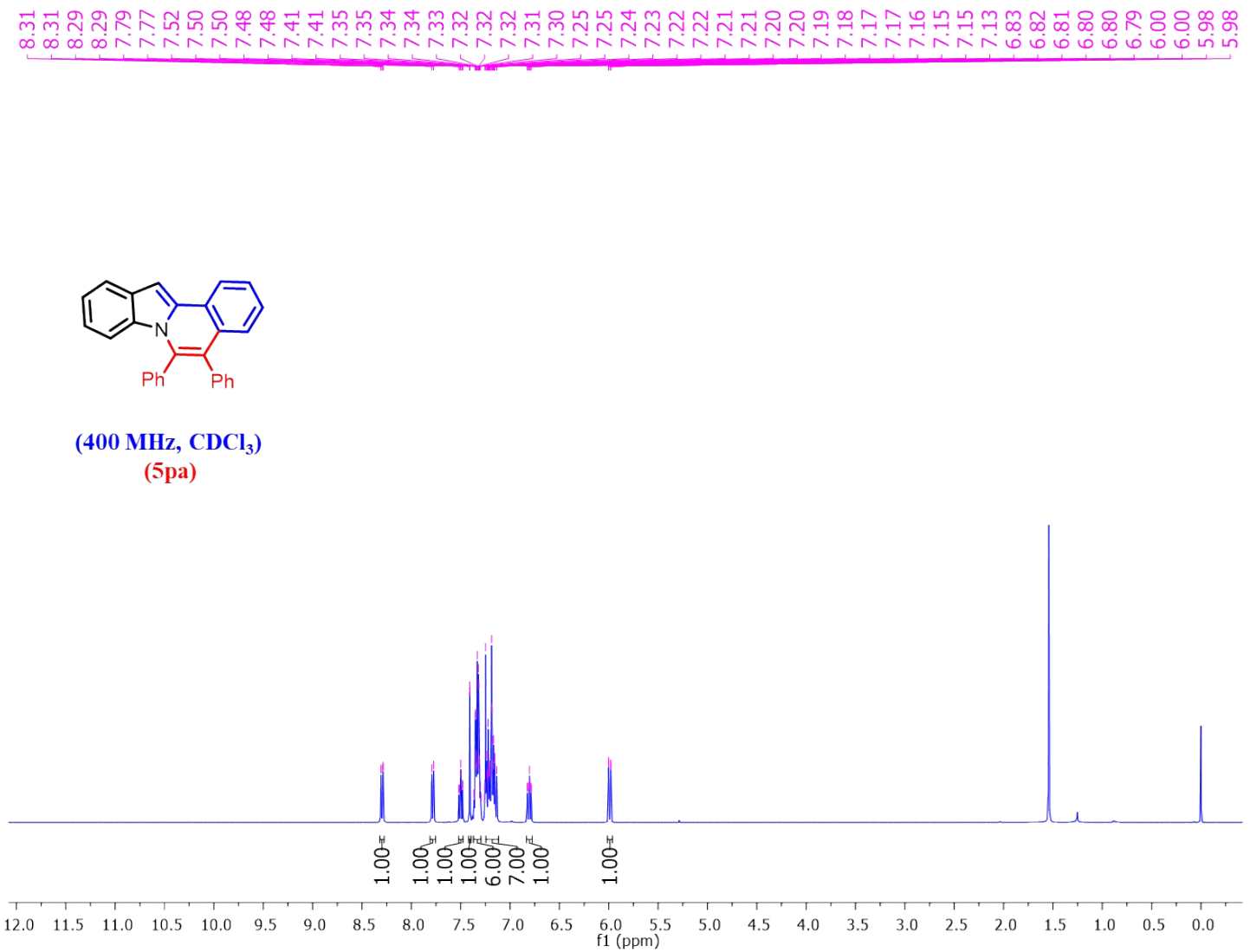


Fig. S88. ^{1}H NMR spectra of diphenylindolo [2,1-a] isoquinoline (**5pa**) in $CDCl_3$.

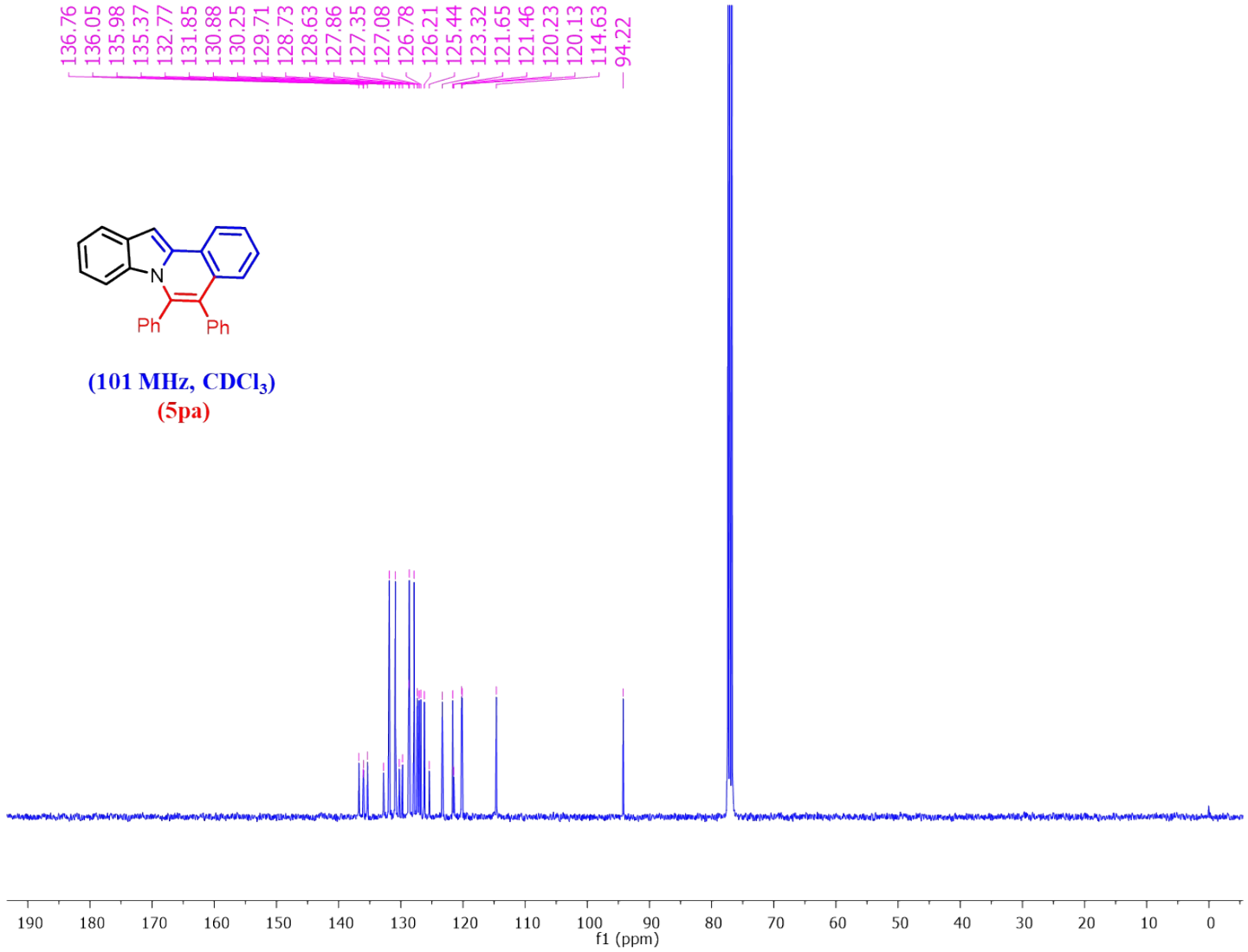


Fig. S89. ^{13}C NMR spectra of diphenylindolo [2,1-a] isoquinoline (**5pa**) in $CDCl_3$.

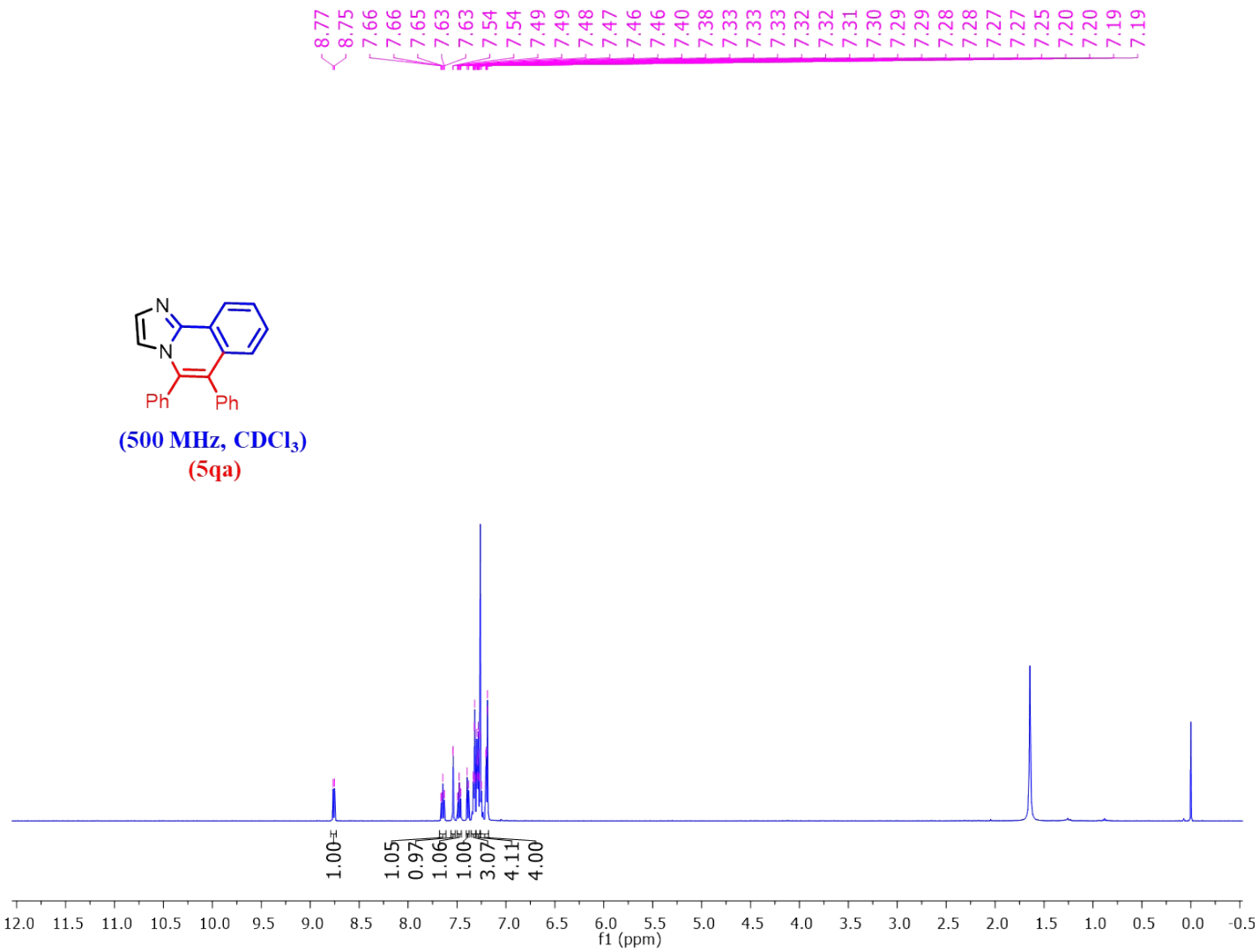


Fig. S90. ^{1}H NMR spectra of 5,6-diphenylimidazo[2,1-a] isoquinoline (**5qa**) in CDC_{l3}.

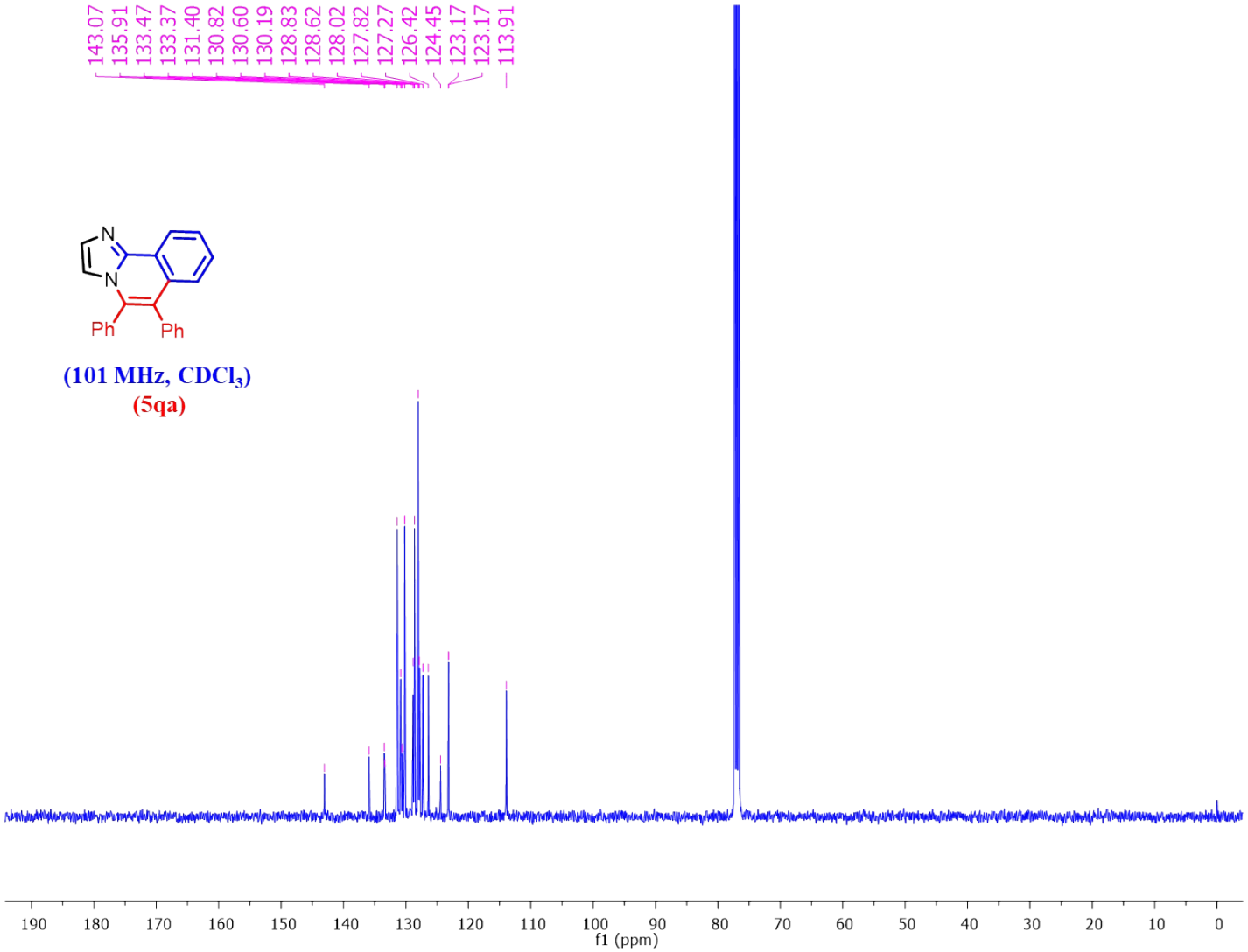


Fig. S91. ^{13}C NMR spectra of 5,6-diphenylimidazo[2,1-a] isoquinoline (**5qa**) in $CDCl_3$.

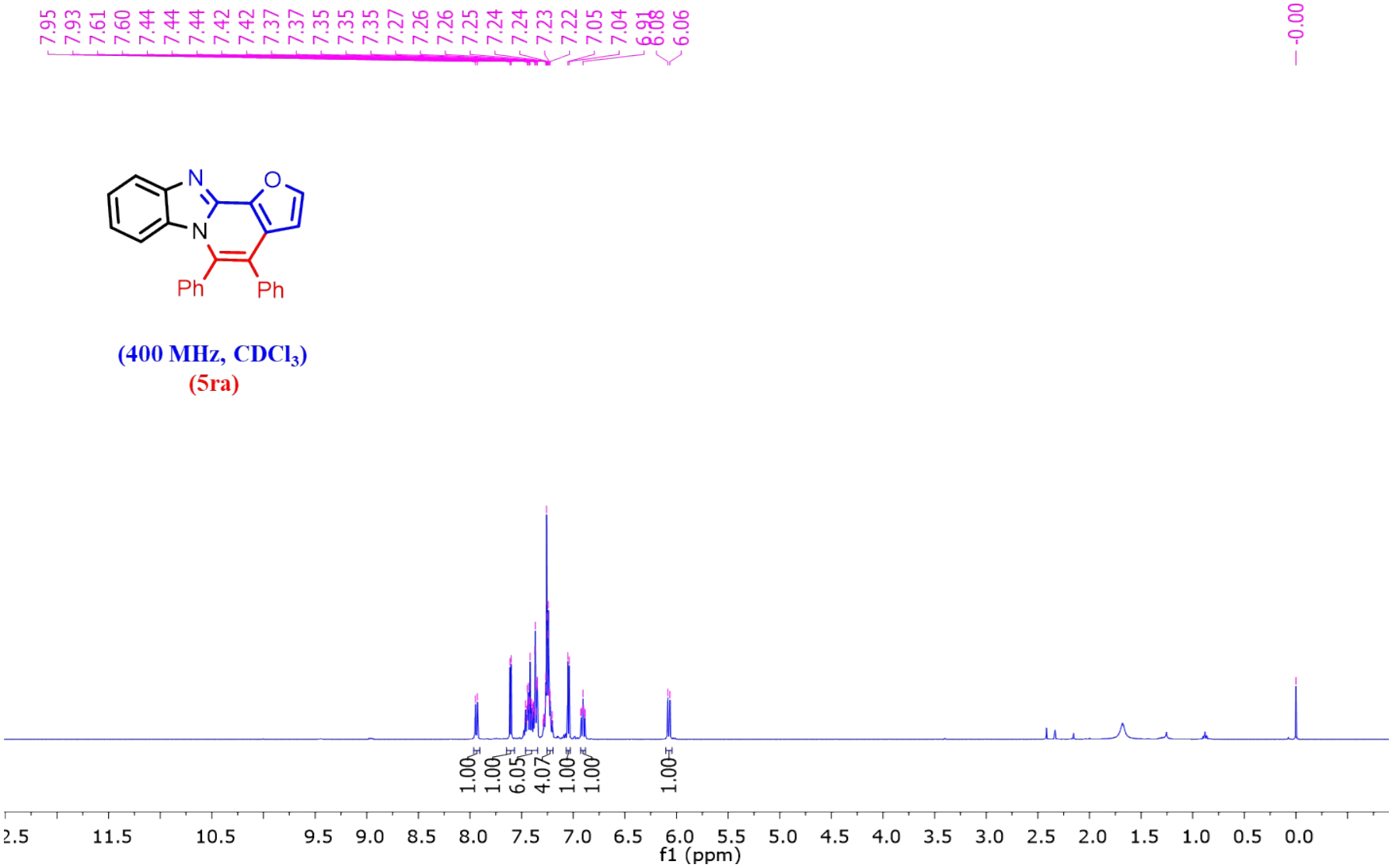


Fig. S92. ^{1}H NMR spectra of 4,5-Diphenylbenzo[4,5]imidazo[1,2-a]furo[2,3-c]pyridine (**5ra**) in $CDCl_3$.

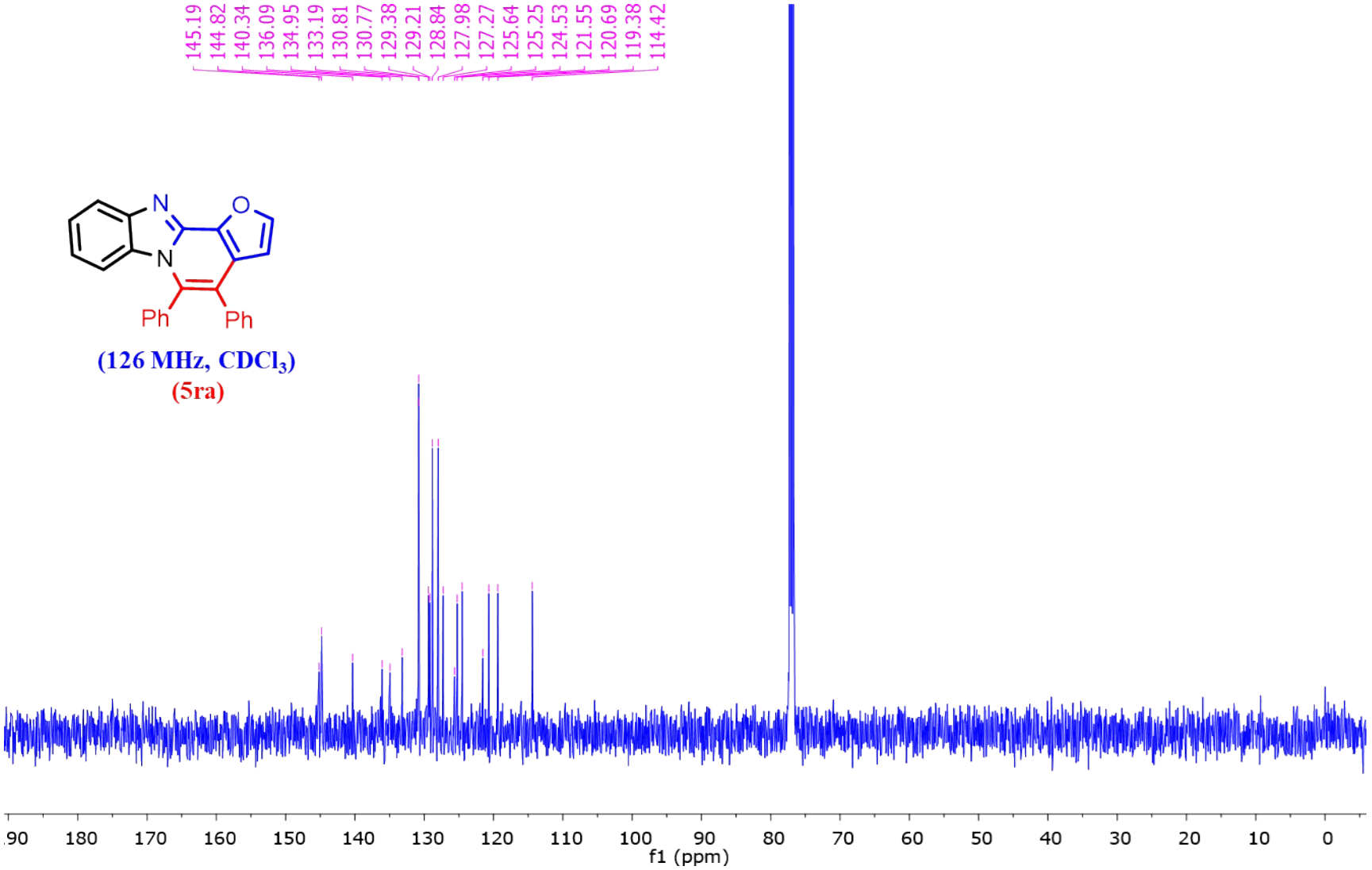


Fig. S93. ^{13}C NMR spectra of 4,5-Diphenylbenzo[4,5]imidazo[1,2-a]furo[2,3-c]pyridine (**5ra**) in $CDCl_3$.

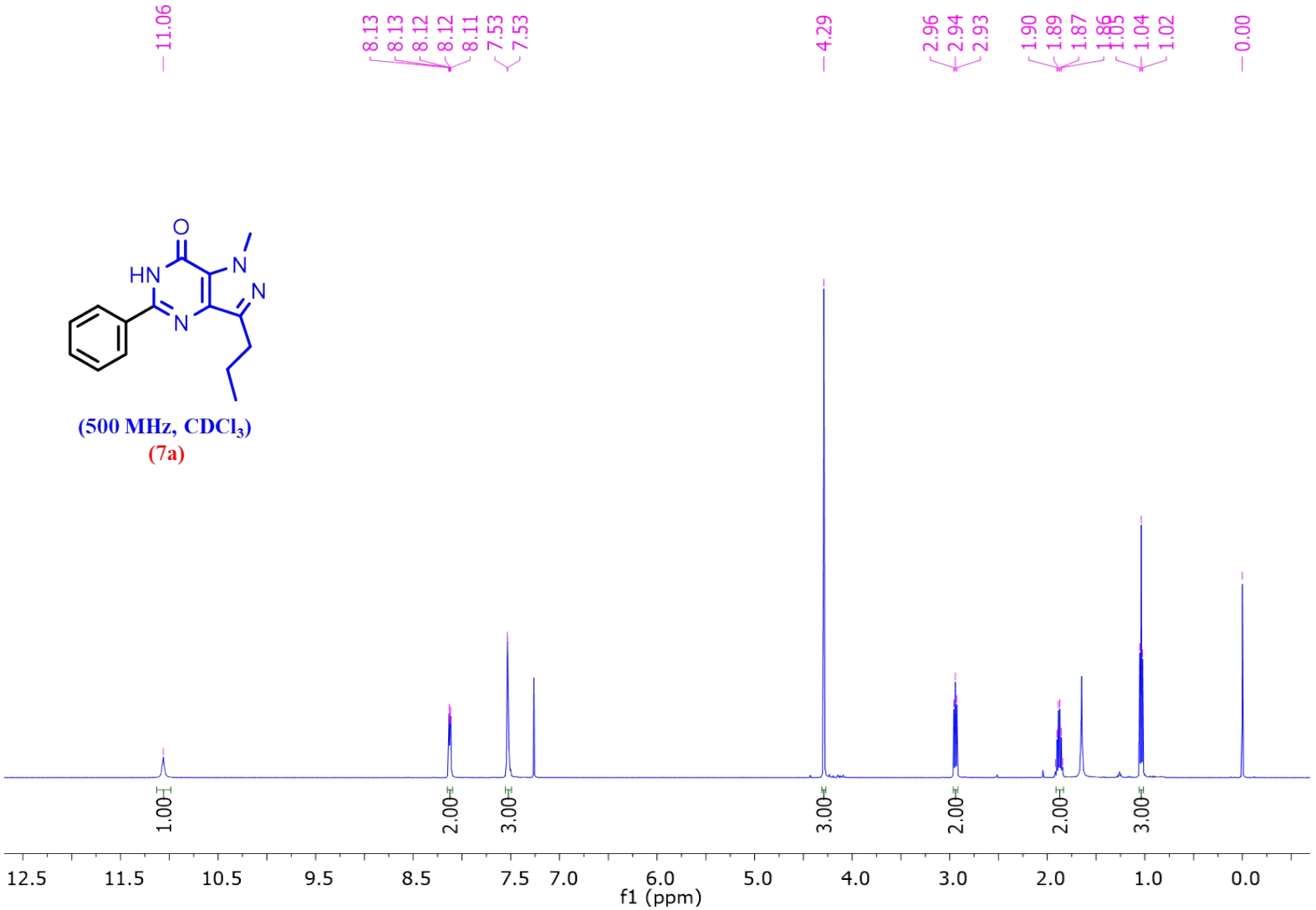


Fig. S94. ^{1}H NMR spectra of 1-Methyl-5-phenyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (**7a**) in $CDCl_3$.

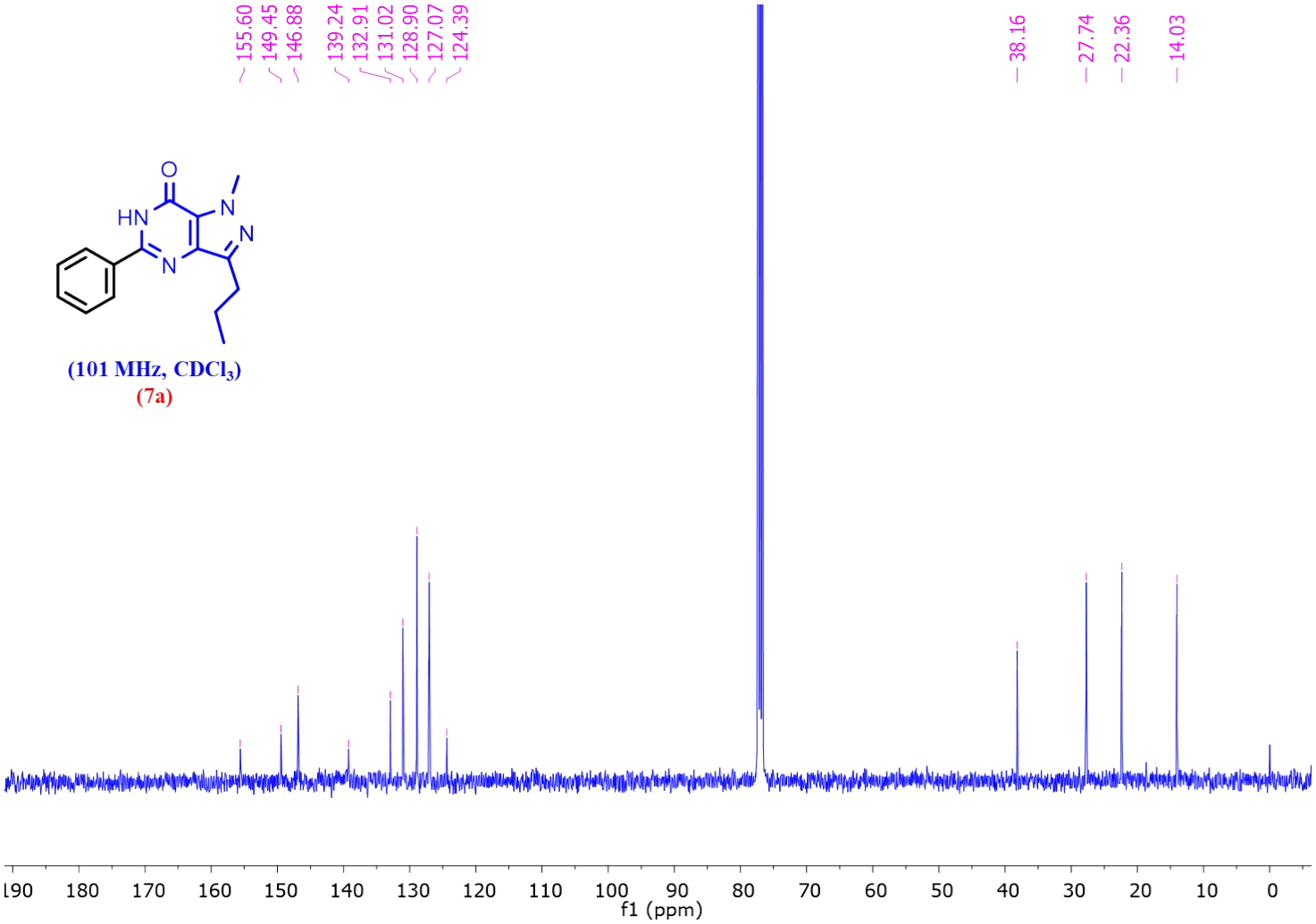


Fig. S95. ^{13}C NMR spectra of 1-Methyl-5-phenyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (**7a**) in $CDCl_3$.

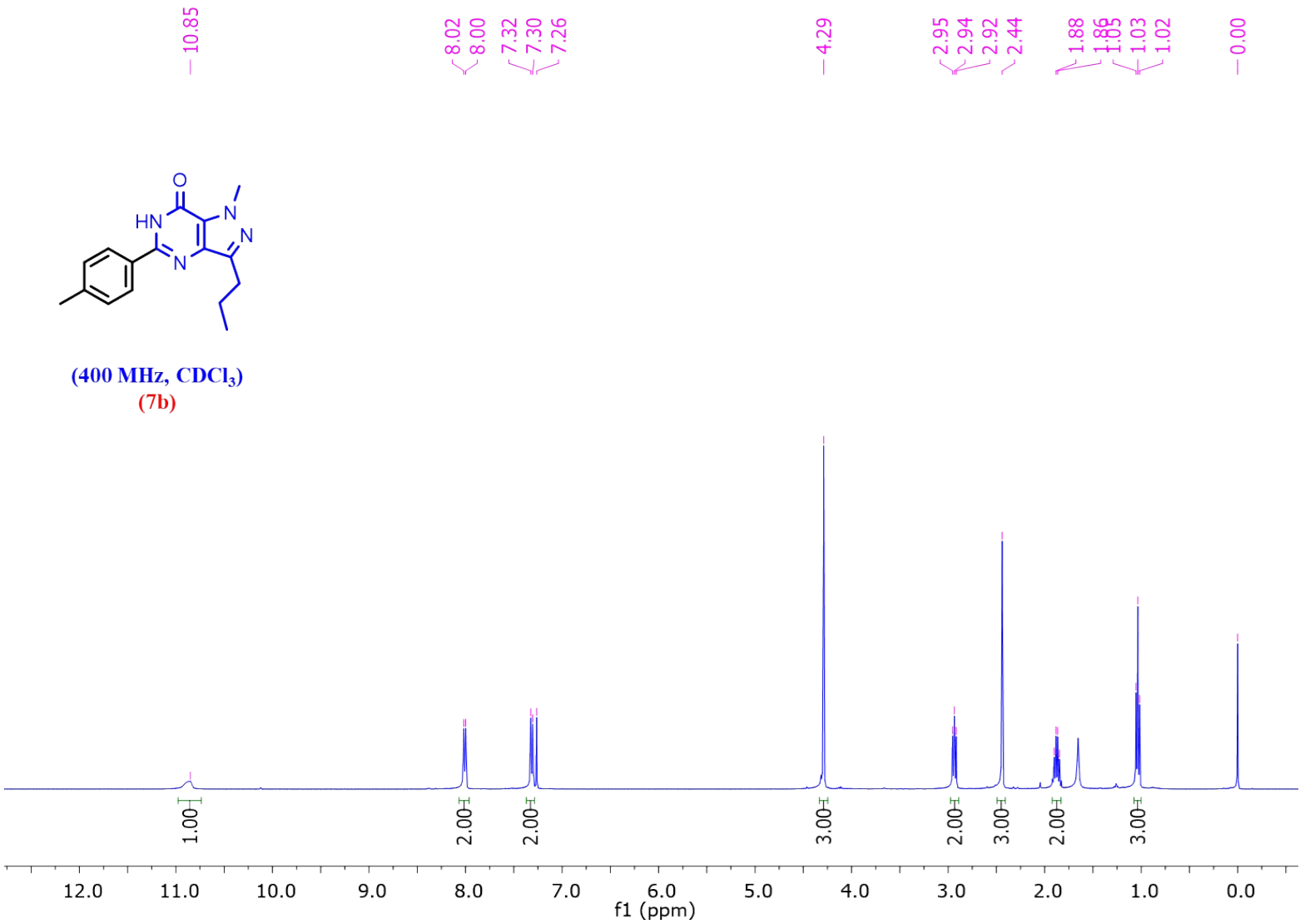


Fig. S96. ^{1}H NMR spectra of 1-Bethyl-3-propyl-5-(p-tolyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7b)** in $CDCl_3$.

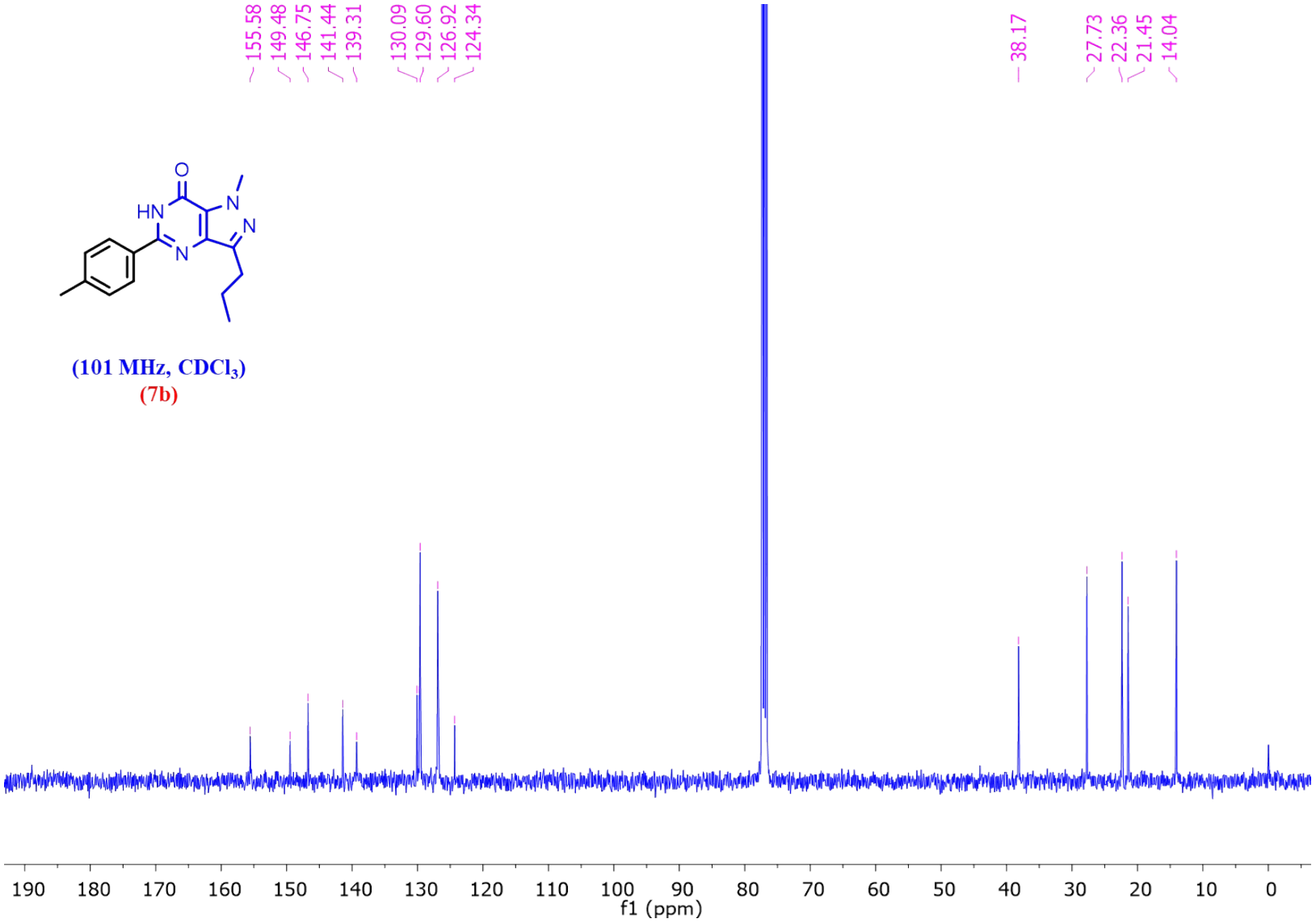


Fig. S97. ^{13}C NMR spectra of 1-Bethyl-3-propyl-5-(p-tolyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7b)** in $CDCl_3$.

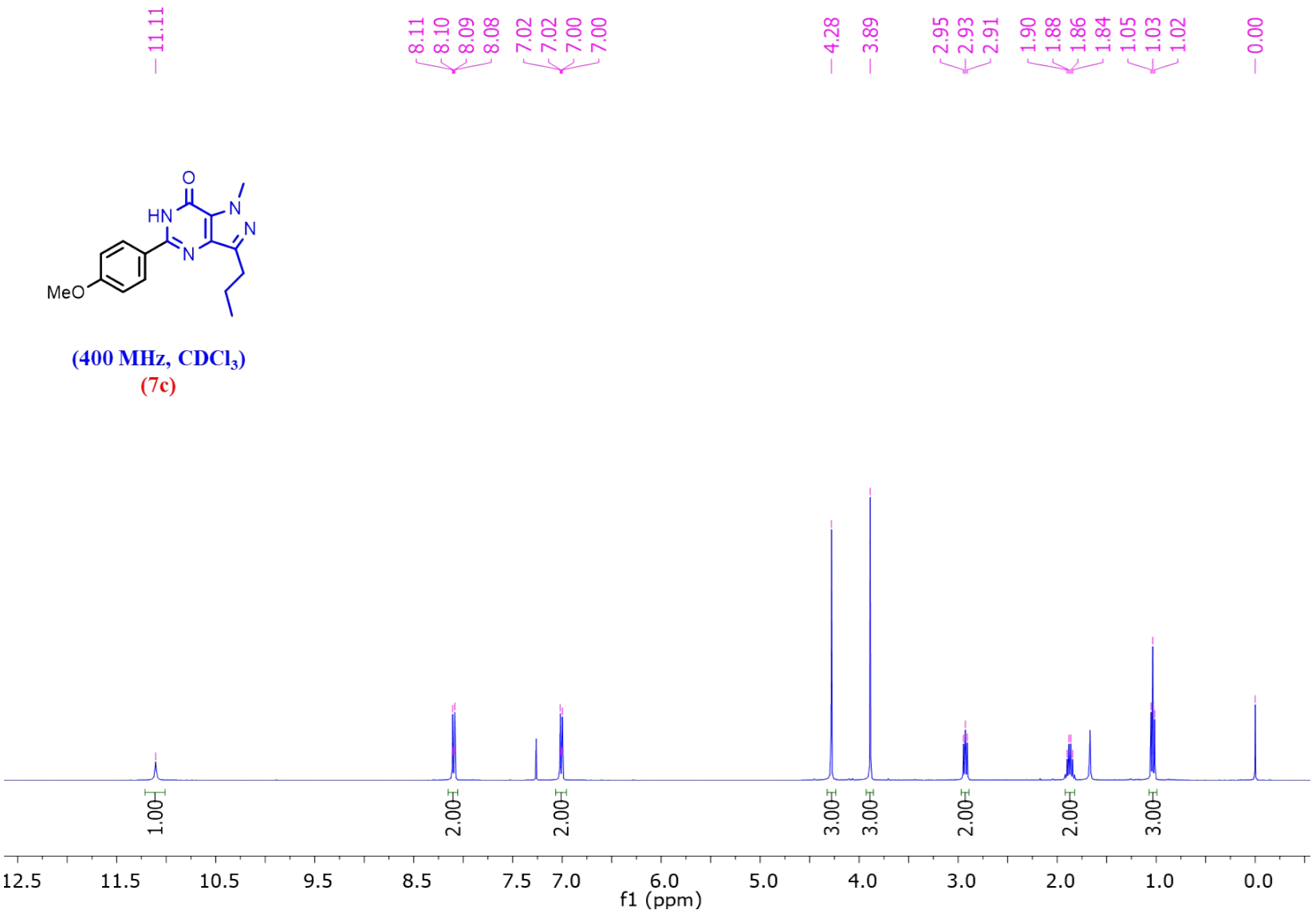


Fig. S98. ^{1}H NMR spectra of 5-(4-Methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7c)** in $CDCl_3$.

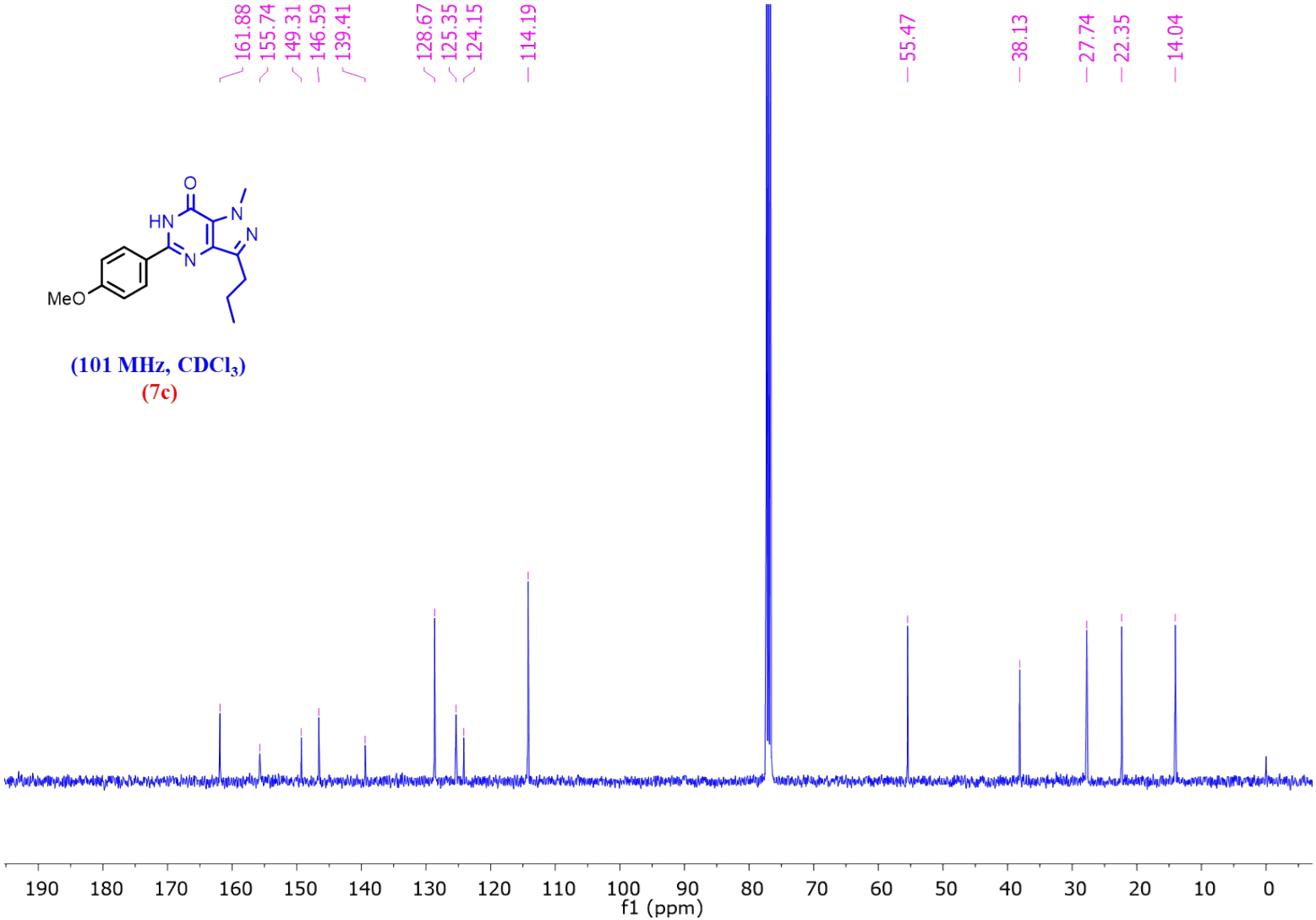


Fig. S99. ^{13}C NMR spectra of 5-(4-Methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7c)** in $CDCl_3$.

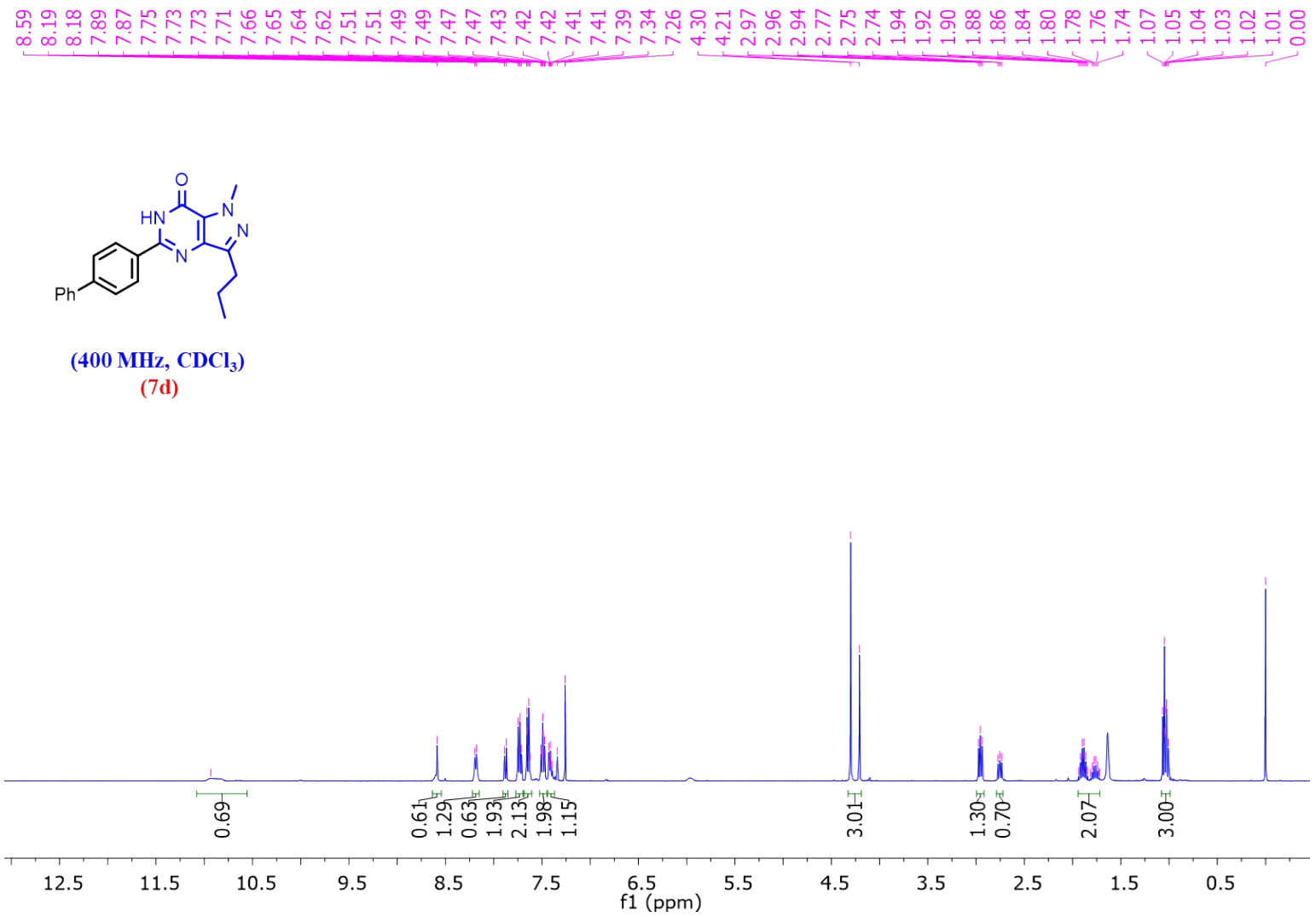


Fig. S100. ^{1}H NMR spectra of 5-([1,1'-Biphenyl]-4-yl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7d)** in $CDCl_3$.

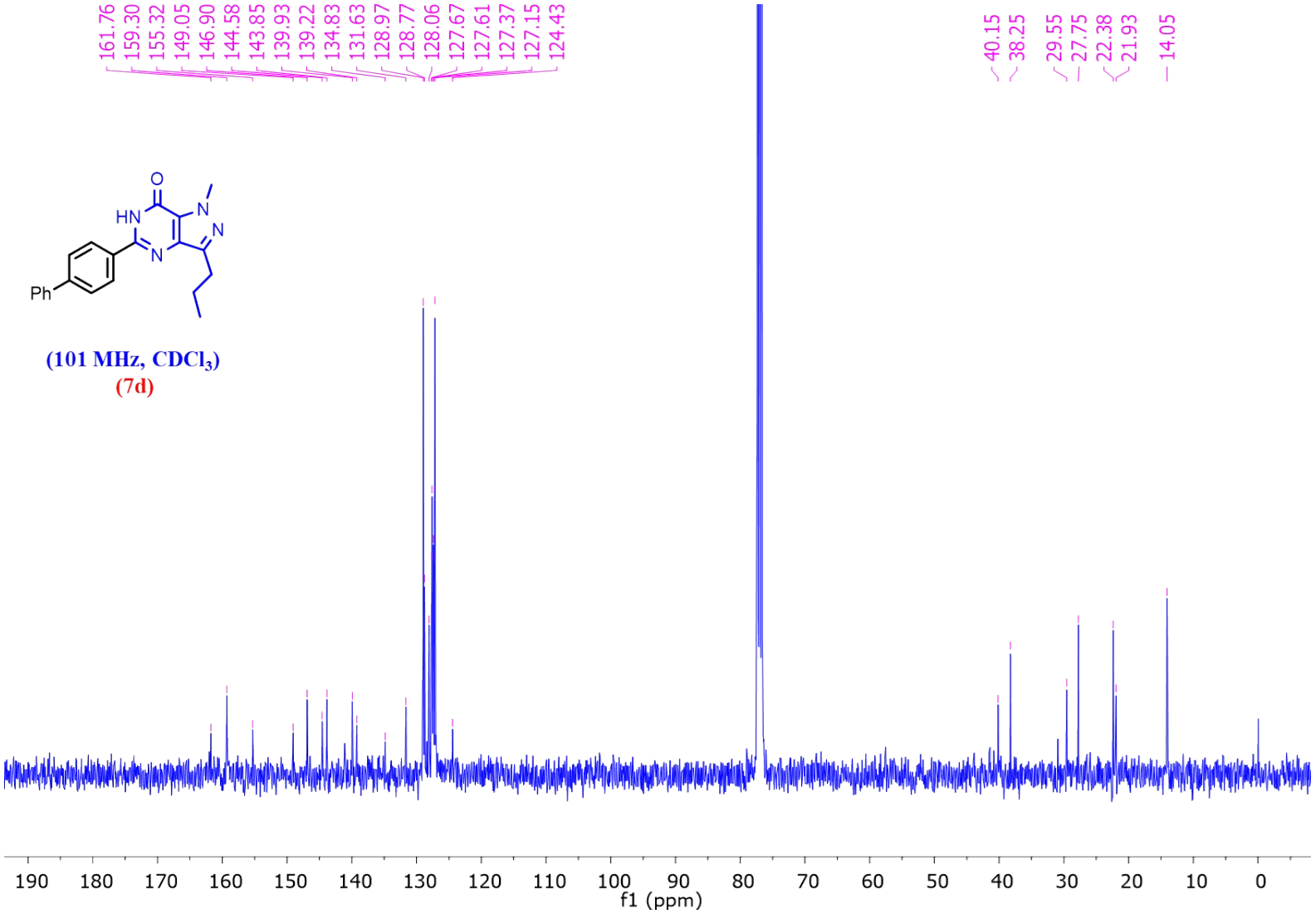


Fig. S101. ^{13}C NMR spectra of 5-([1,1'-Biphenyl]-4-yl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7d)** in $CDCl_3$.

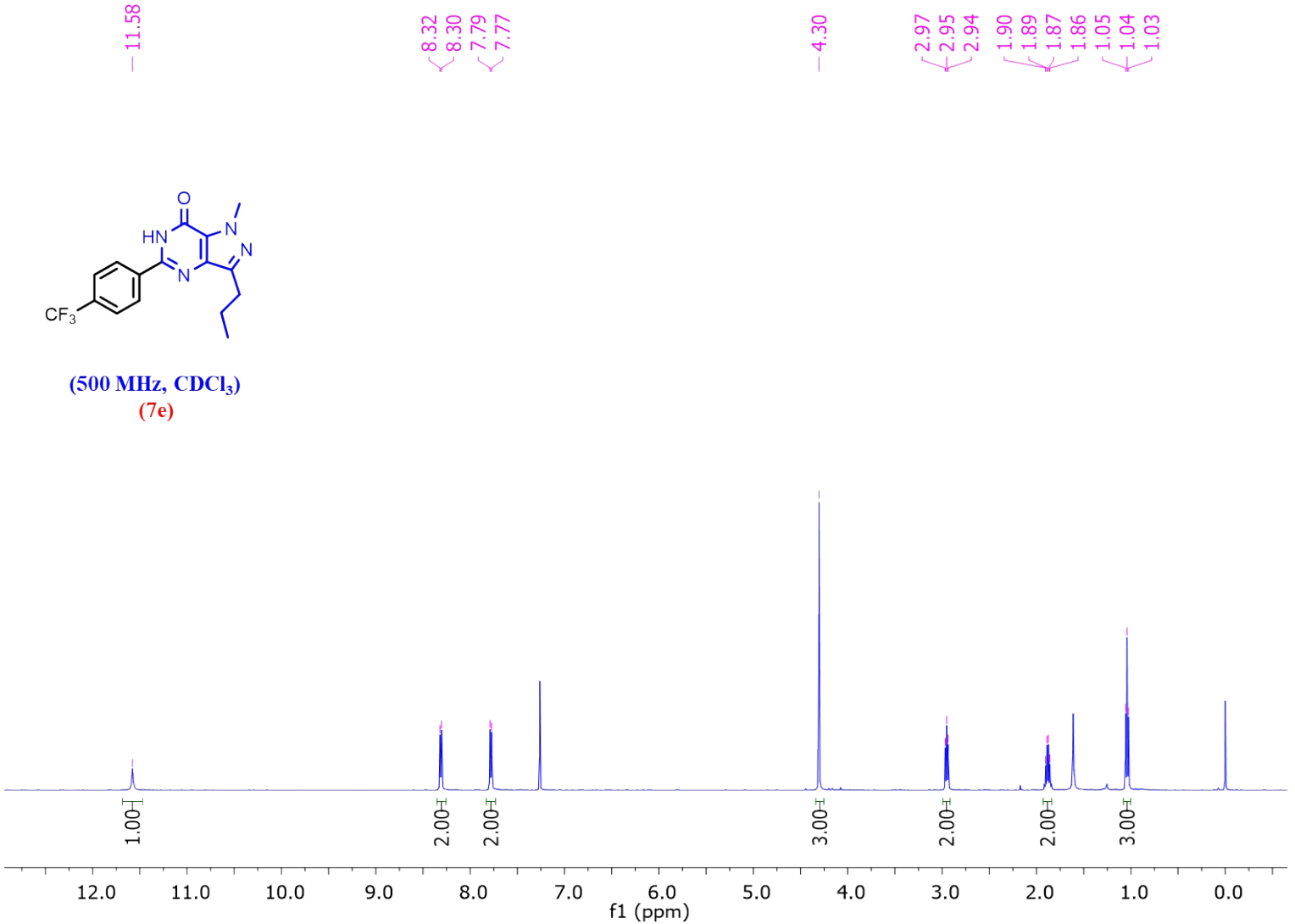


Fig. S102. ^{1}H NMR spectra of 1-Methyl-3-propyl-5-(4-(trifluoromethyl)phenyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7e)** in $CDCl_3$.

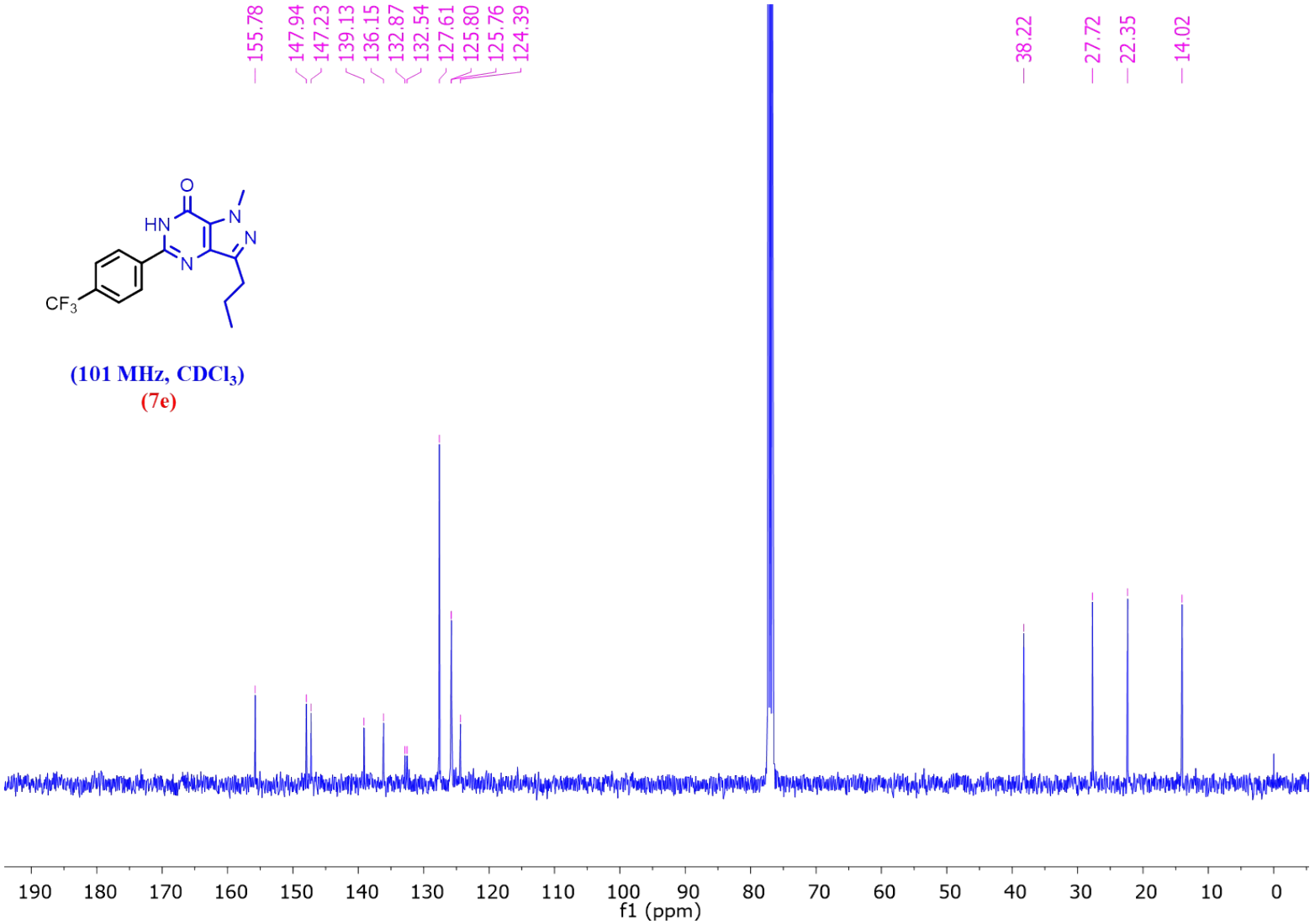


Fig. S103. ^{13}C NMR spectra of 1-Methyl-3-propyl-5-(4-(trifluoromethyl)phenyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7e)** in $CDCl_3$

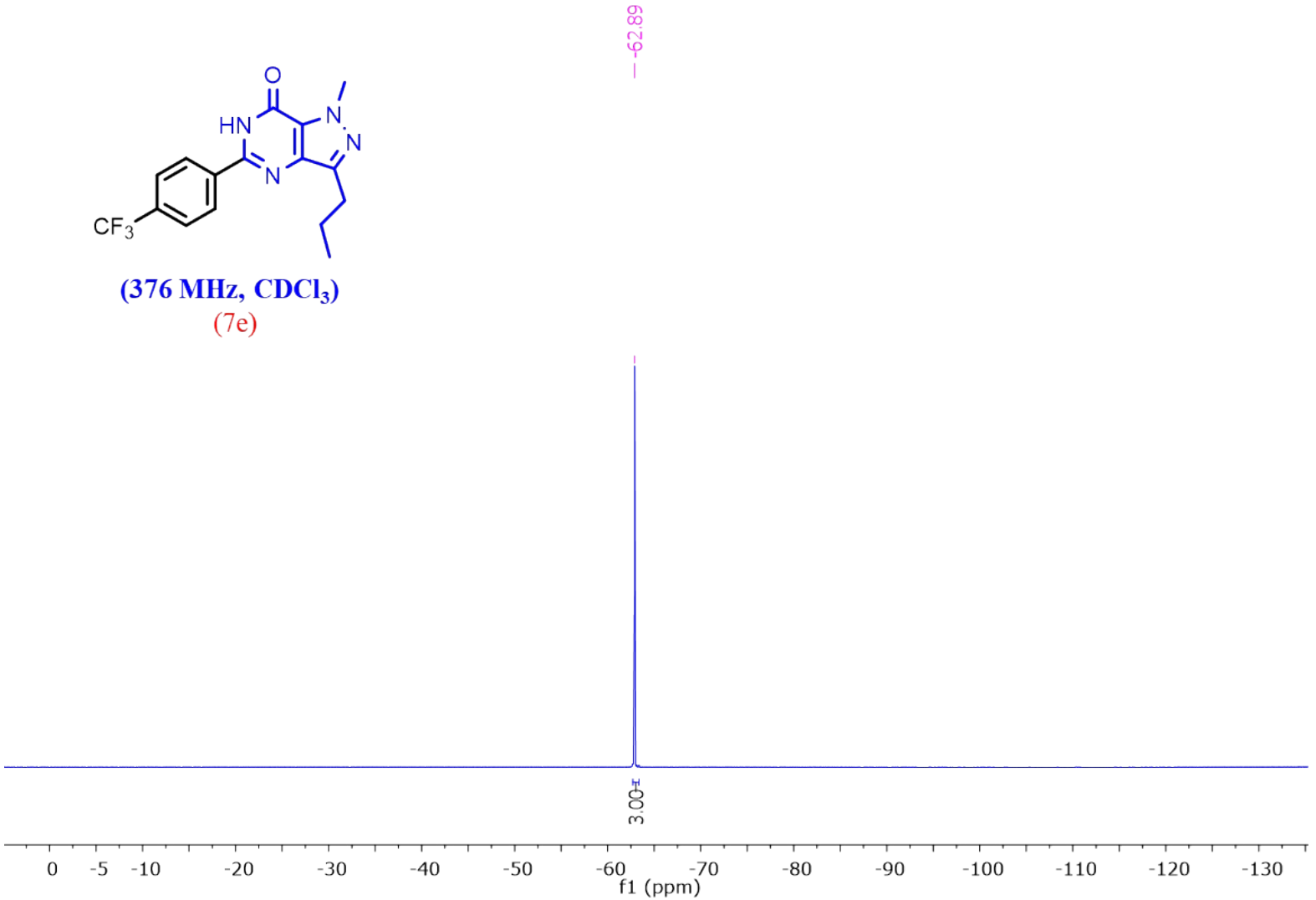


Fig. S104. ^{19}F NMR spectra of 1-Methyl-3-propyl-5-(4-(trifluoromethyl)phenyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7e)** in $CDCl_3$

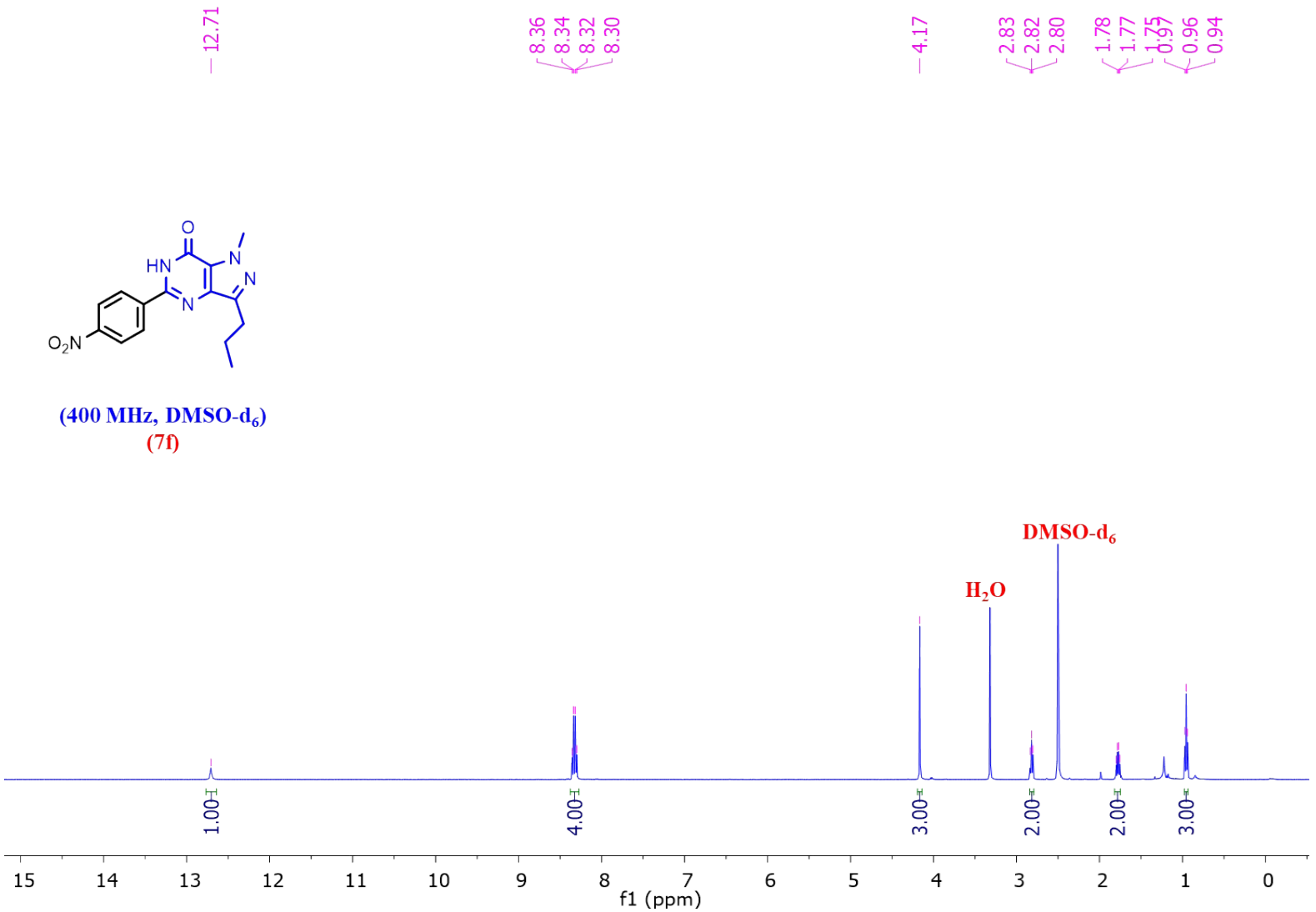


Fig. S105. ^{1}H NMR spectra of 1-Methyl-5-(4-nitrophenyl)-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7f)** in DMSO-d_6.

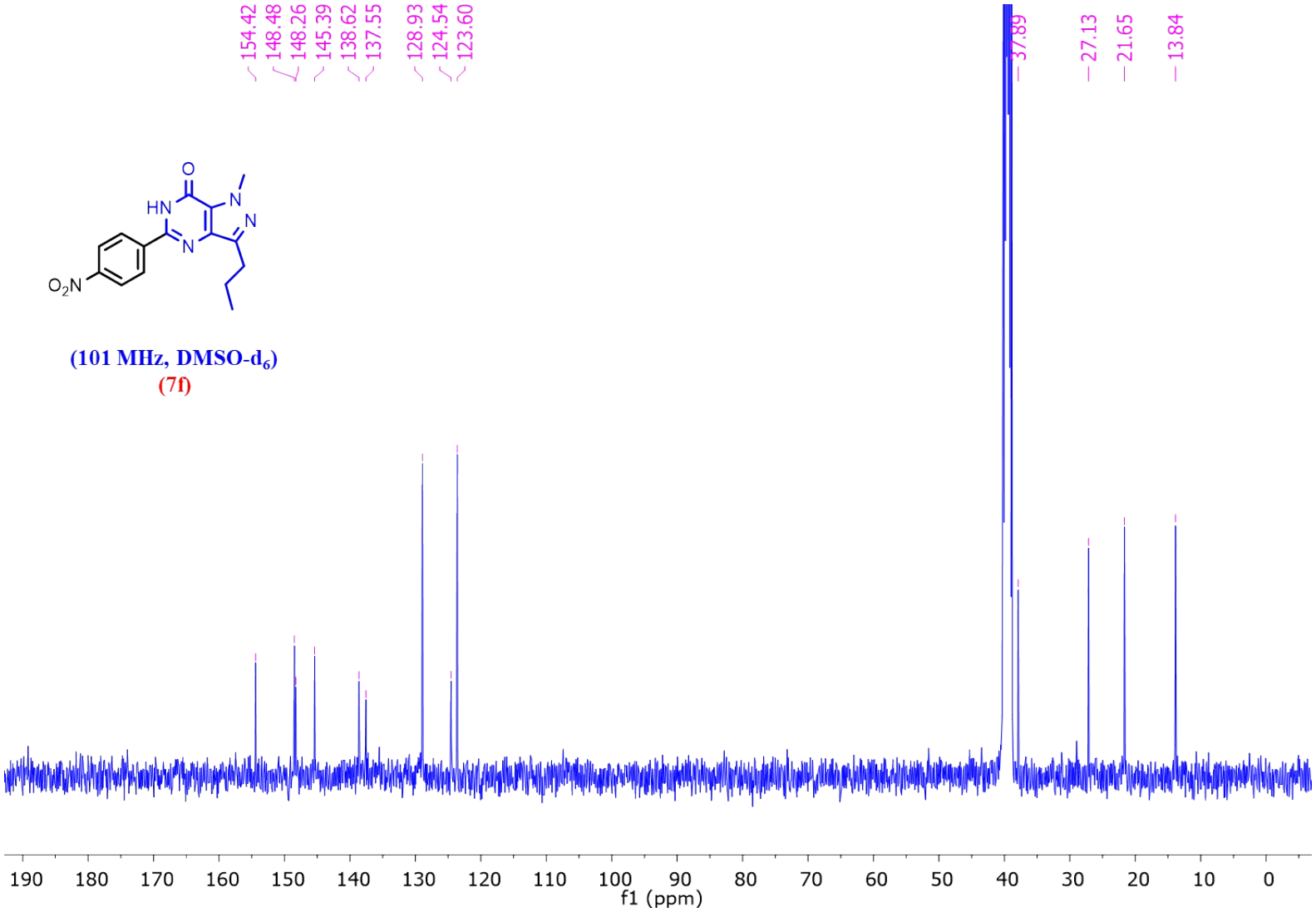


Fig. S106. ^{13}C NMR spectra of 1-Methyl-5-(4-nitrophenyl)-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7f)** in DMSO-d_6.

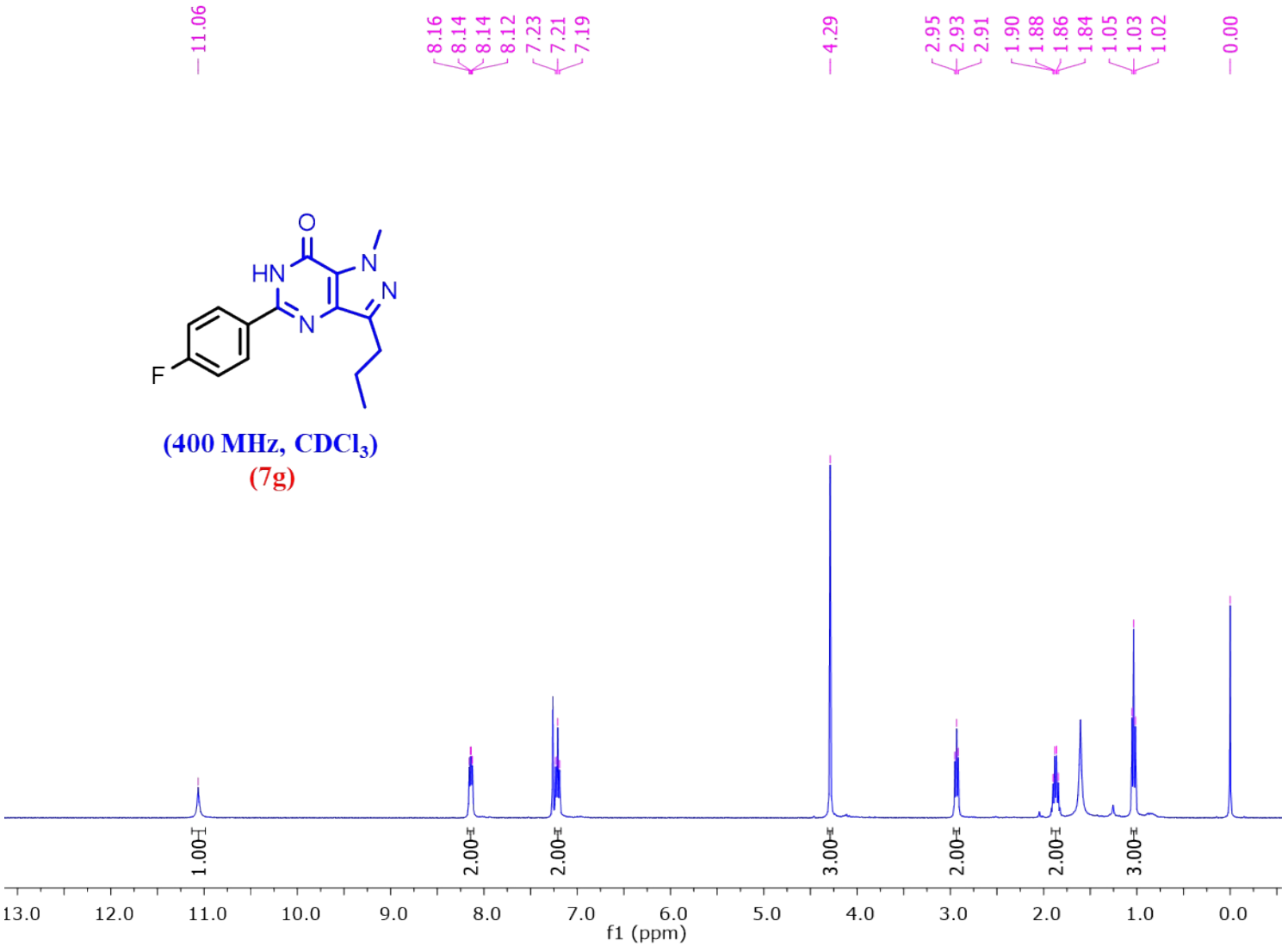


Fig. S107. ^{1}H NMR spectra of 5-(4-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7g)** in $CDCl_3$.

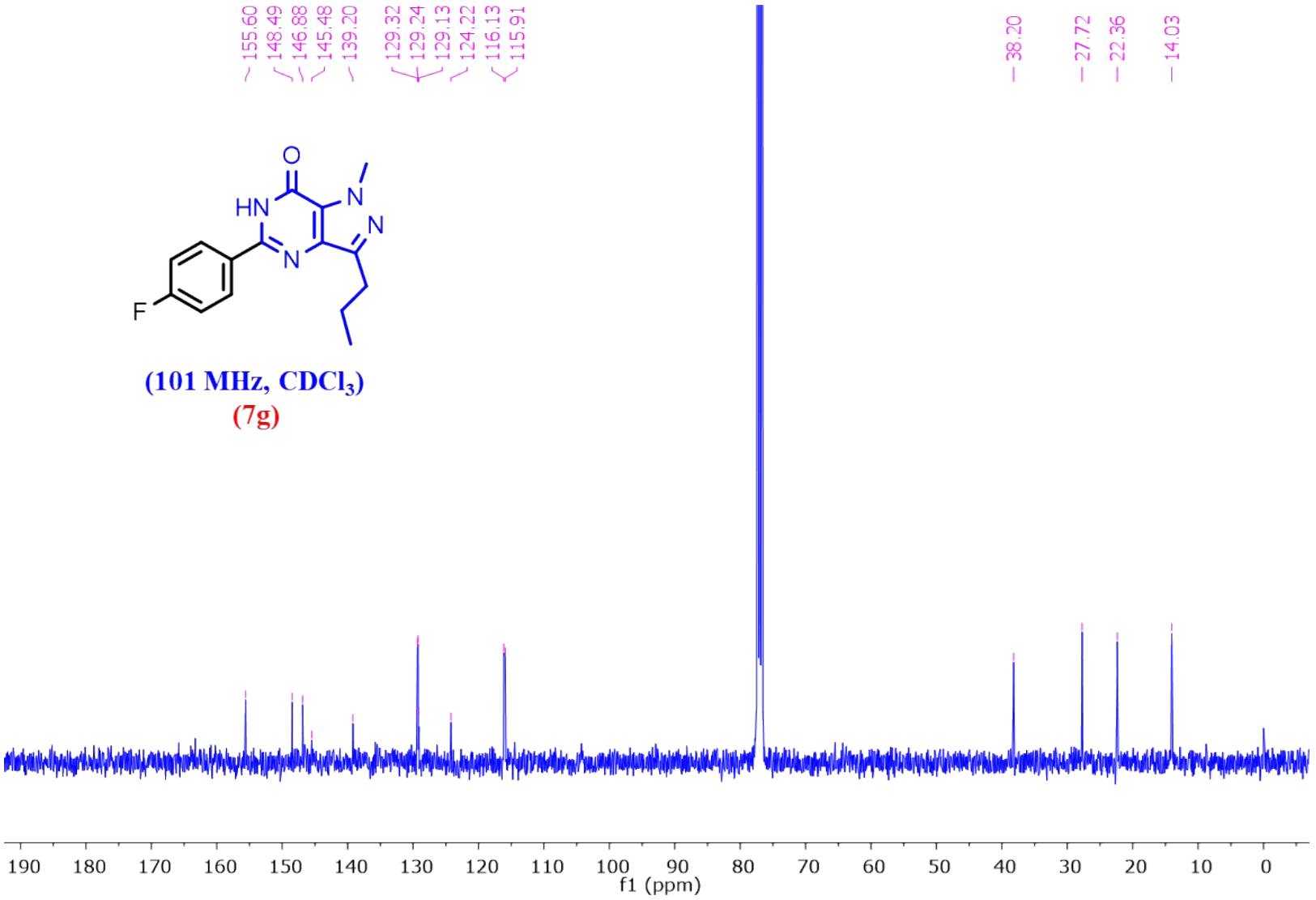


Fig. S108. ^{13}C NMR spectra of 5-(4-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7g)** in $CDCl_3$.

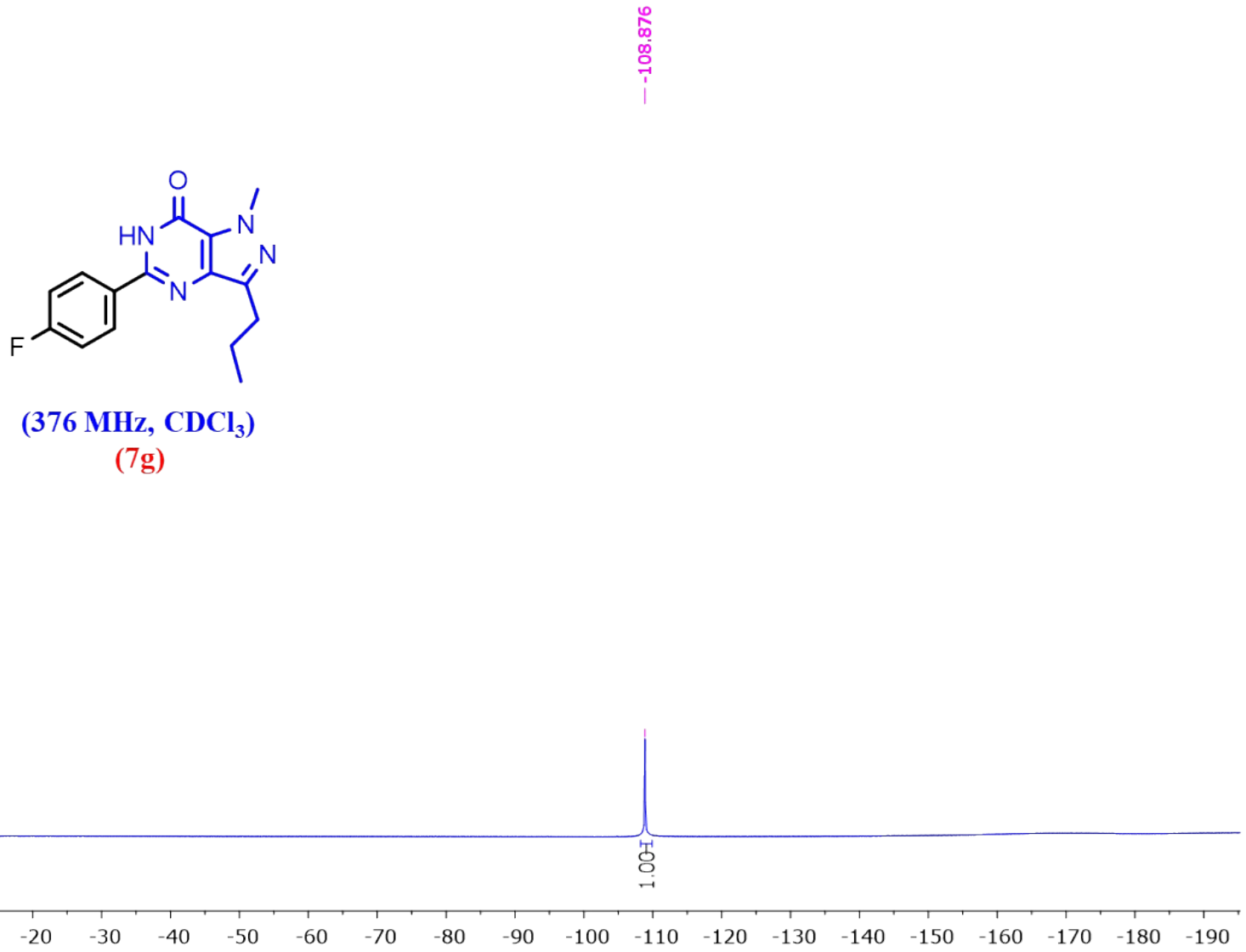


Fig. S109. ^{19}F NMR spectra of 5-(4-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7g)** in $CDCl_3$.

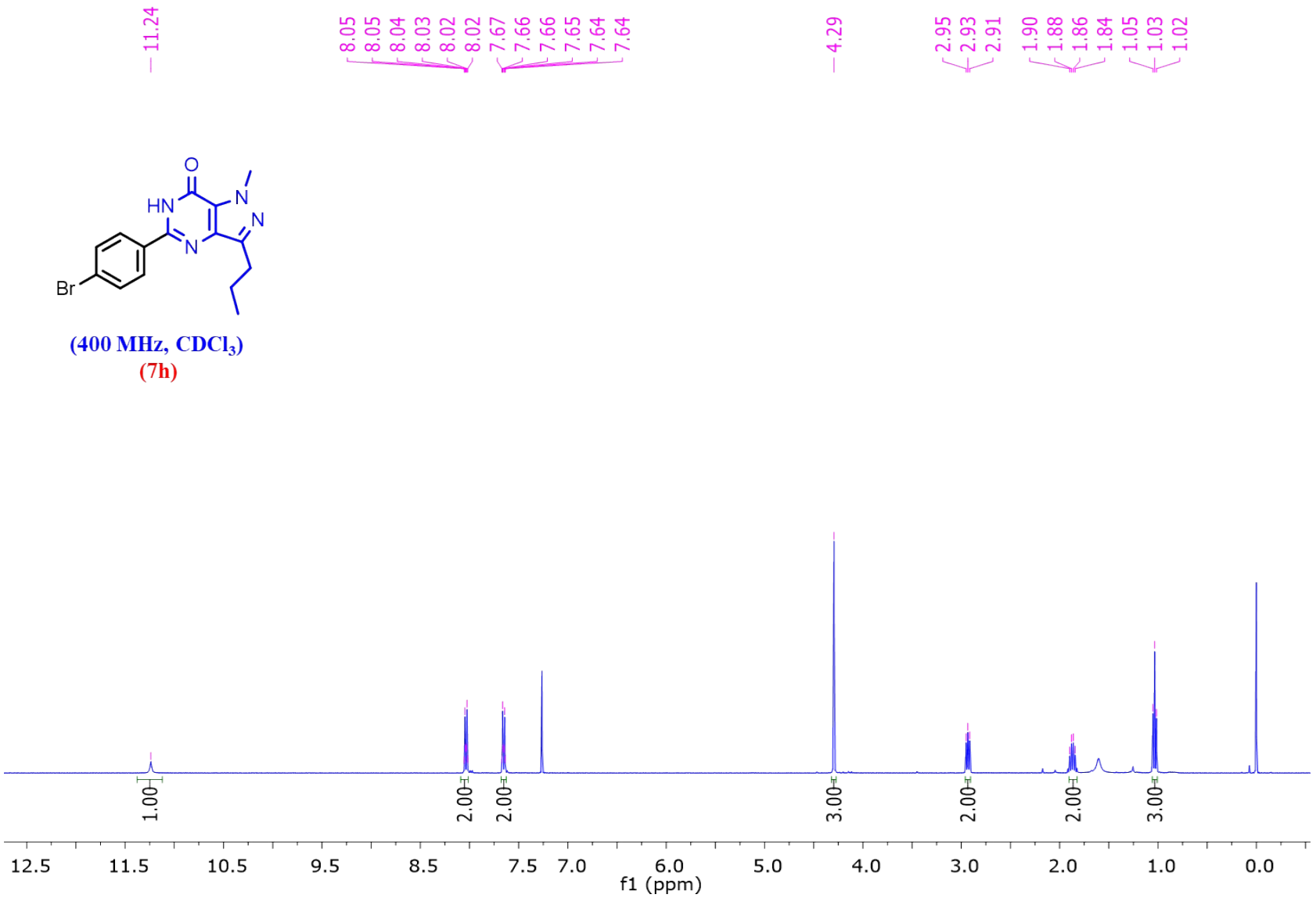


Fig. S110. [1]H NMR spectra of 5-(4-Bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7h)** in $CDCl_3$.

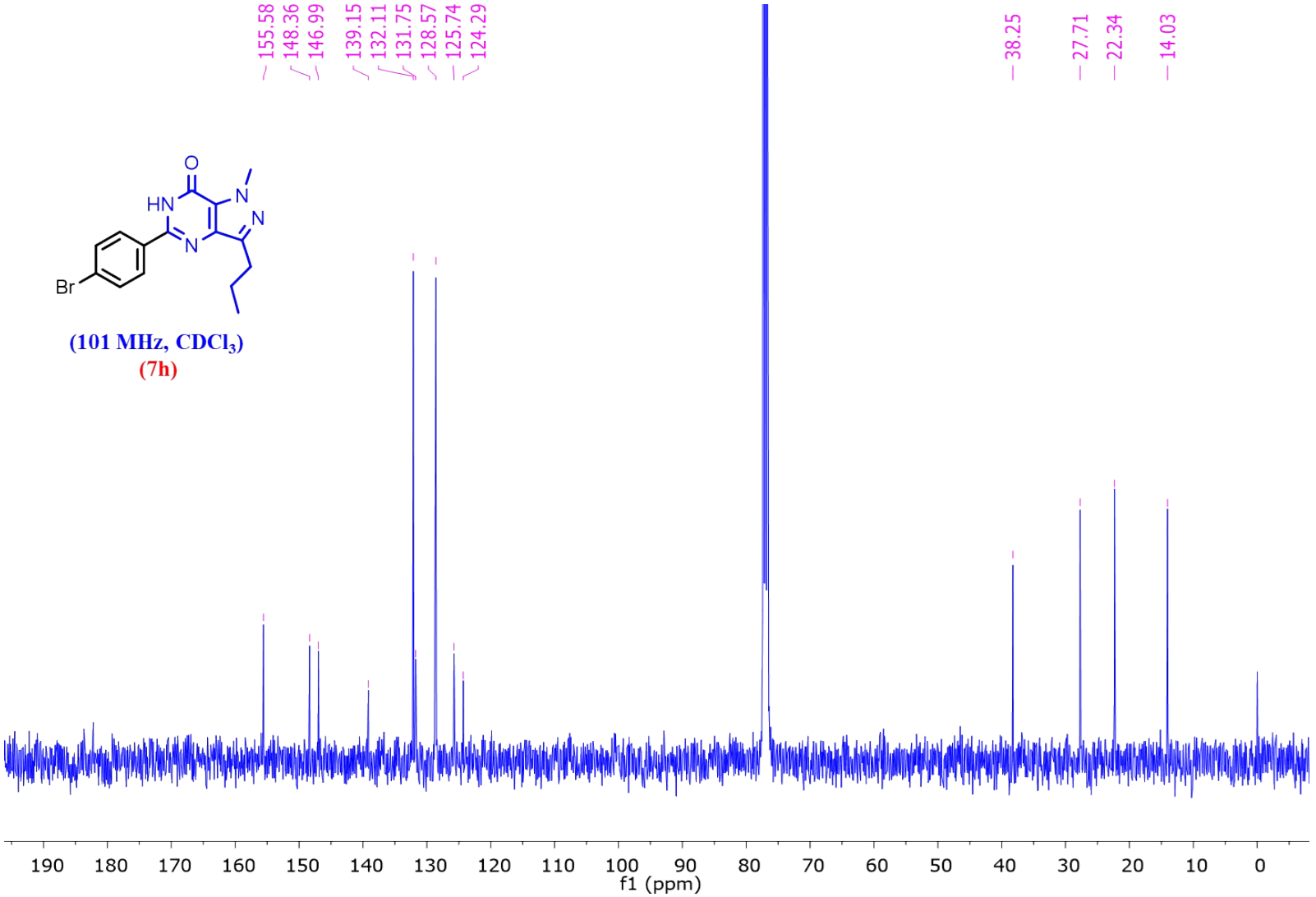


Fig. S111. ^{13}C NMR spectra of 5-(4-Bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7h)** in $CDCl_3$.

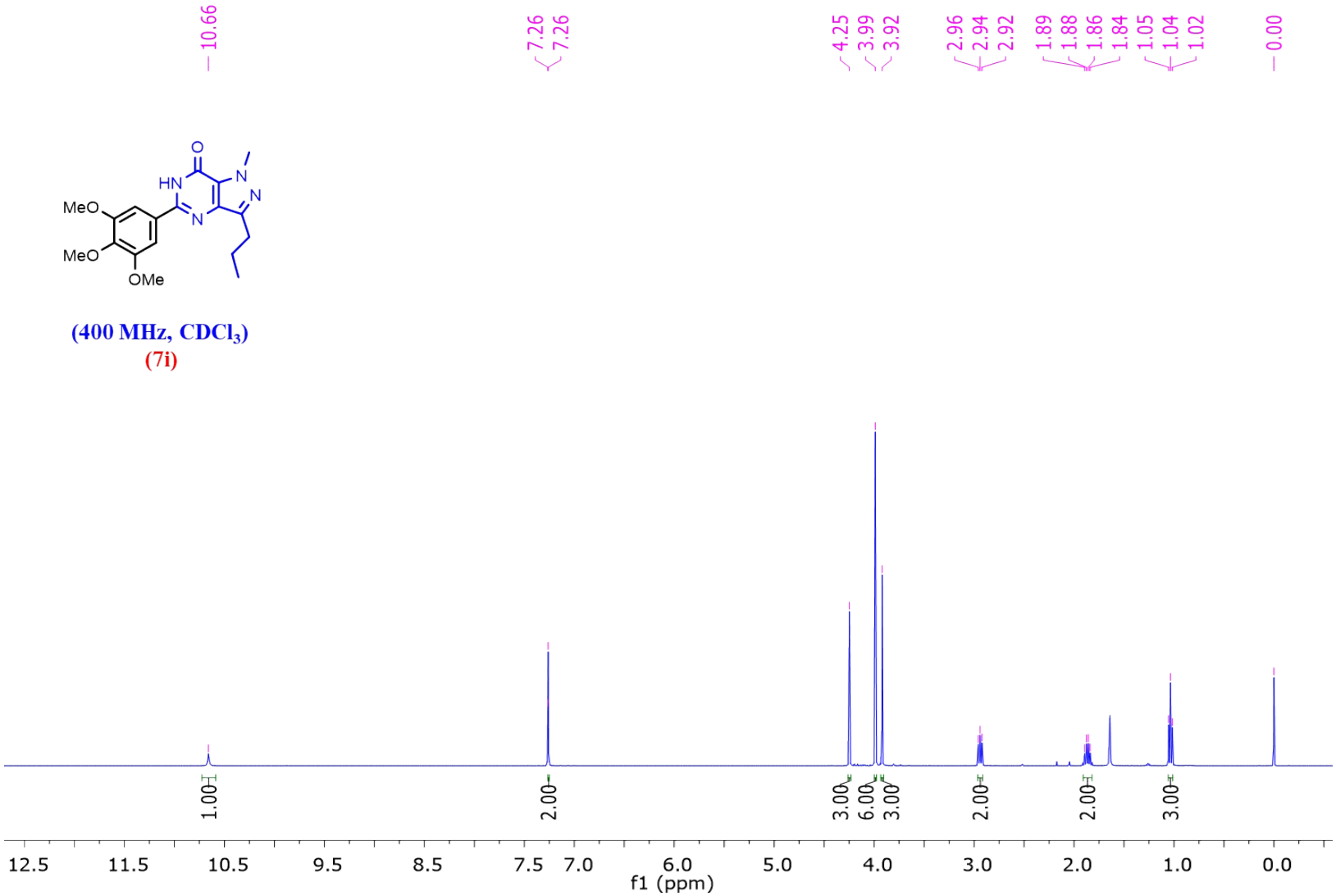


Fig. S112. ^{1}H NMR spectra of 1-Methyl-3-propyl-5-(3,4,5-trimethoxyphenyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7i)** in $CDCl_3$.

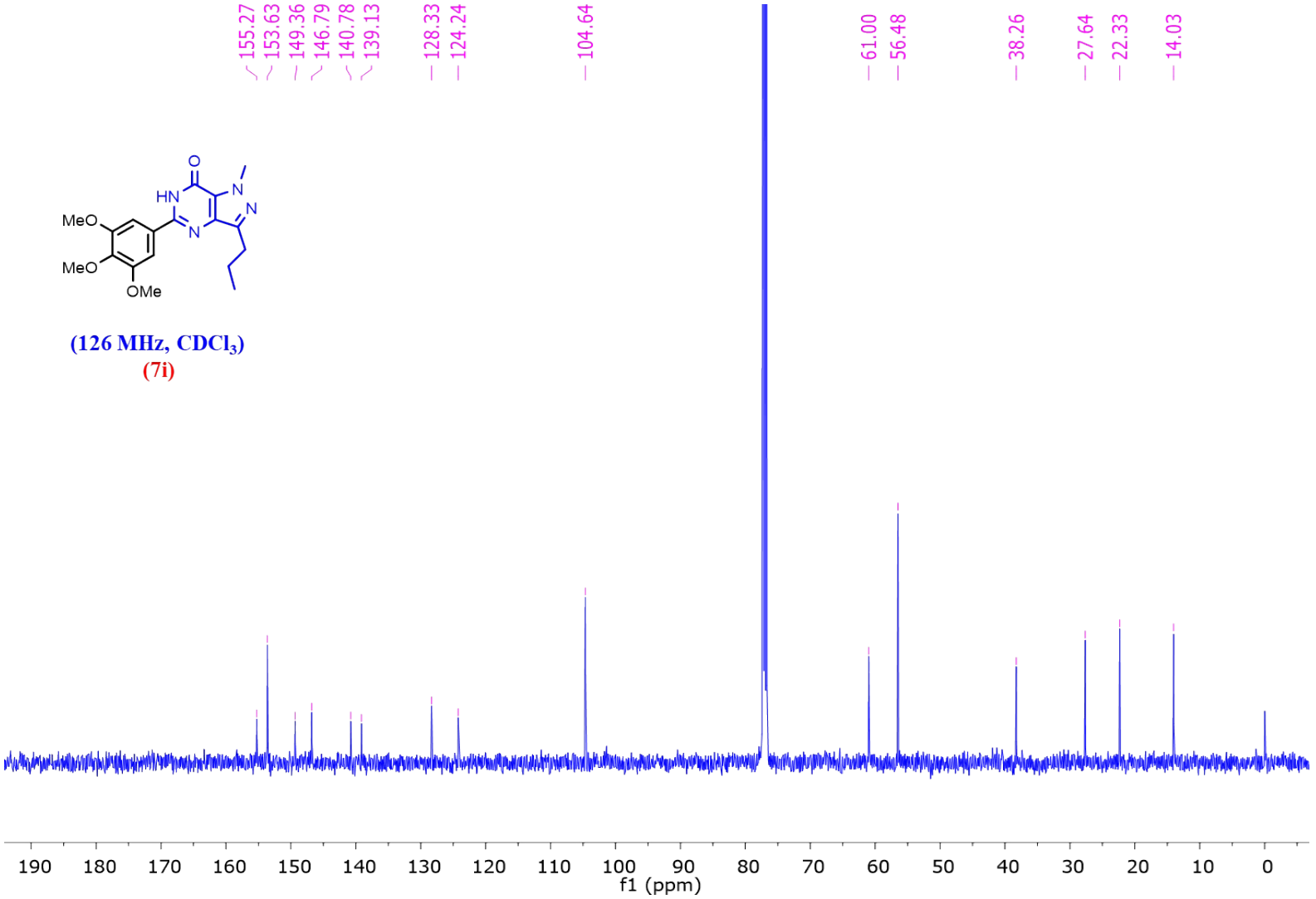


Fig. S113. ^{13}C NMR spectra of 1-Methyl-3-propyl-5-(3,4,5-trimethoxyphenyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7i)** in $CDCl_3$

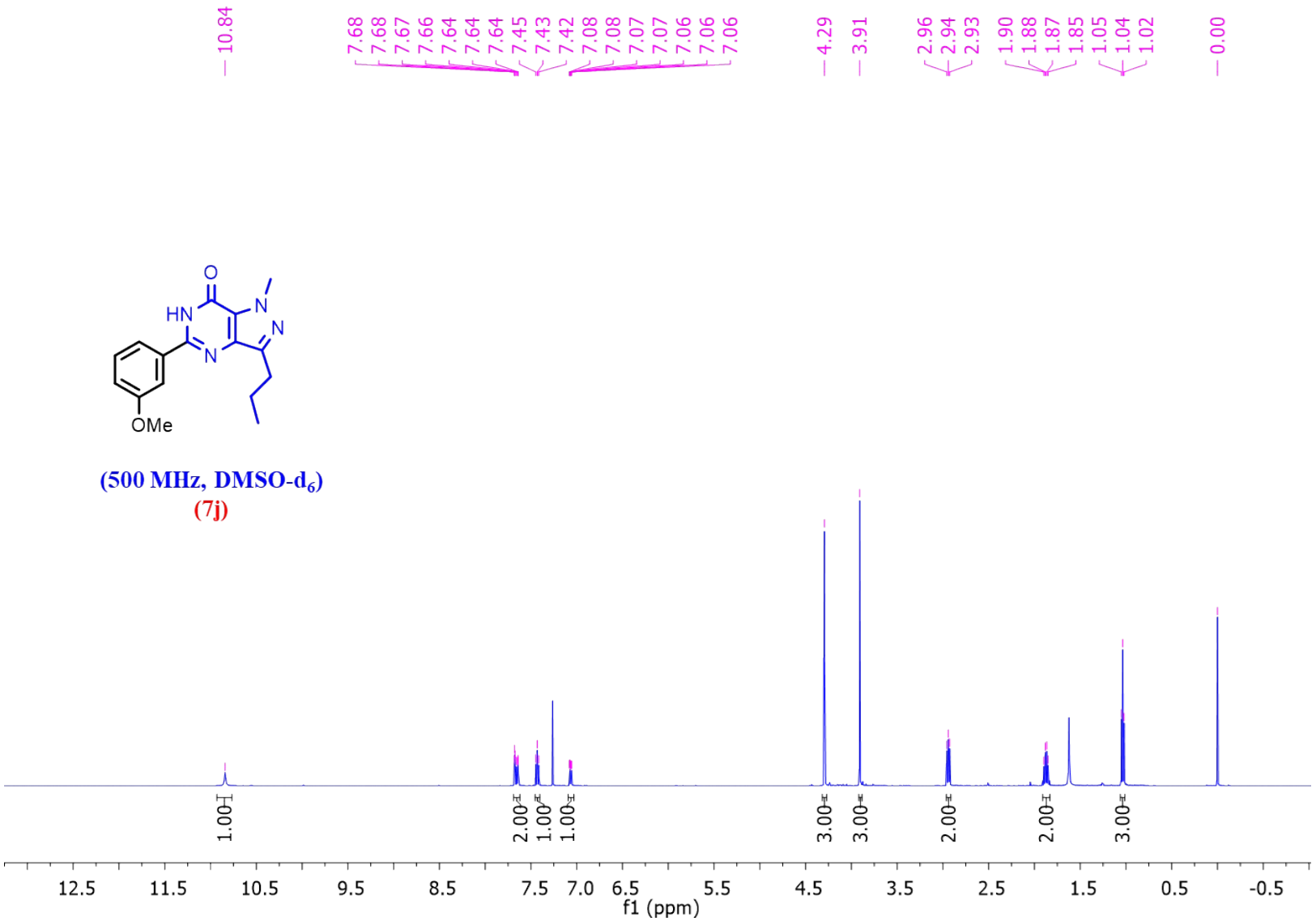


Fig. S114. ^{1}H NMR spectra of 1-Methyl-3-propyl-5-(m-tolyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7j)** in $CDCl_3$.

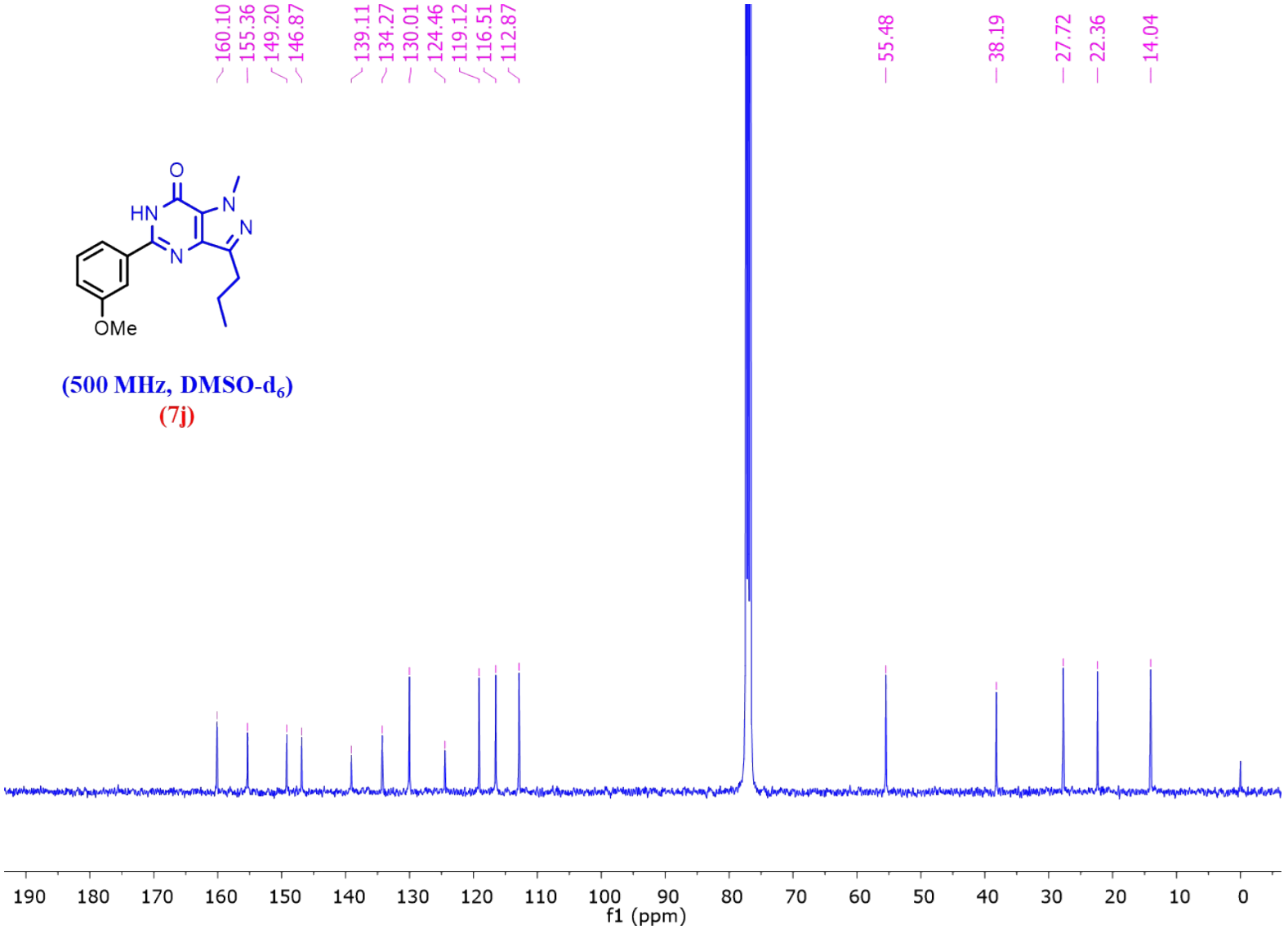


Fig. S115. ^{13}C NMR spectra of 1-Methyl-3-propyl-5-(m-tolyl)-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7j)** in $CDCl_3$.

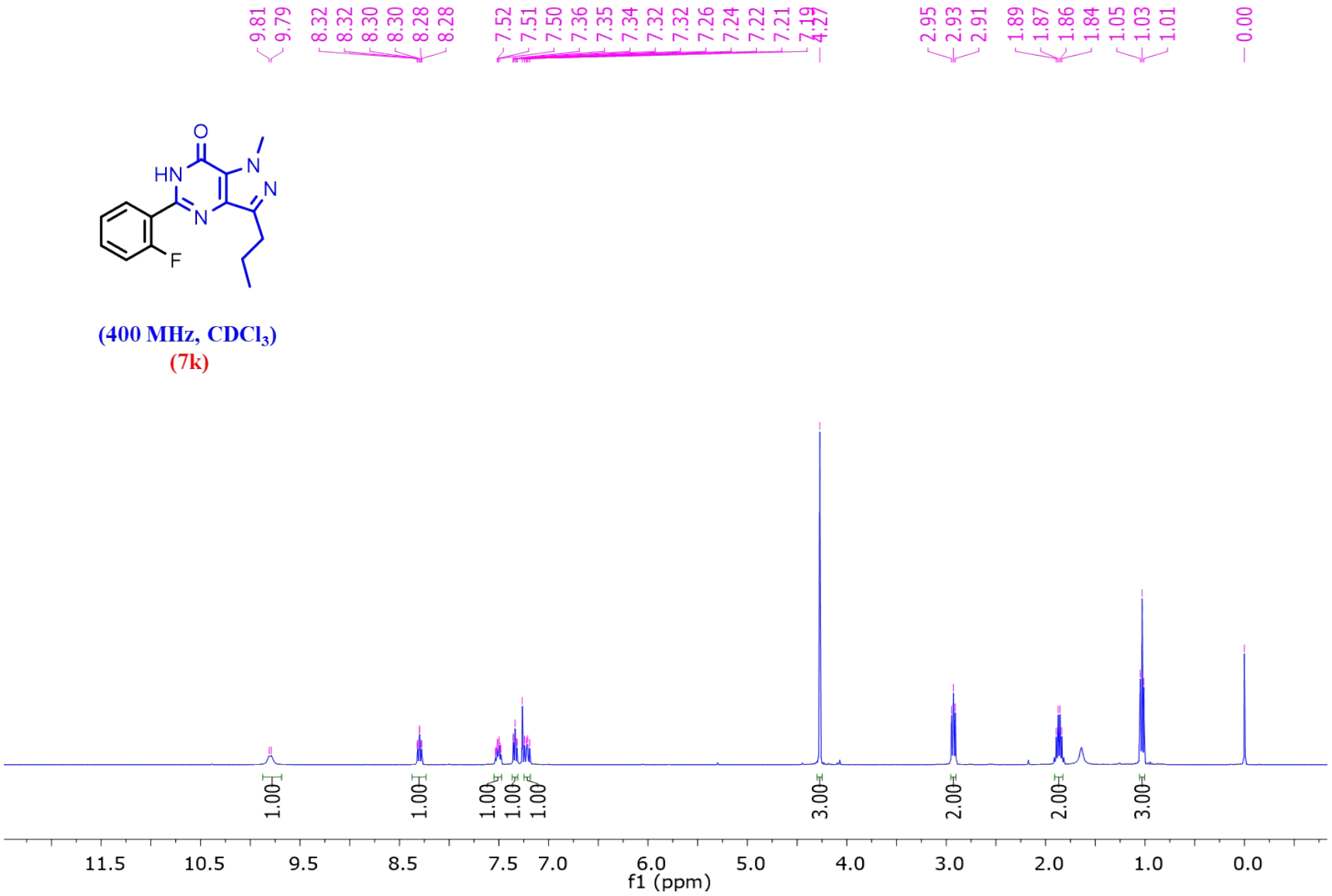


Fig. S116. ^{1}H NMR spectra of 5-(2-Fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7k)** in $CDCl_3$.

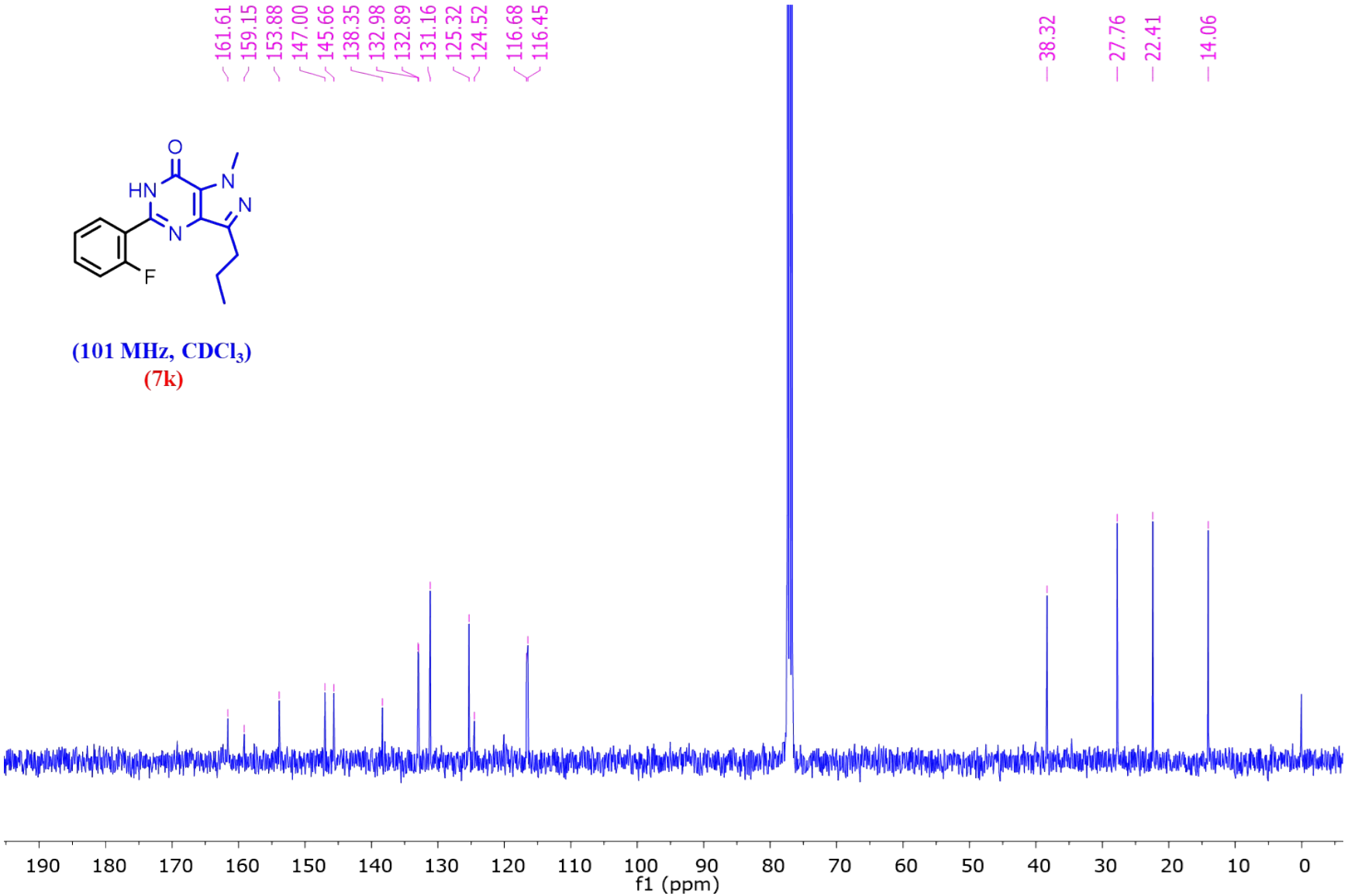


Fig. S117. ^{13}C NMR spectra of 5-(2-Fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7k)** in $CDCl_3$.

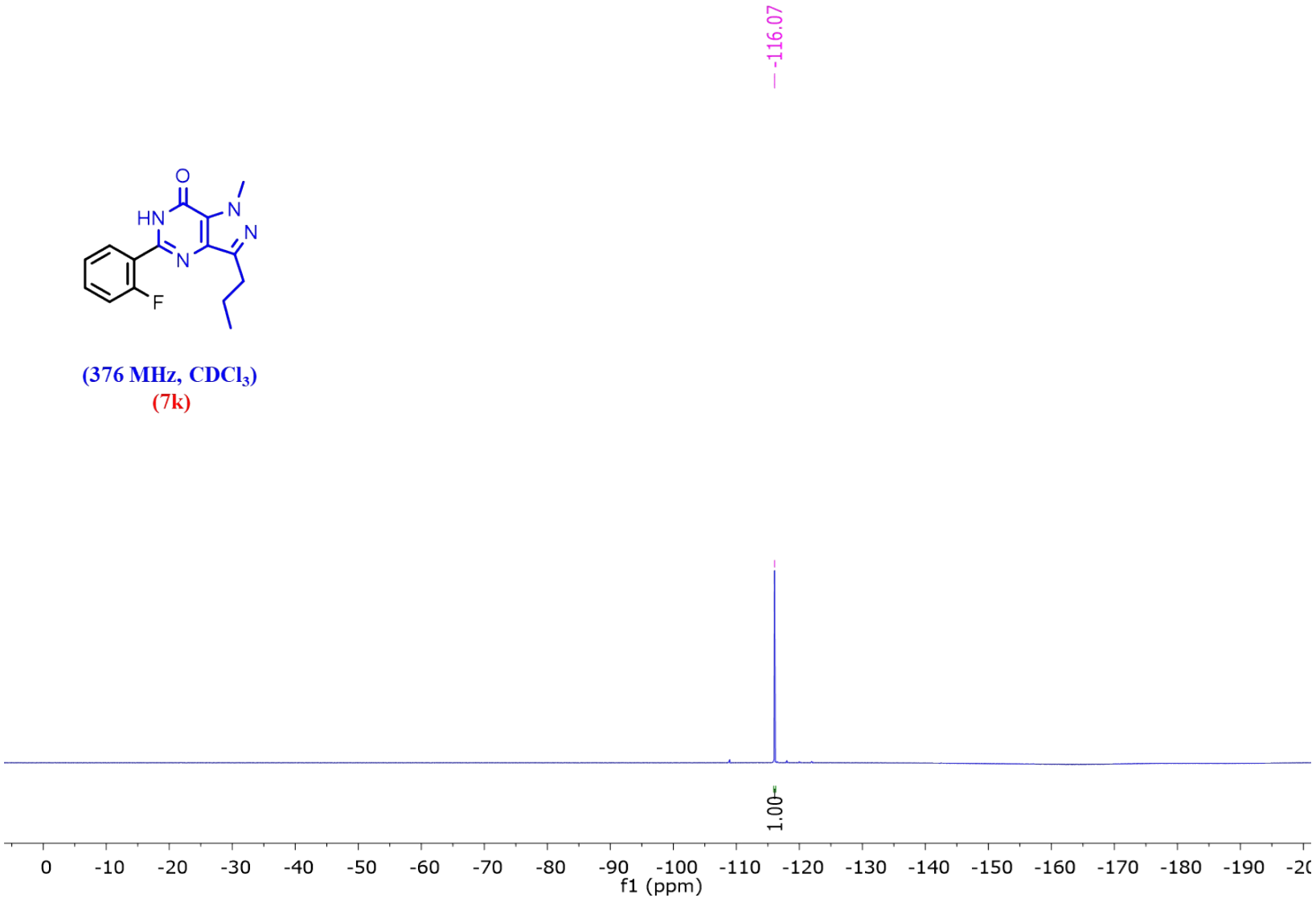


Fig. S118. ^{19}F NMR spectra of 5-(2-Fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7k)** in $CDCl_3$.

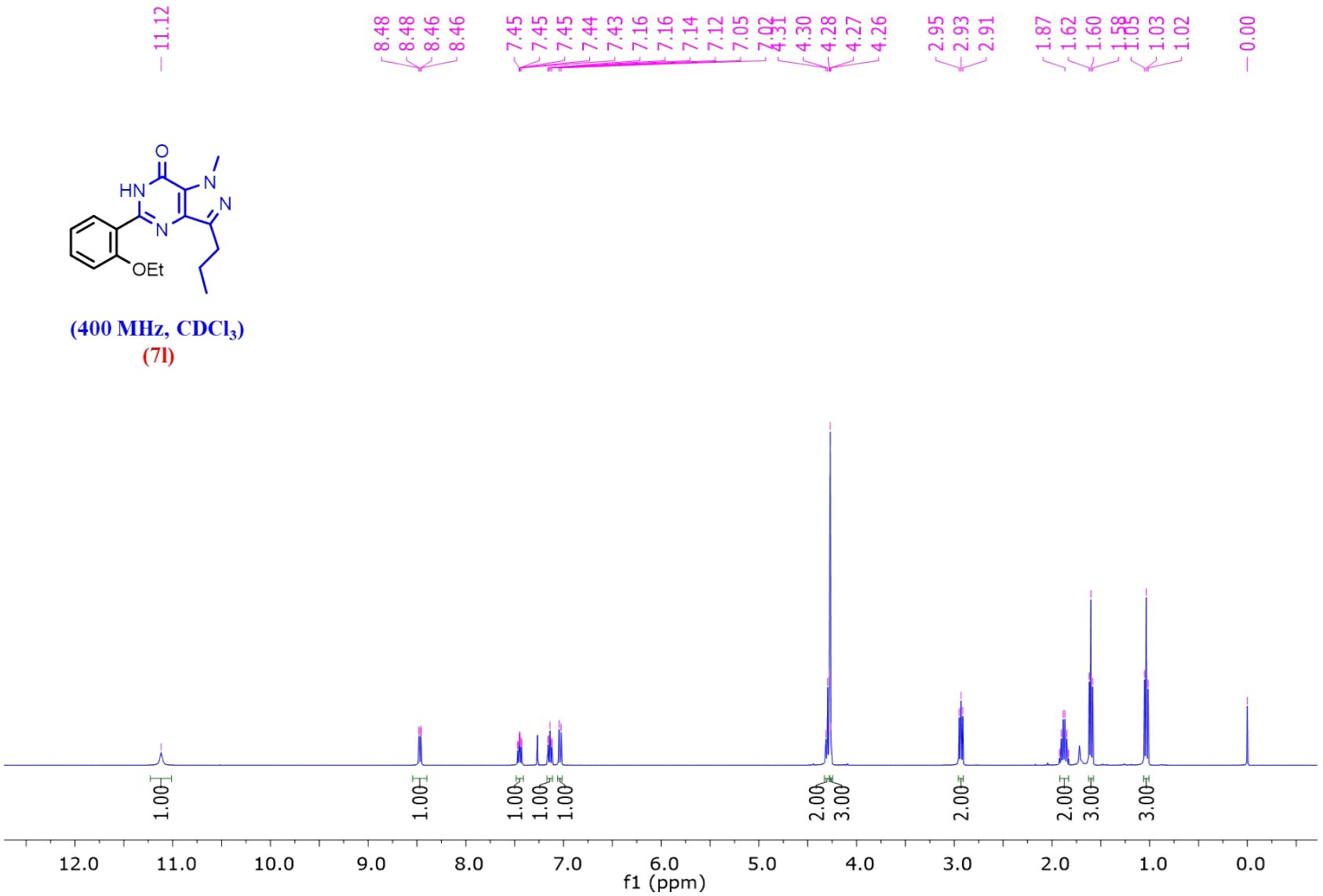


Fig. S119. ^{1}H NMR spectra of 5-(2-Ethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7l)** in $CDCl_3$.

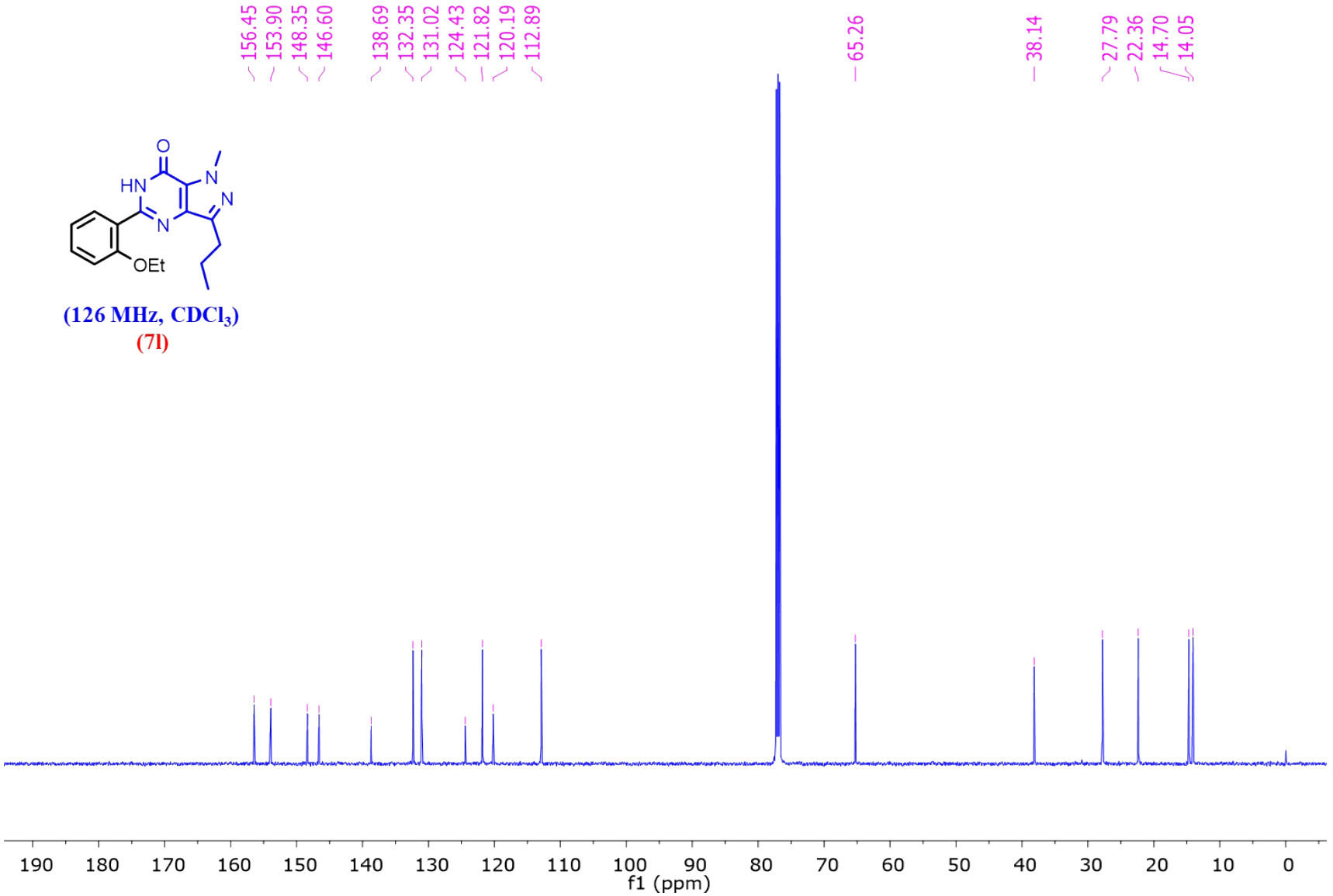


Fig. S120. ^{13}C NMR spectra of 5-(2-Ethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **(7l)** in $CDCl_3$.

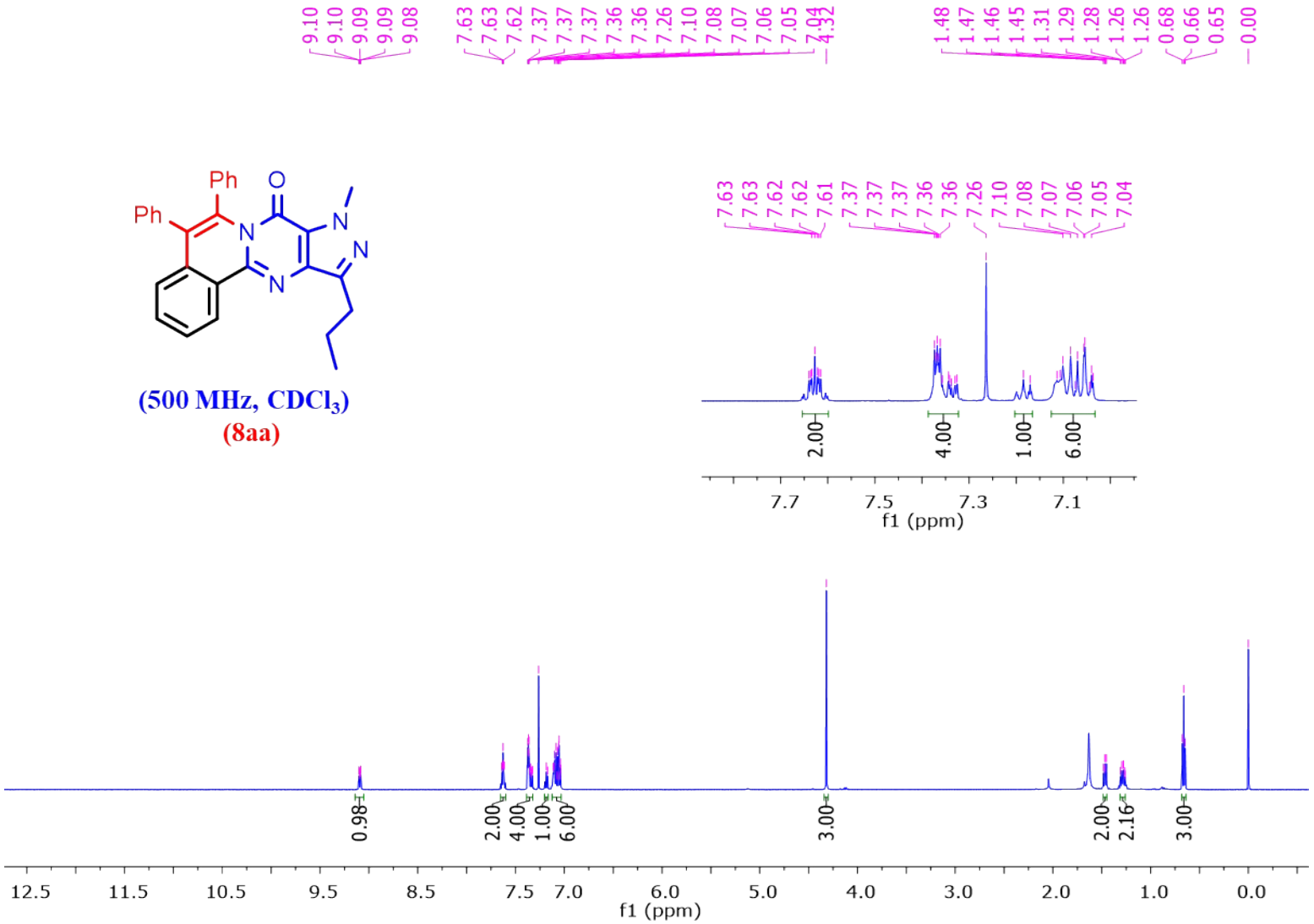


Fig. S121. ^{1}H NMR spectra of 9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8aa)** in $CDCl_3$.

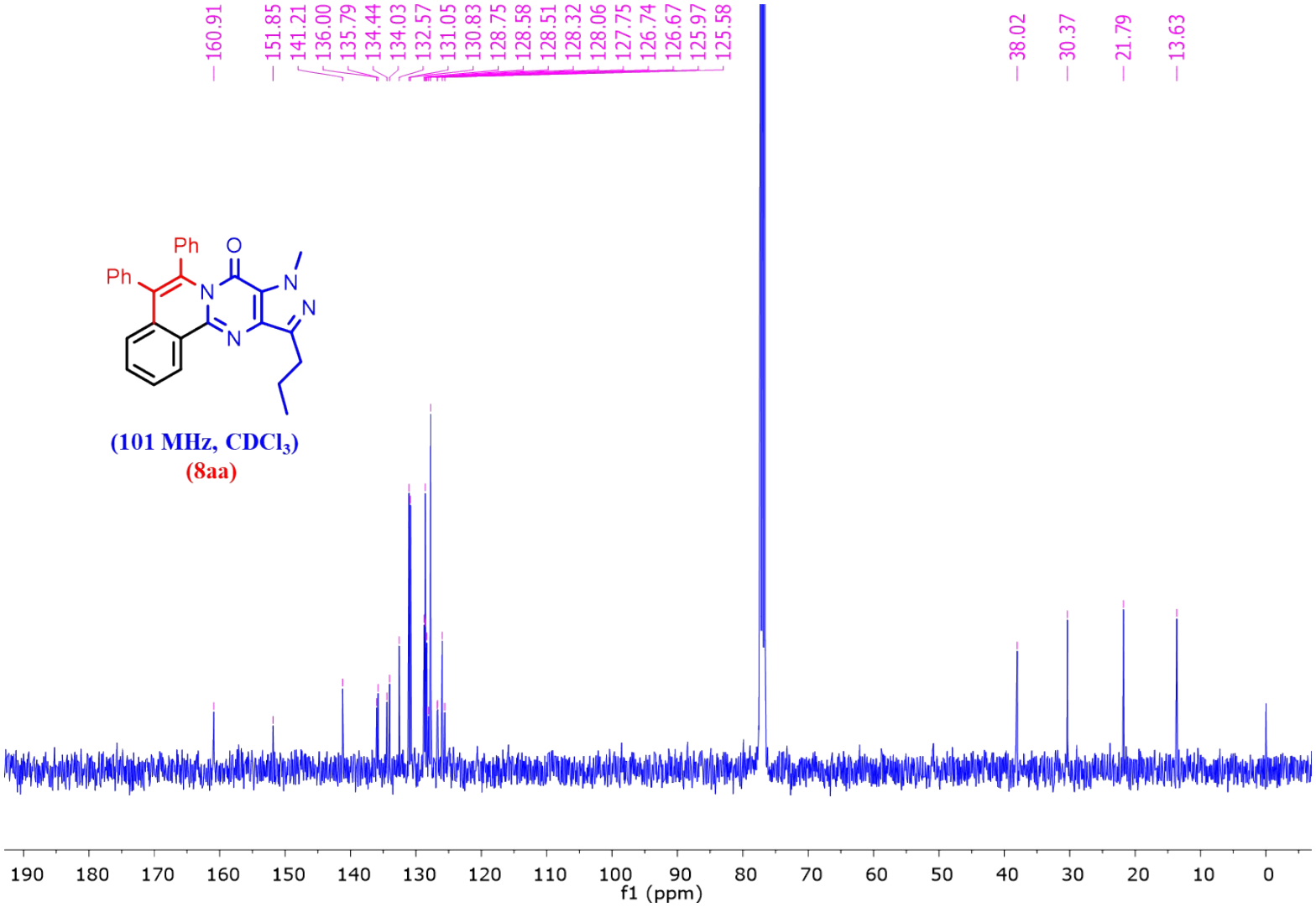


Fig. S122. ^{13}C NMR spectra of 9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8aa)** in $CDCl_3$.

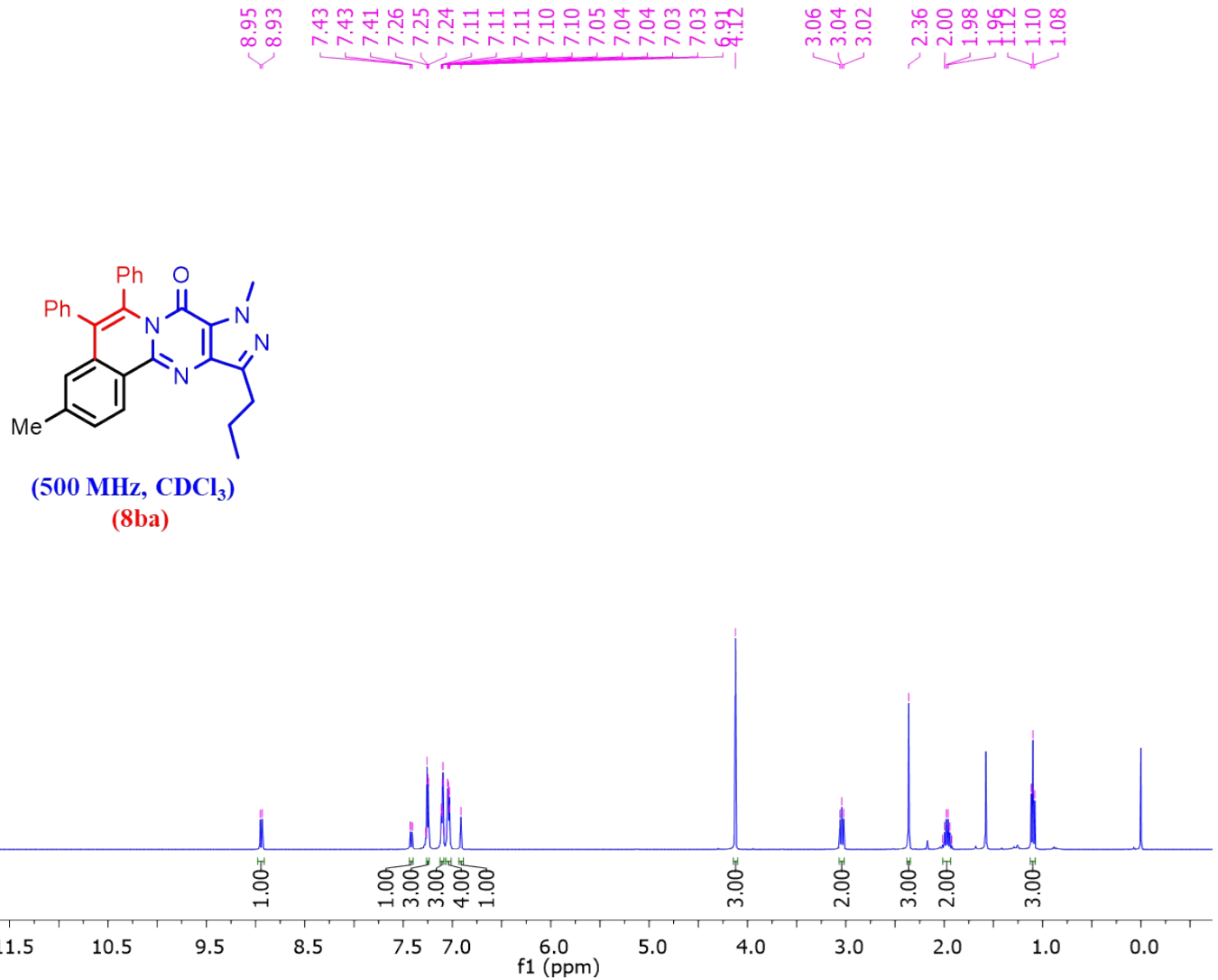


Fig. S123 ^{1}H NMR spectra of 3,9-Mimethyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ba)** in $CDCl_3$.

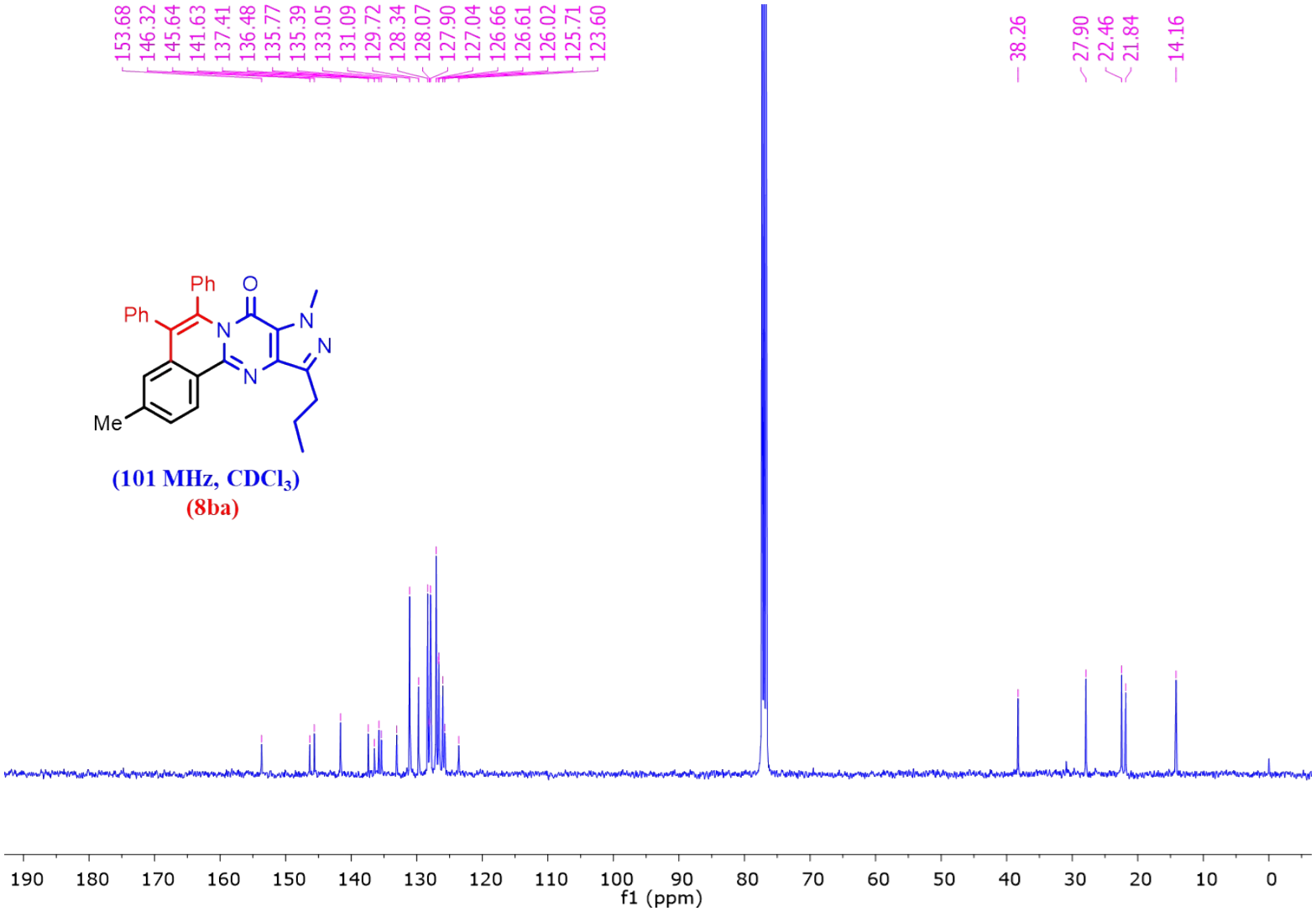


Fig. S124. ^{13}C NMR spectra of 3,9-Mimethyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ba)** in $CDCl_3$.

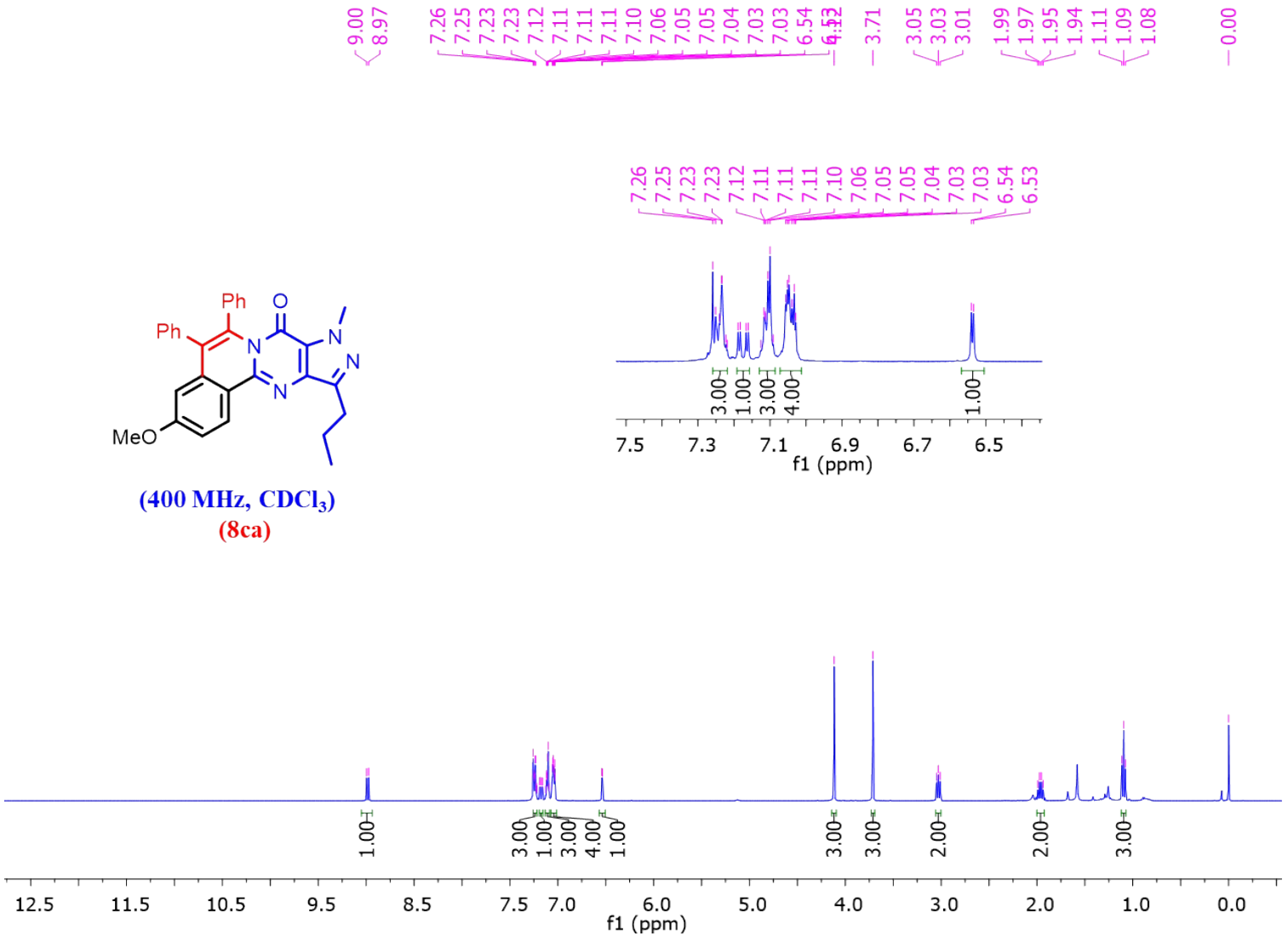


Fig. S125. ^{1}H NMR spectra of 3-Methoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ca)** in $CDCl_3$.

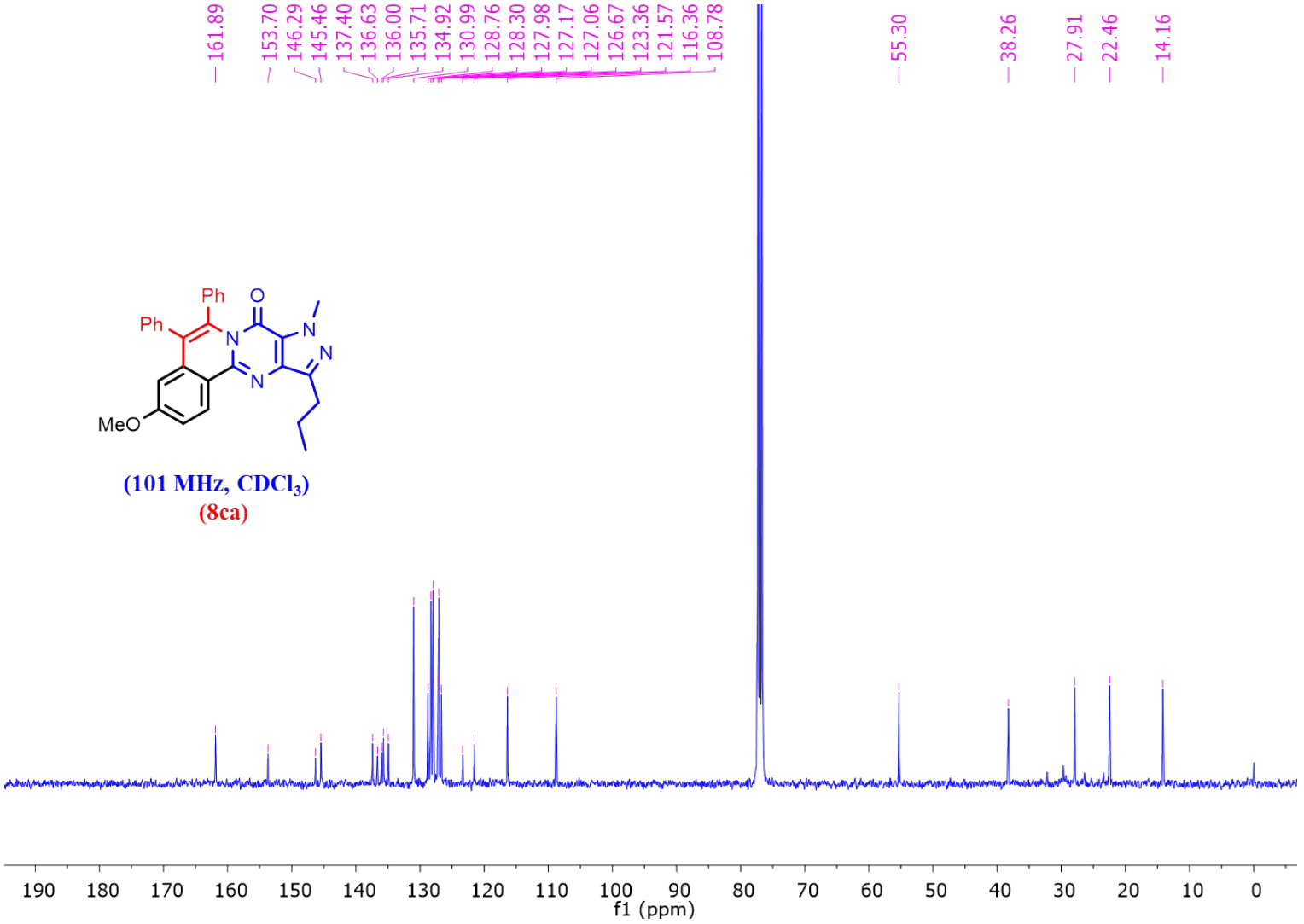


Fig. S126. ^{13}C NMR spectra of 3-Methoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ca)** in $CDCl_3$.

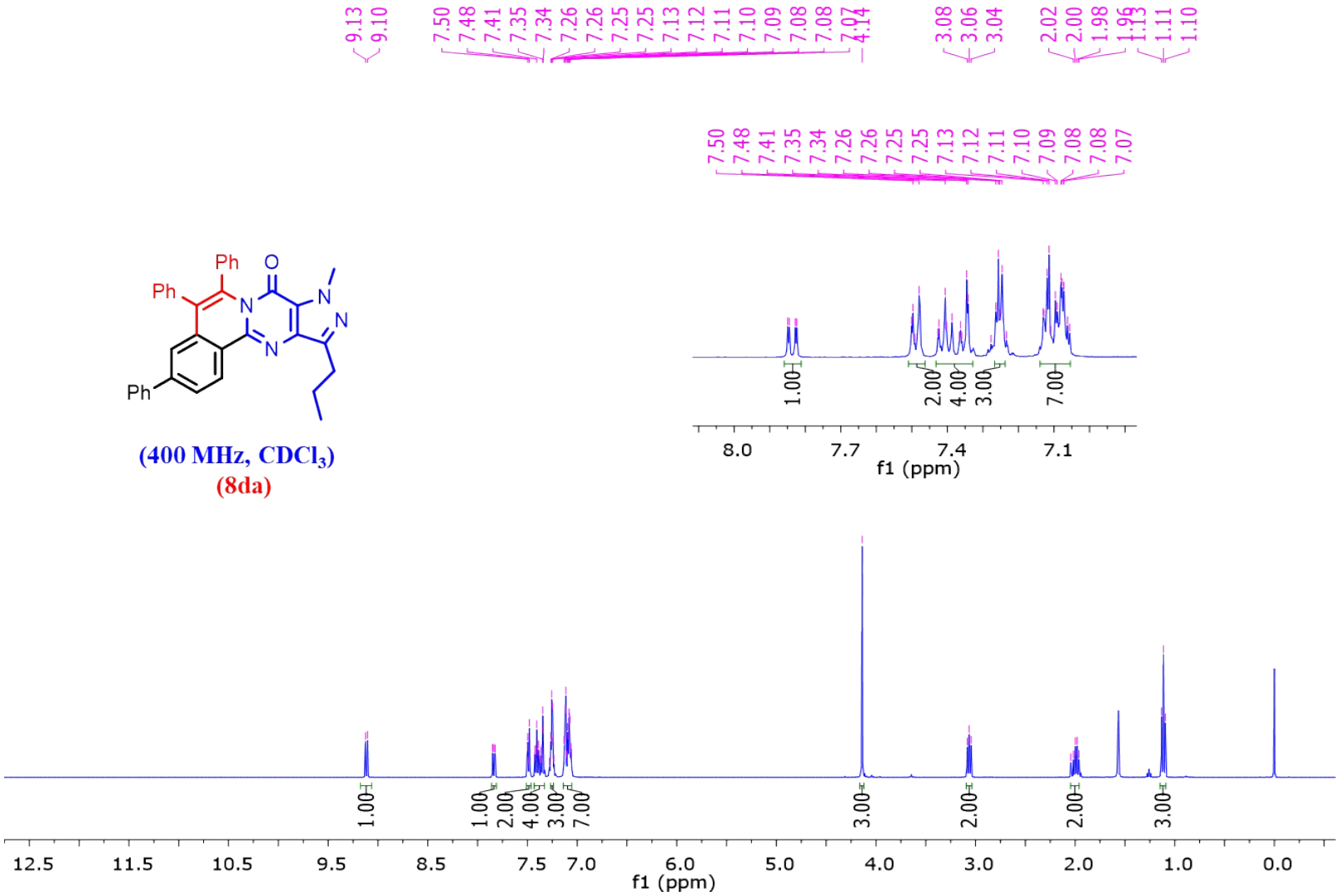


Fig. S127. ^{1}H NMR spectra of 9-Methyl-3,5,6-triphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8da)** in $CDCl_3$.

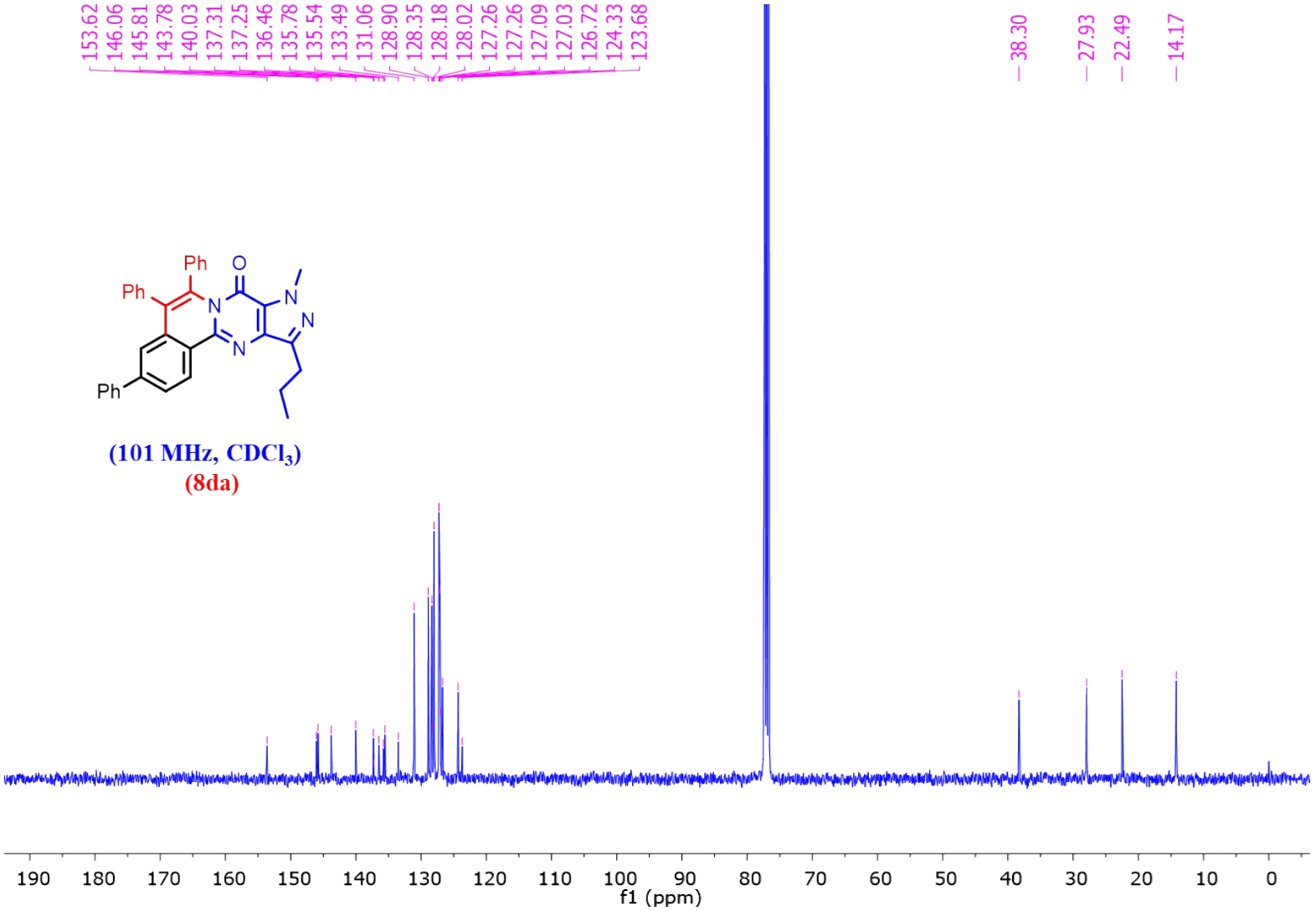


Fig. S128. ^{13}C NMR spectra of 9-Methyl-3,5,6-triphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8da)** in $CDCl_3$.

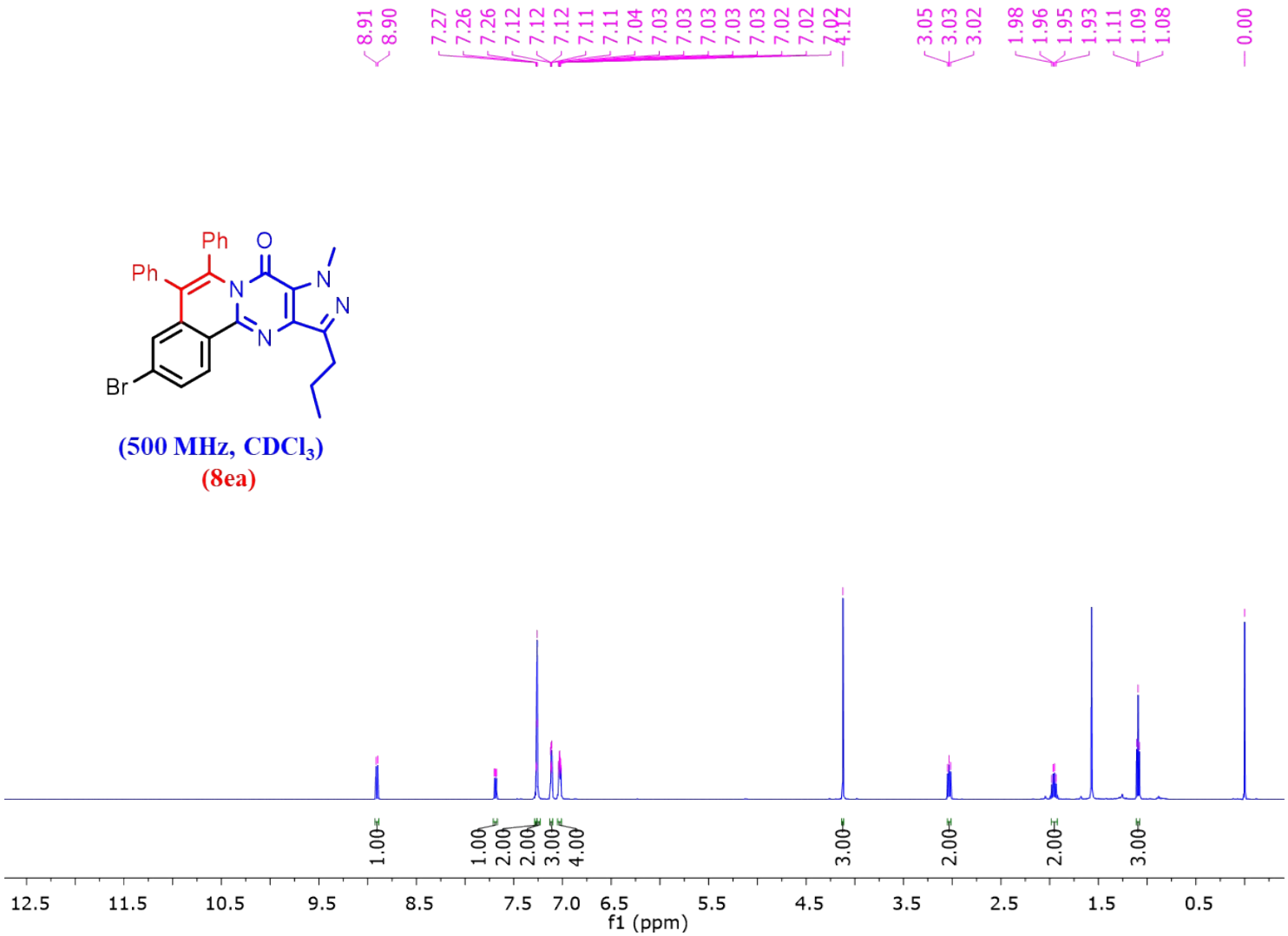


Fig. S139. ^{1}H NMR spectra of 3-Bromo-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ea)** in $CDCl_3$.

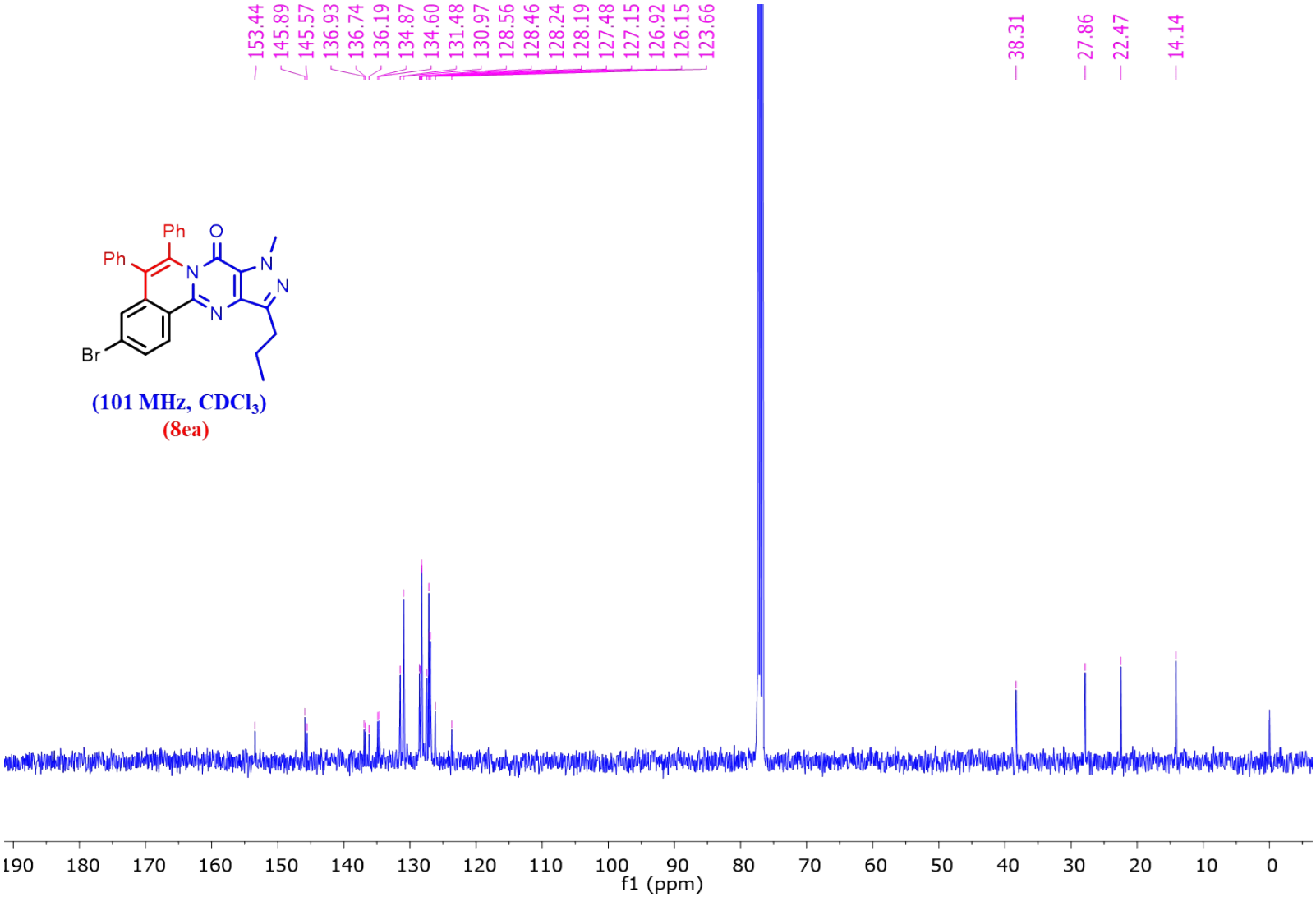


Fig. S130. ^{13}C NMR spectra of 3-Bromo-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ea)** in $CDCl_3$.

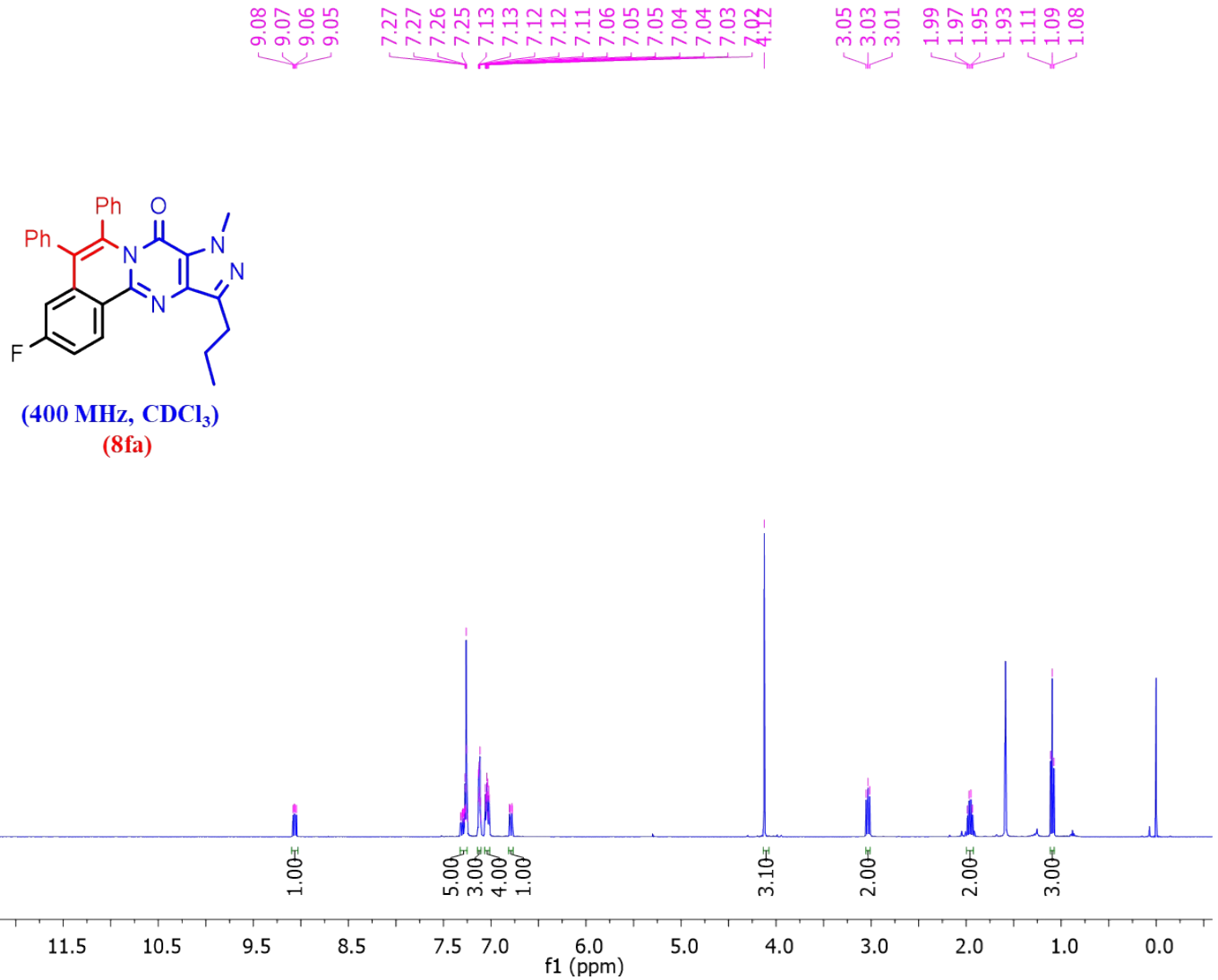


Fig. S131. ^{1}H NMR spectra of 3-fluoro-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8fa)** in $CDCl_3$.

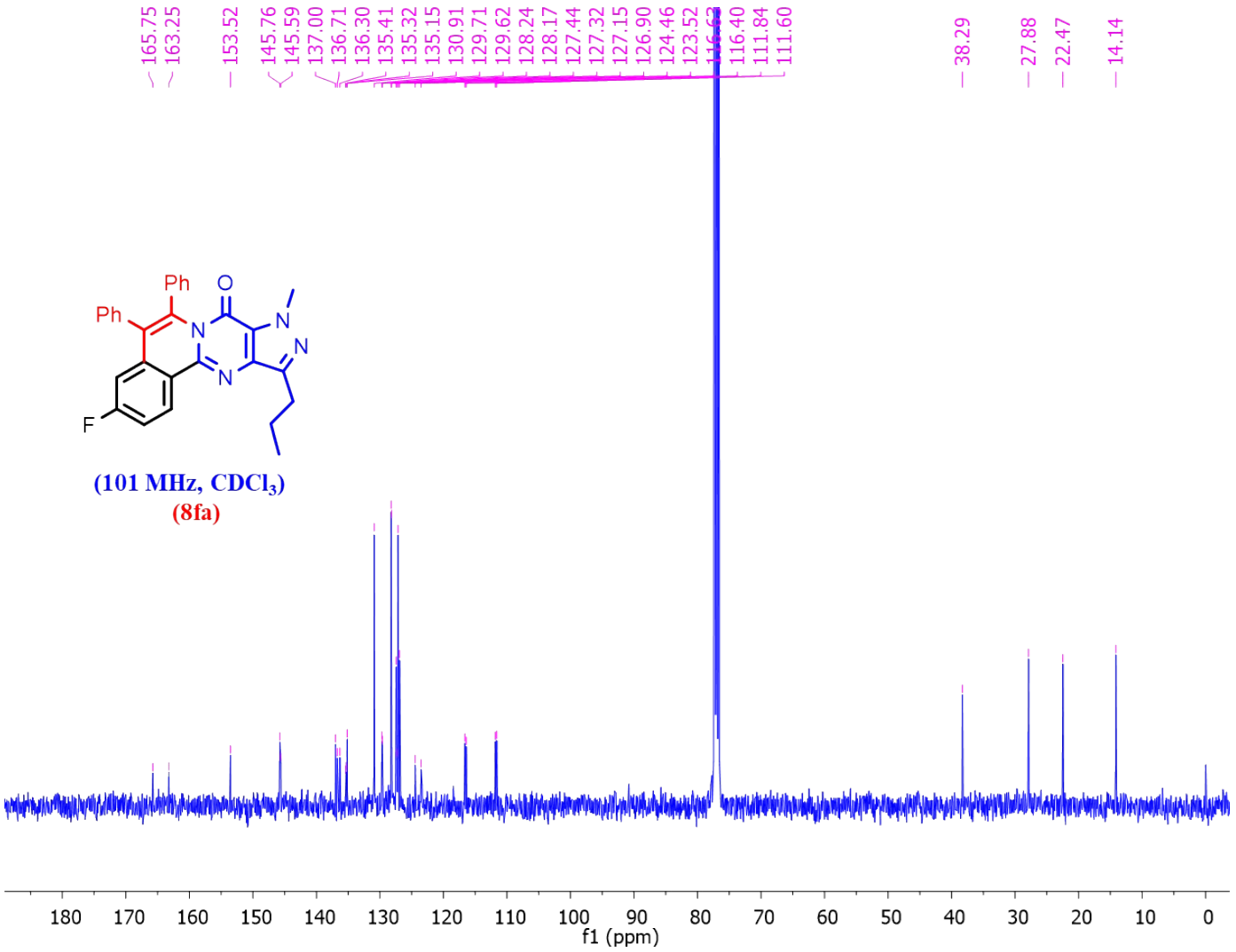
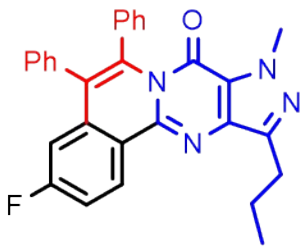


Fig. S132. ^{13}C NMR spectra of 3-fluoro-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8fa)** in $CDCl_3$.



(376 MHz, $CDCl_3$)
(8fa)

Fig. S133. ^{19}F NMR spectra of 3-fluoro-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8fa)** in $CDCl_3$.

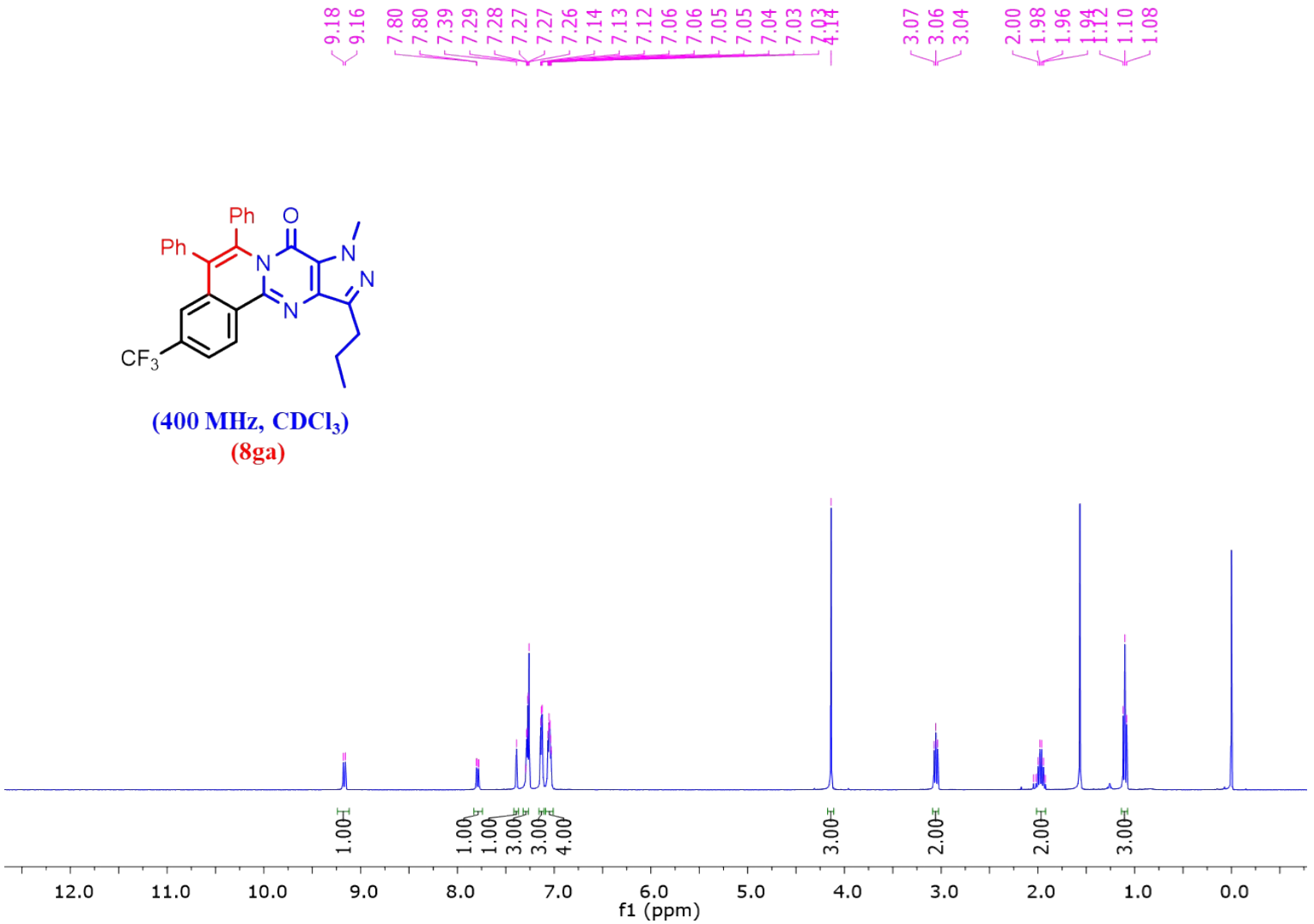


Fig. S134. ^{1}H NMR spectra of 9-Methyl-5,6-diphenyl-11-propyl-3-(trifluoromethyl)pyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ga)** in $CDCl_3$.

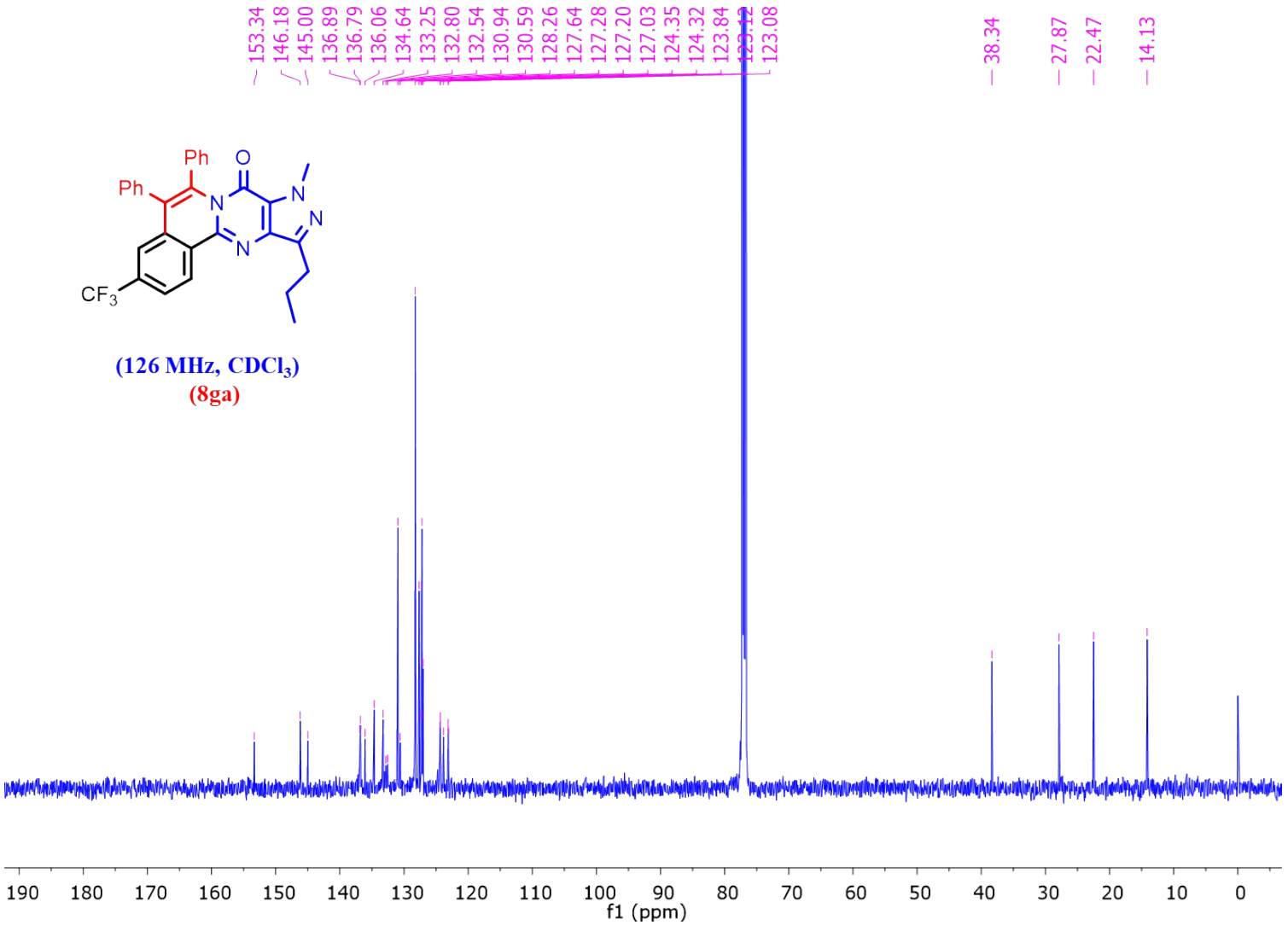


Fig. S135. ^{13}C NMR spectra of 9-Methyl-5,6-diphenyl-11-propyl-3-(trifluoromethyl)pyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ga)** in $CDCl_3$.

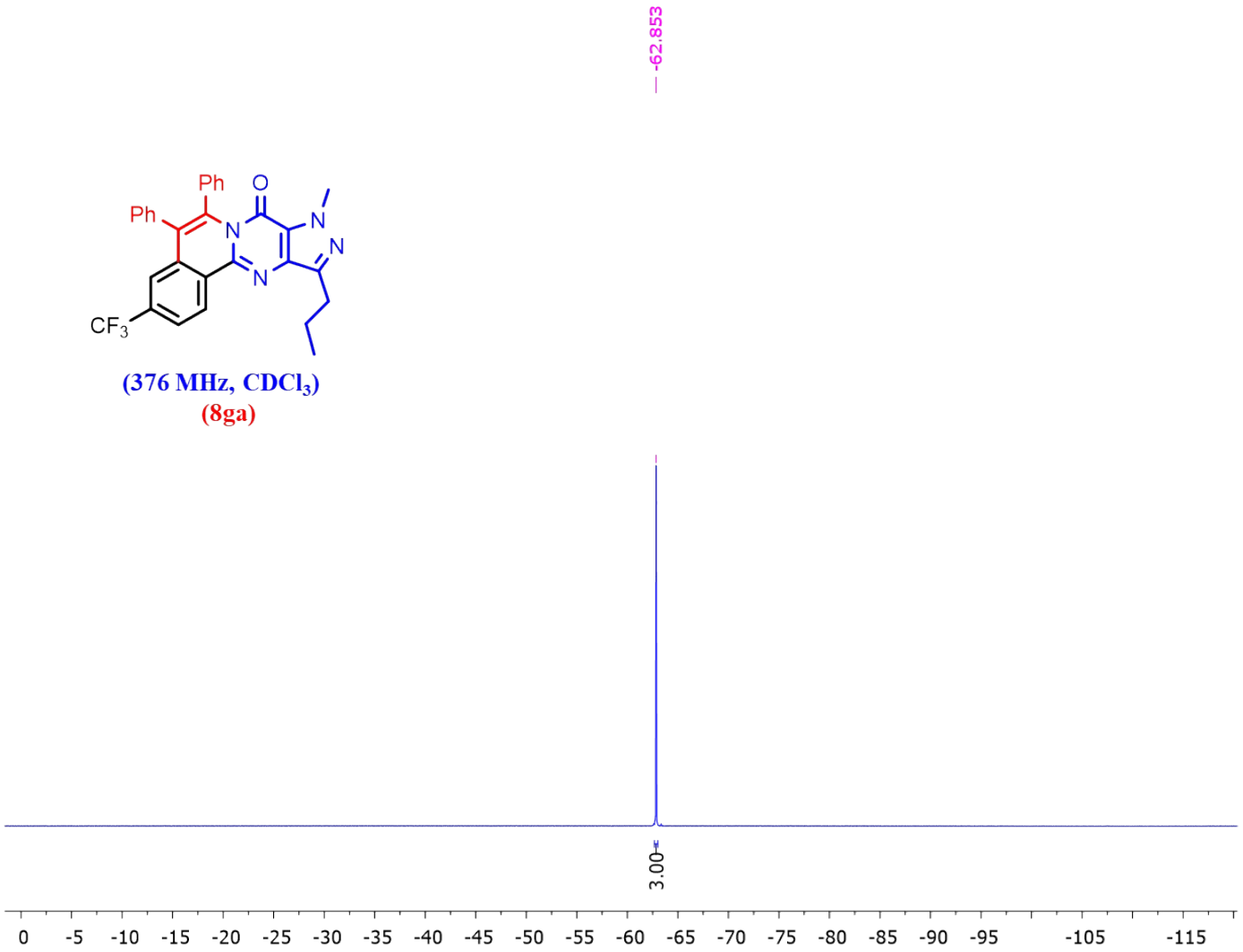


Fig. S136. ^{19}F NMR spectra of 9-Methyl-5,6-diphenyl-11-propyl-3-(trifluoromethyl)pyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ga)** in $CDCl_3$.

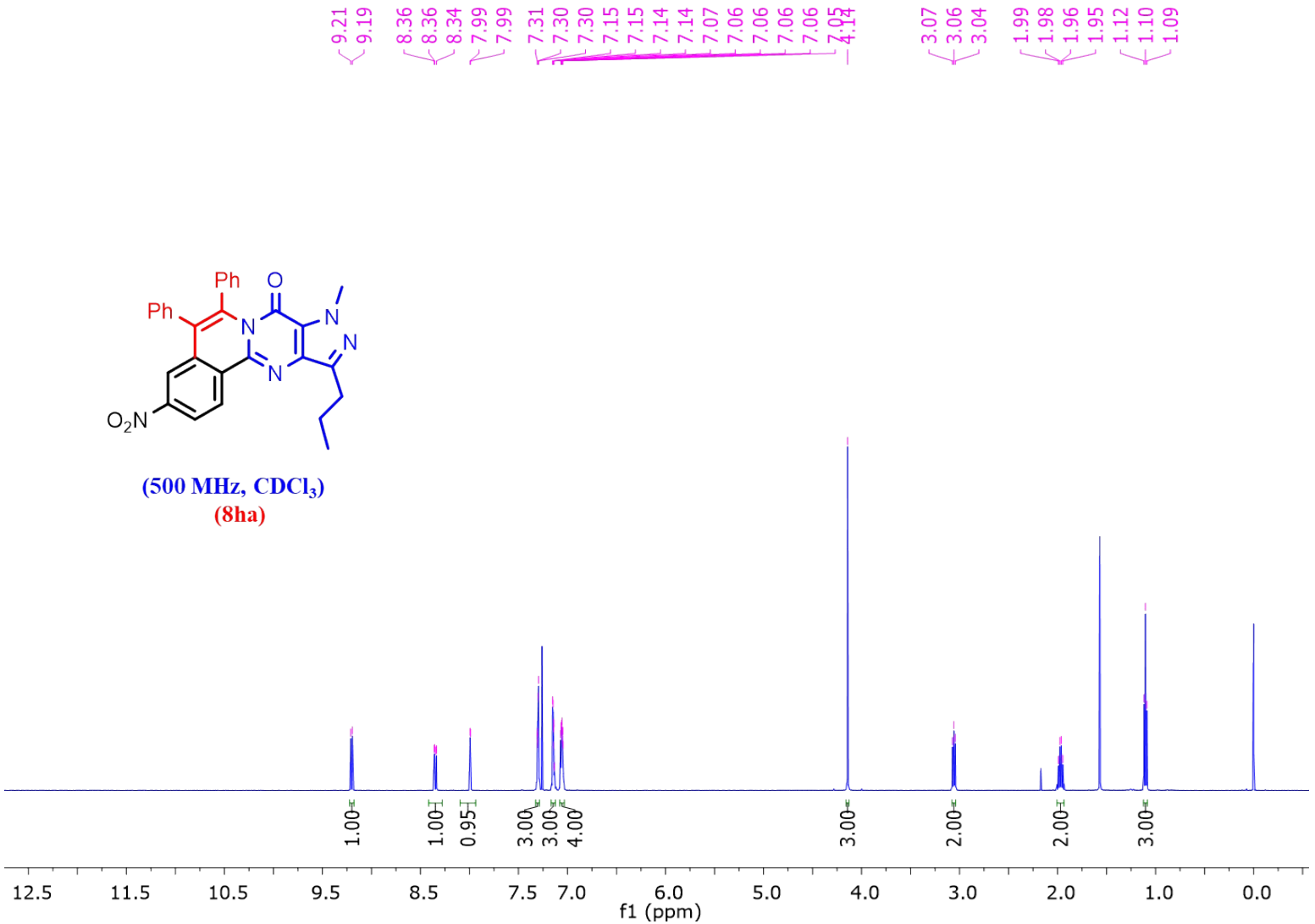


Fig. S137. ^{1}H NMR spectra of 9-Methyl-3-nitro-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8 (9H)-one **(8ha)** in $CDCl_3$.

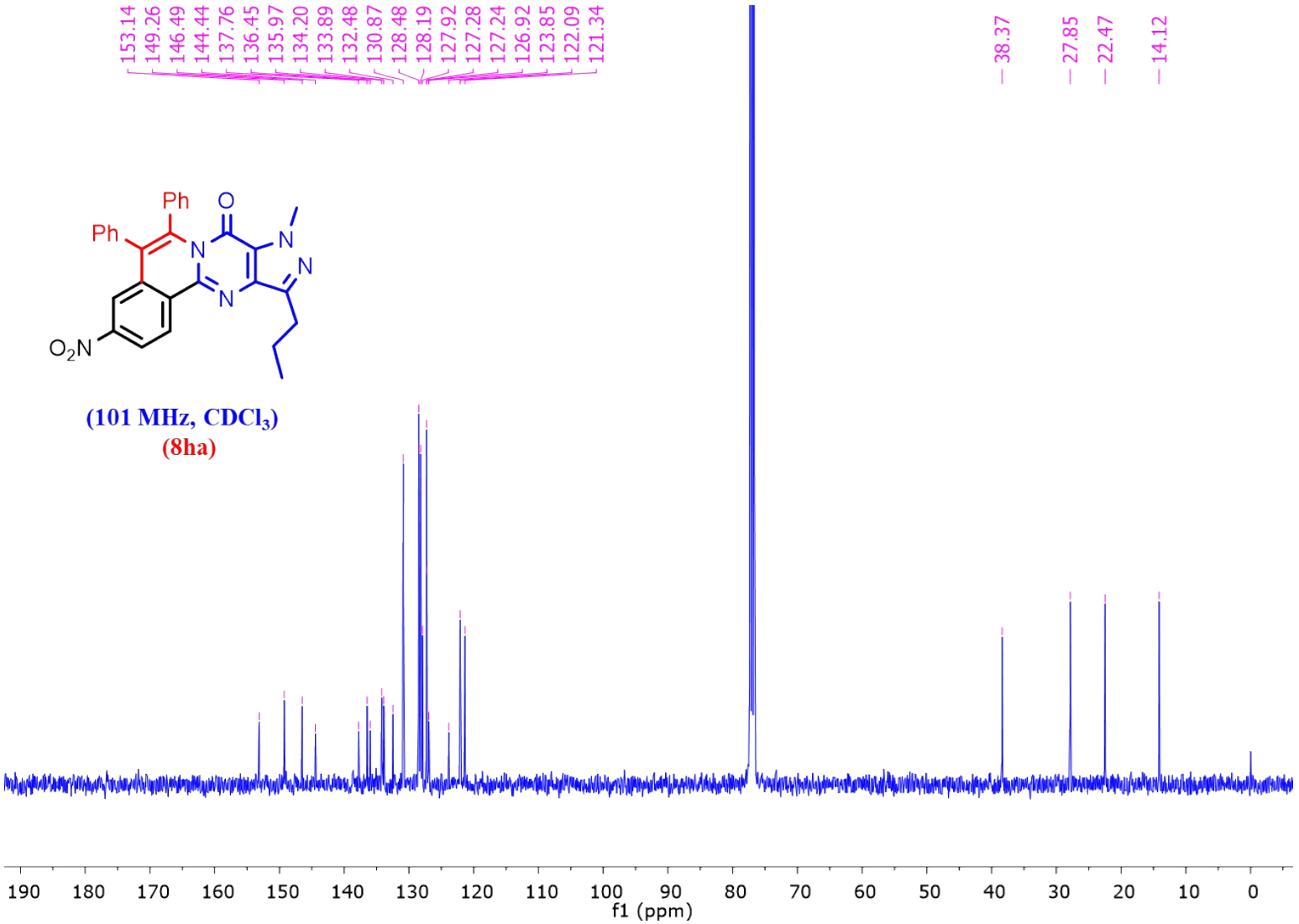


Fig. S138. ^{13}C NMR spectra of 9-Methyl-3-nitro-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8 (9H)-one **(8ha)** in $CDCl_3$.

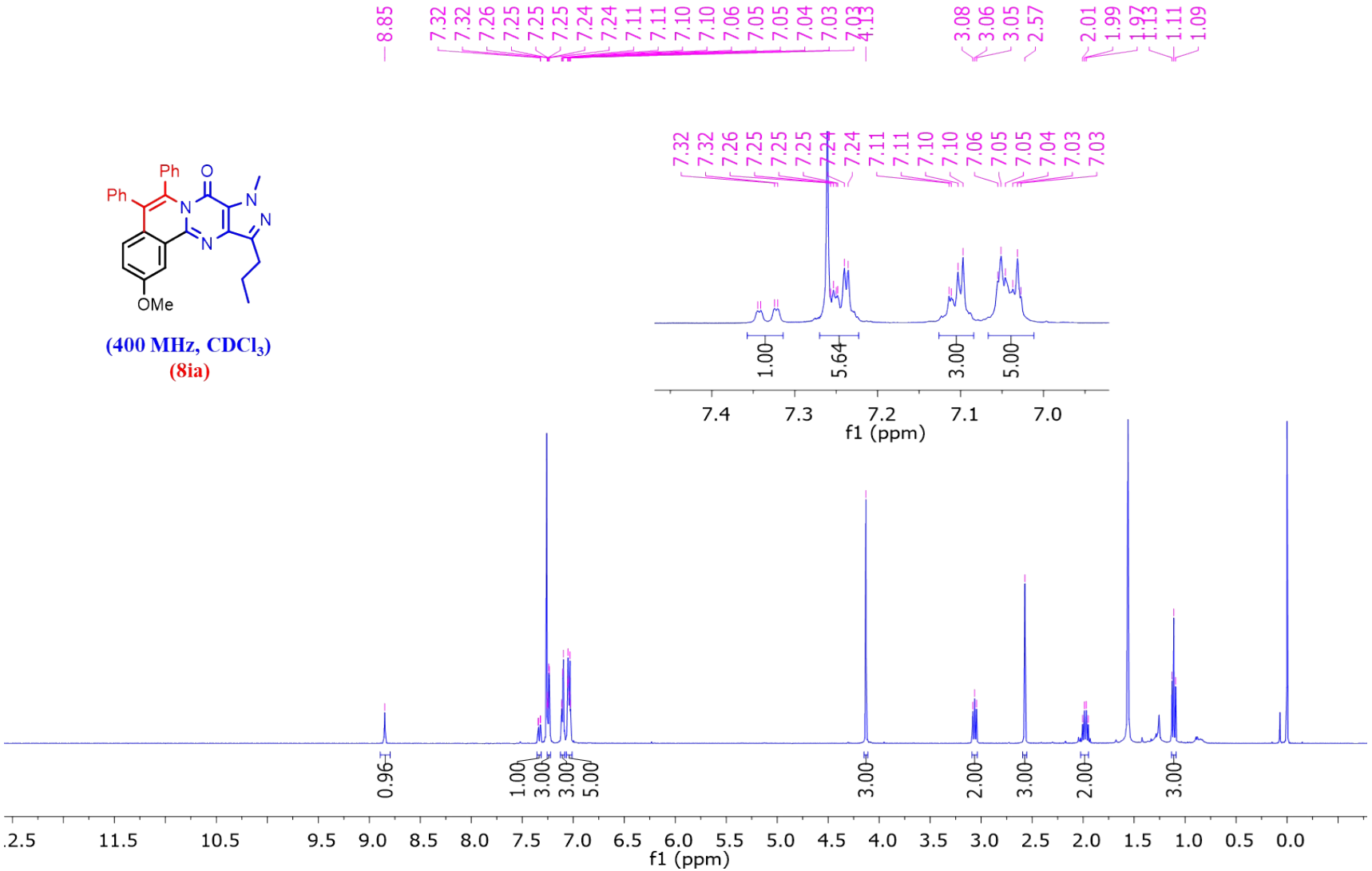


Fig. S139. ^{1}H NMR spectra of 3,9-Mimethyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ia)** in $CDCl_3$.

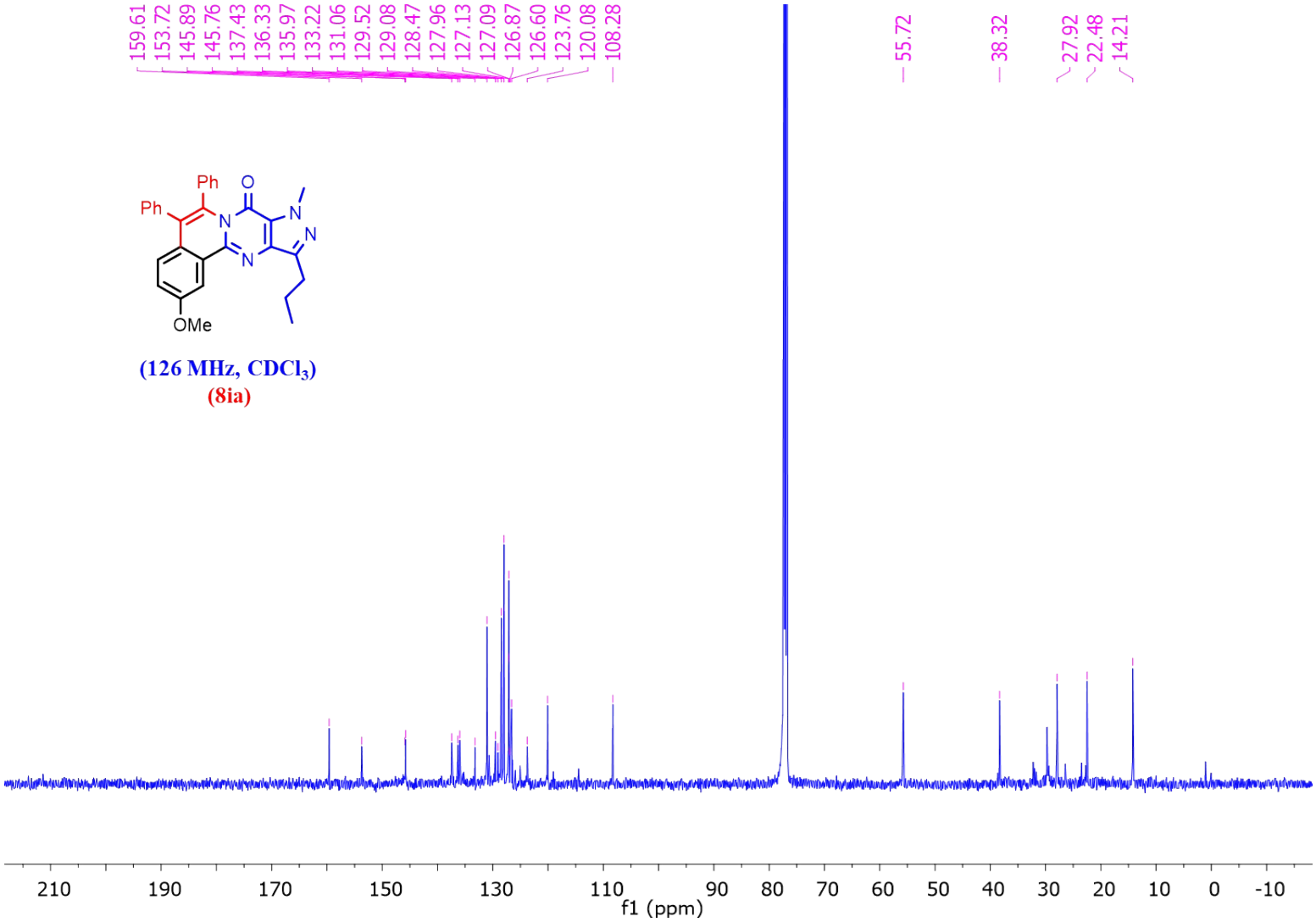


Fig. S140. ^{13}C NMR spectra of 3,9-Mimethyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ia)** in $CDCl_3$.

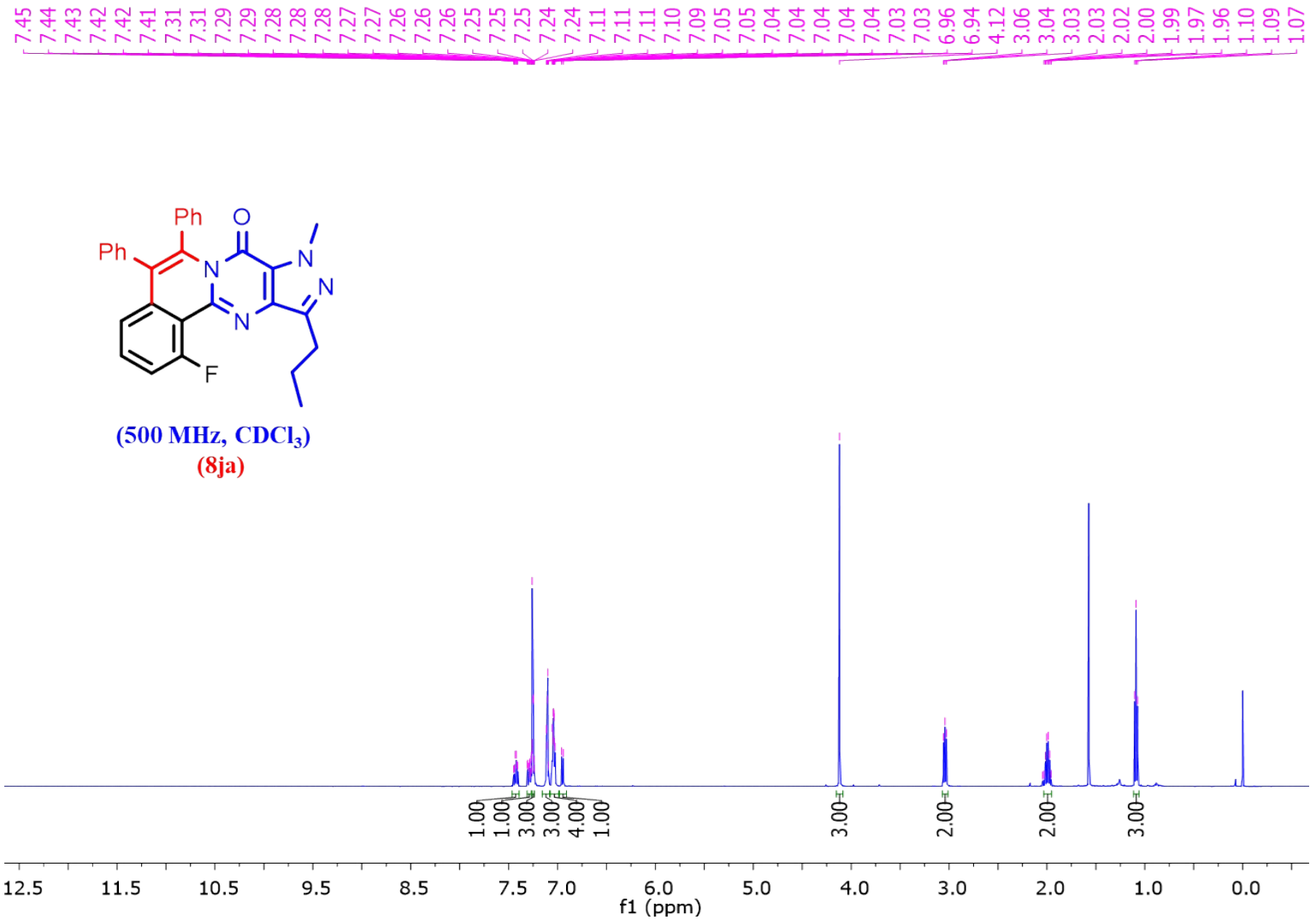


Fig. S141. ^{1}H NMR spectra of 1-Fluoro-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ja)** in $CDCl_3$.

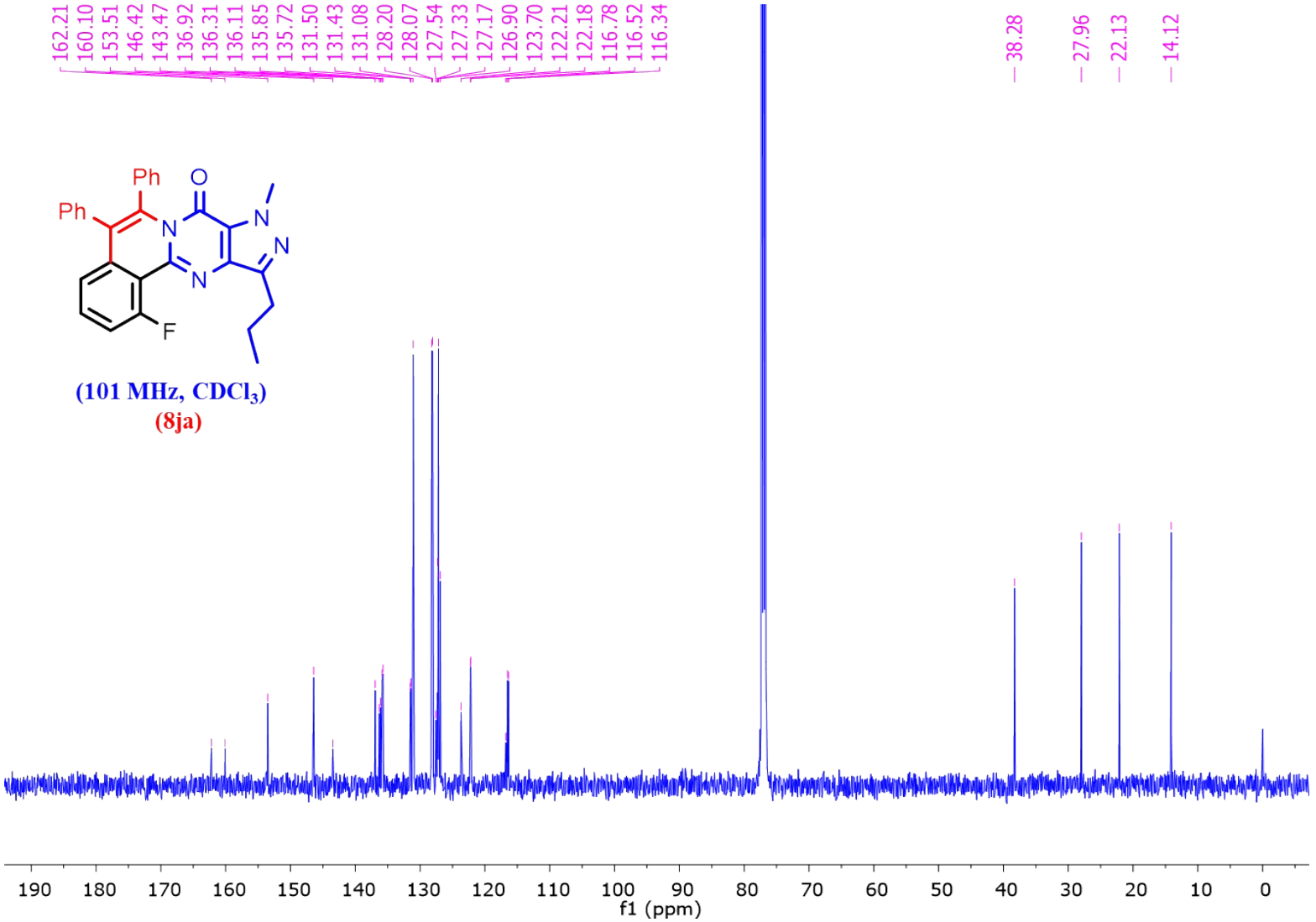


Fig. S142. ^{13}C NMR spectra of 1-Fluoro-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ja)** in $CDCl_3$.

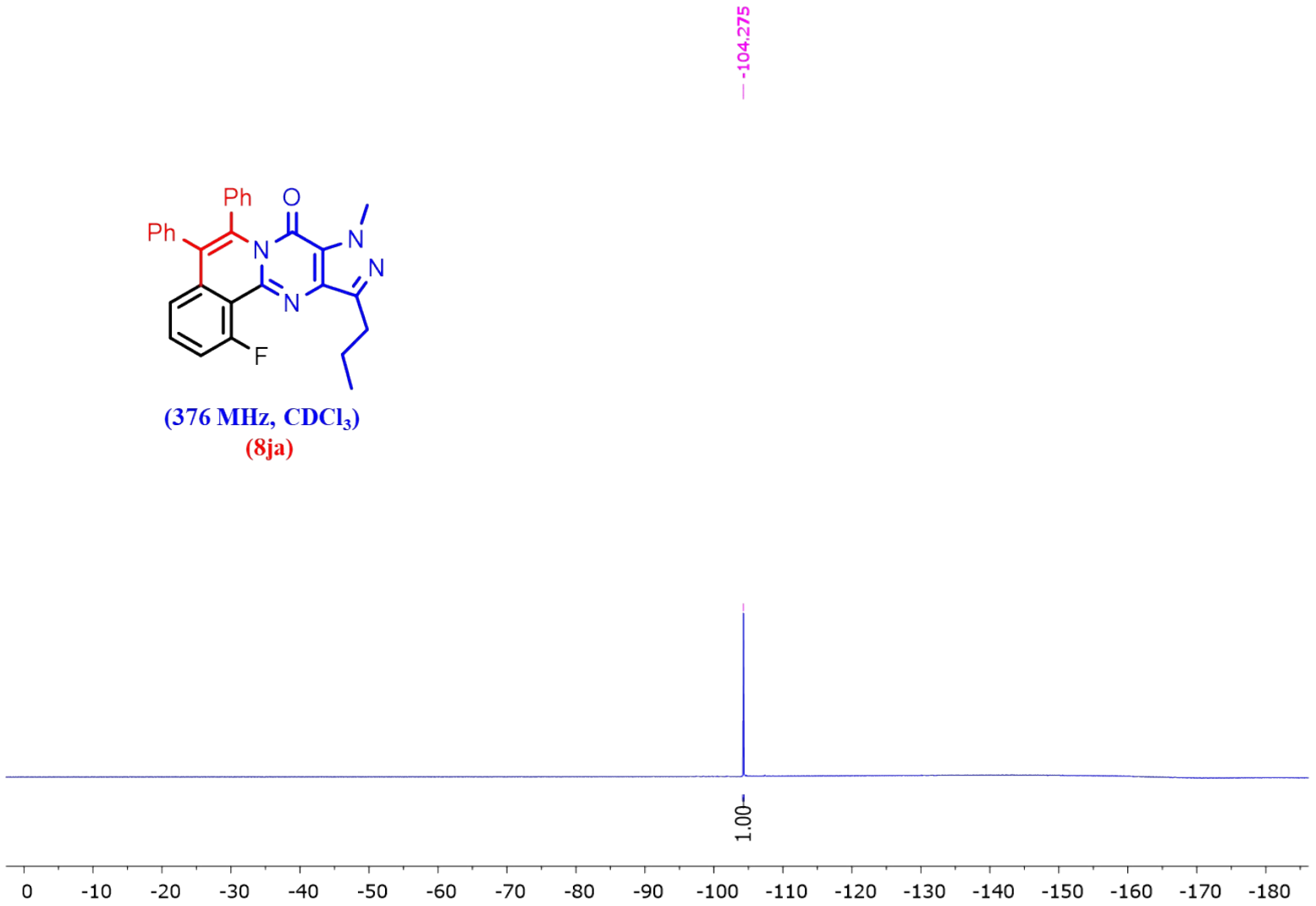


Fig. S143. ^{19}F NMR spectra of 1-Fluoro-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ja)** in $CDCl_3$

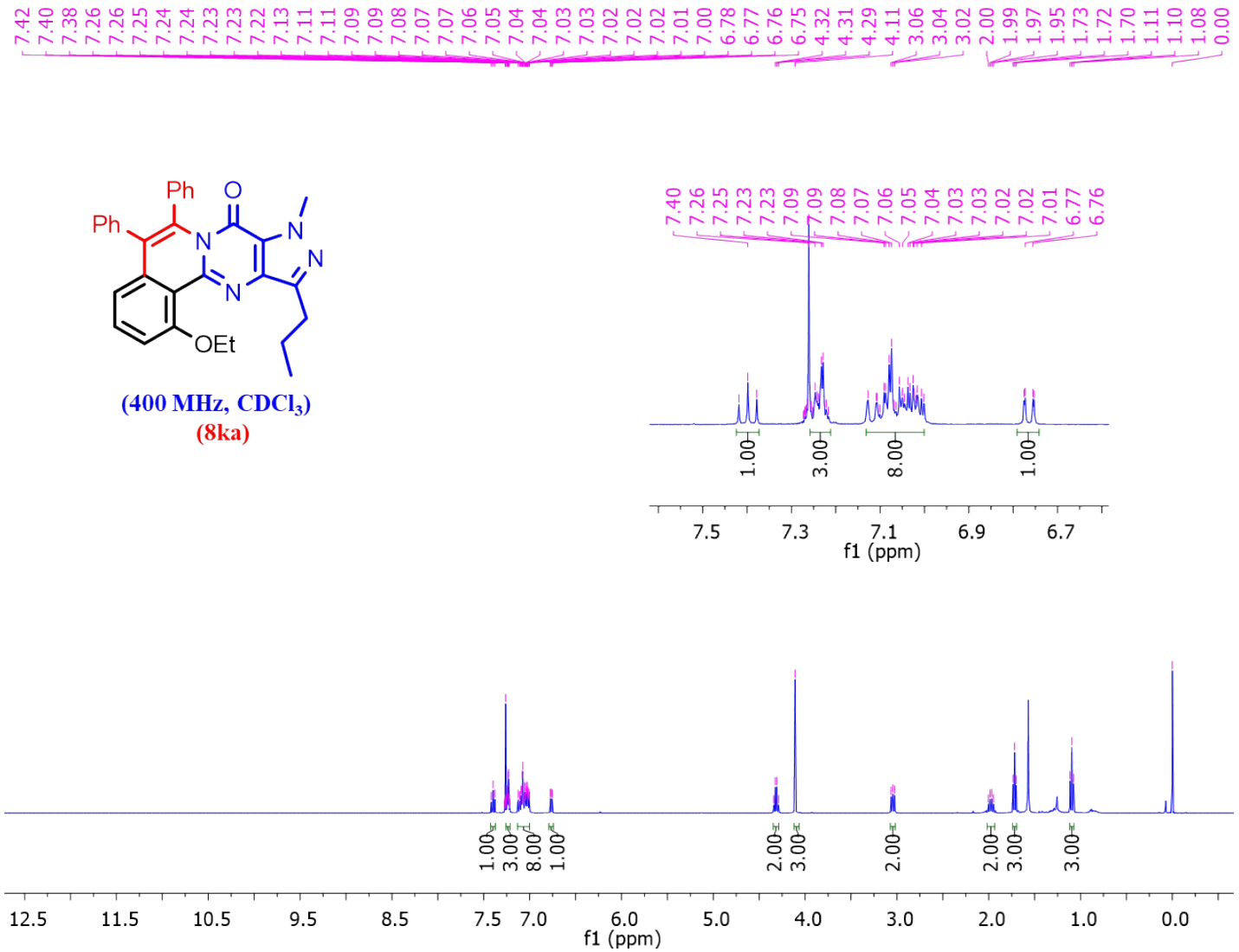


Fig. S144. ^{1}H NMR spectra of 1-Ethoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a] isoquinolin-8 (9H)-one **(8ka)** in $CDCl_3$.

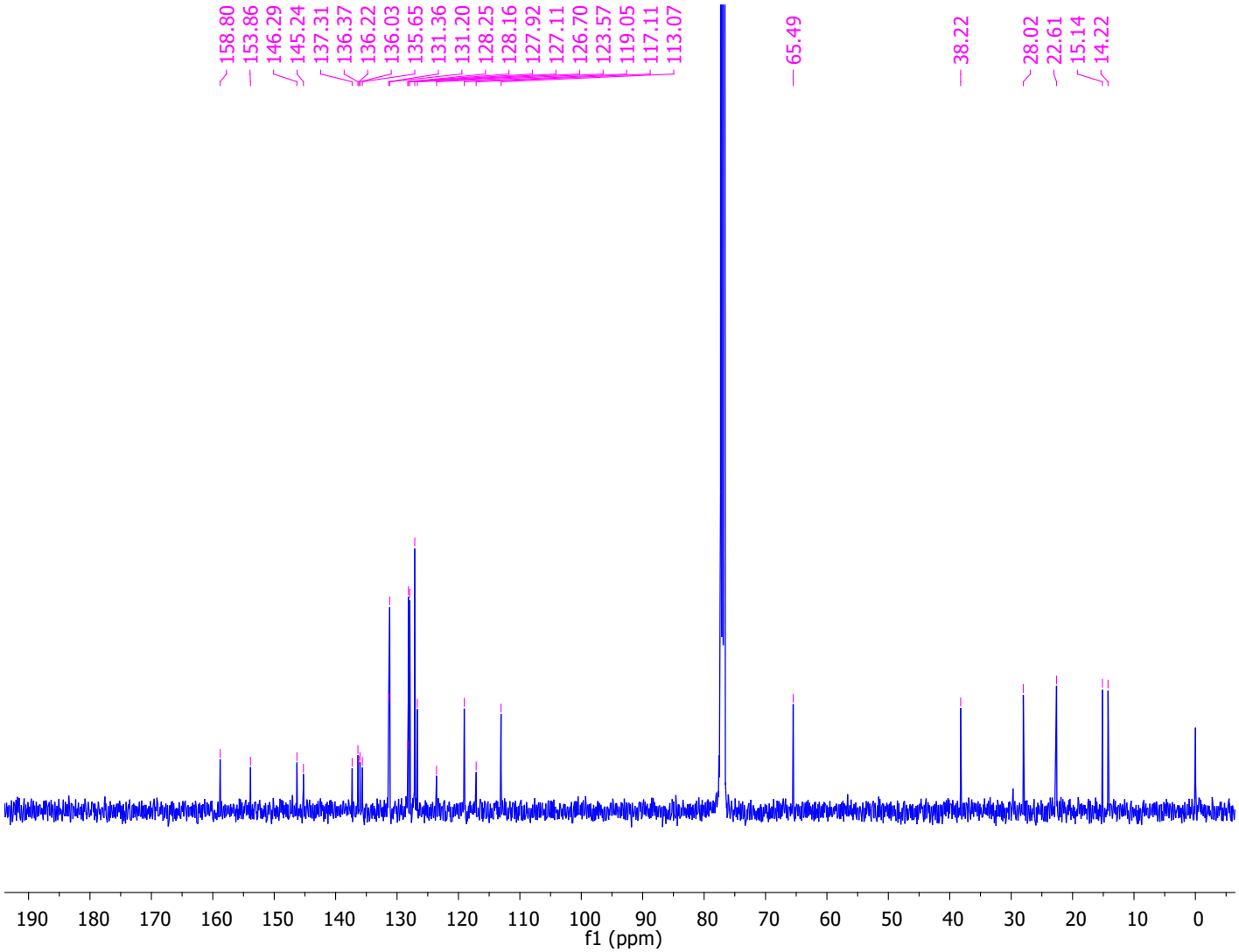


Fig. S145. ^{13}C NMR spectra of 1-Ethoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a] isoquinolin-8 (9H)-one **(8ka)** in $CDCl_3$.

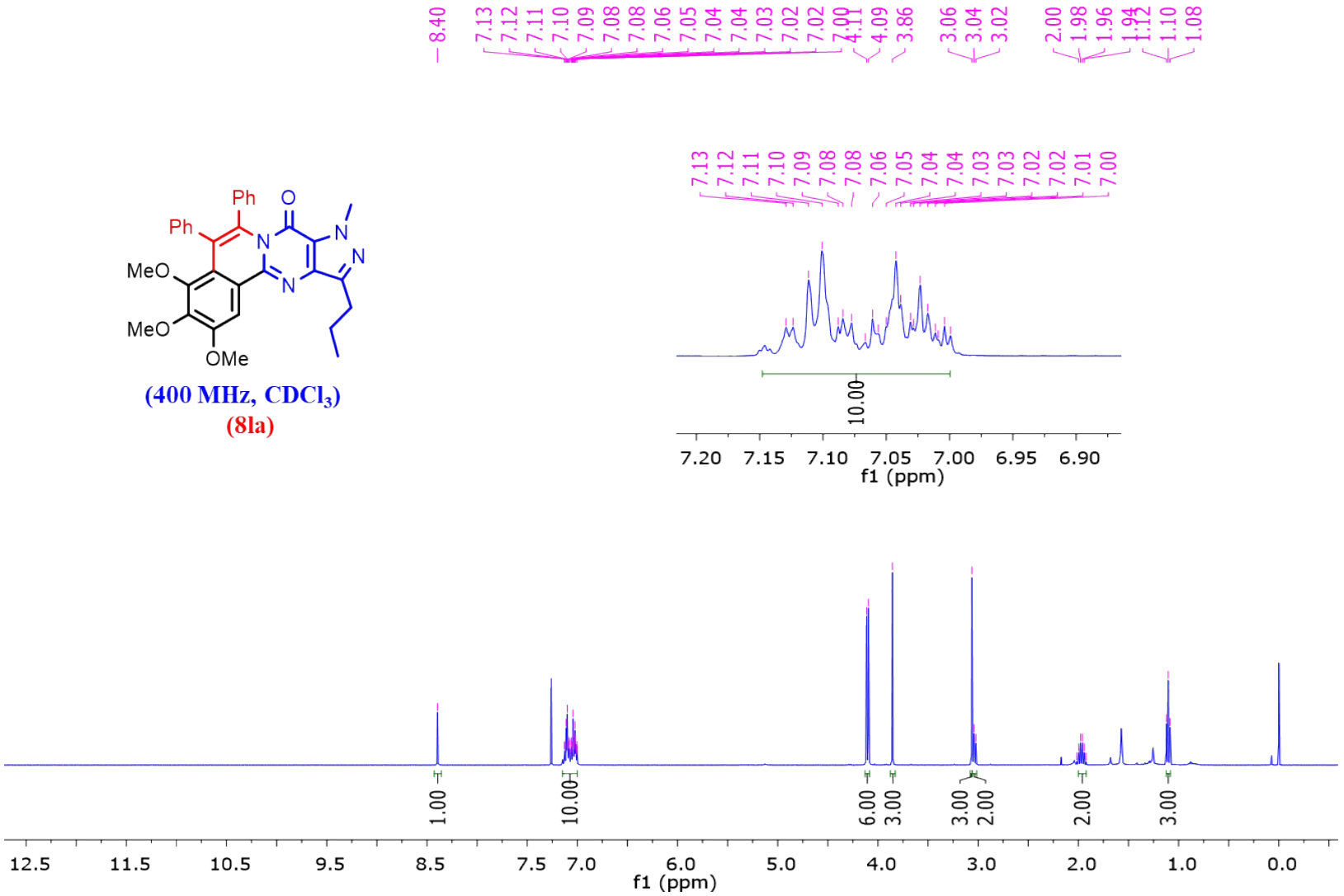


Fig. S146. ^{1}H NMR spectra of 2,3,4-Mrimethoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8la)** in $CDCl_3$.

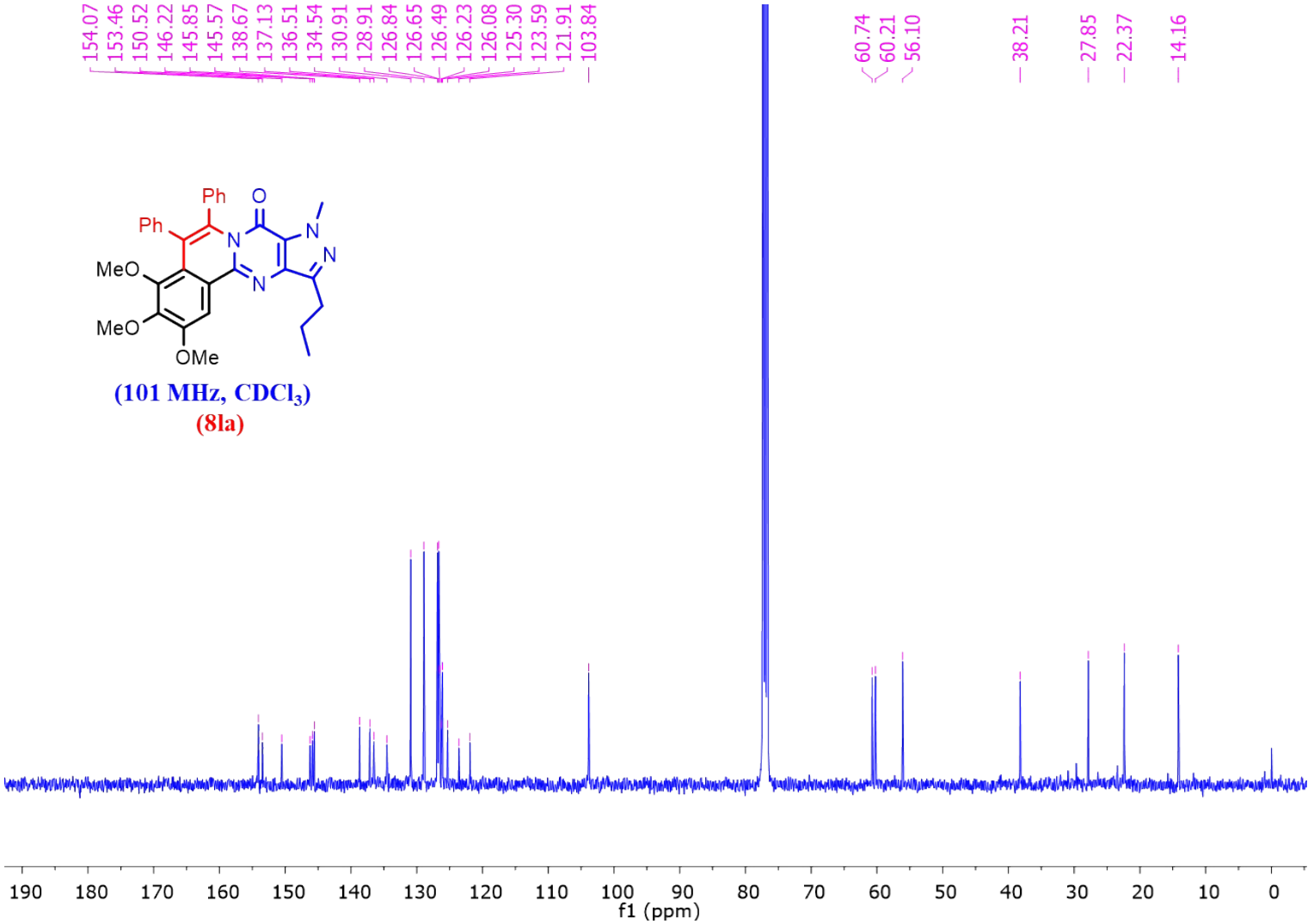


Fig. S147. ^{13}C NMR spectra of 2,3,4-Mrimethoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8la)** in $CDCl_3$.

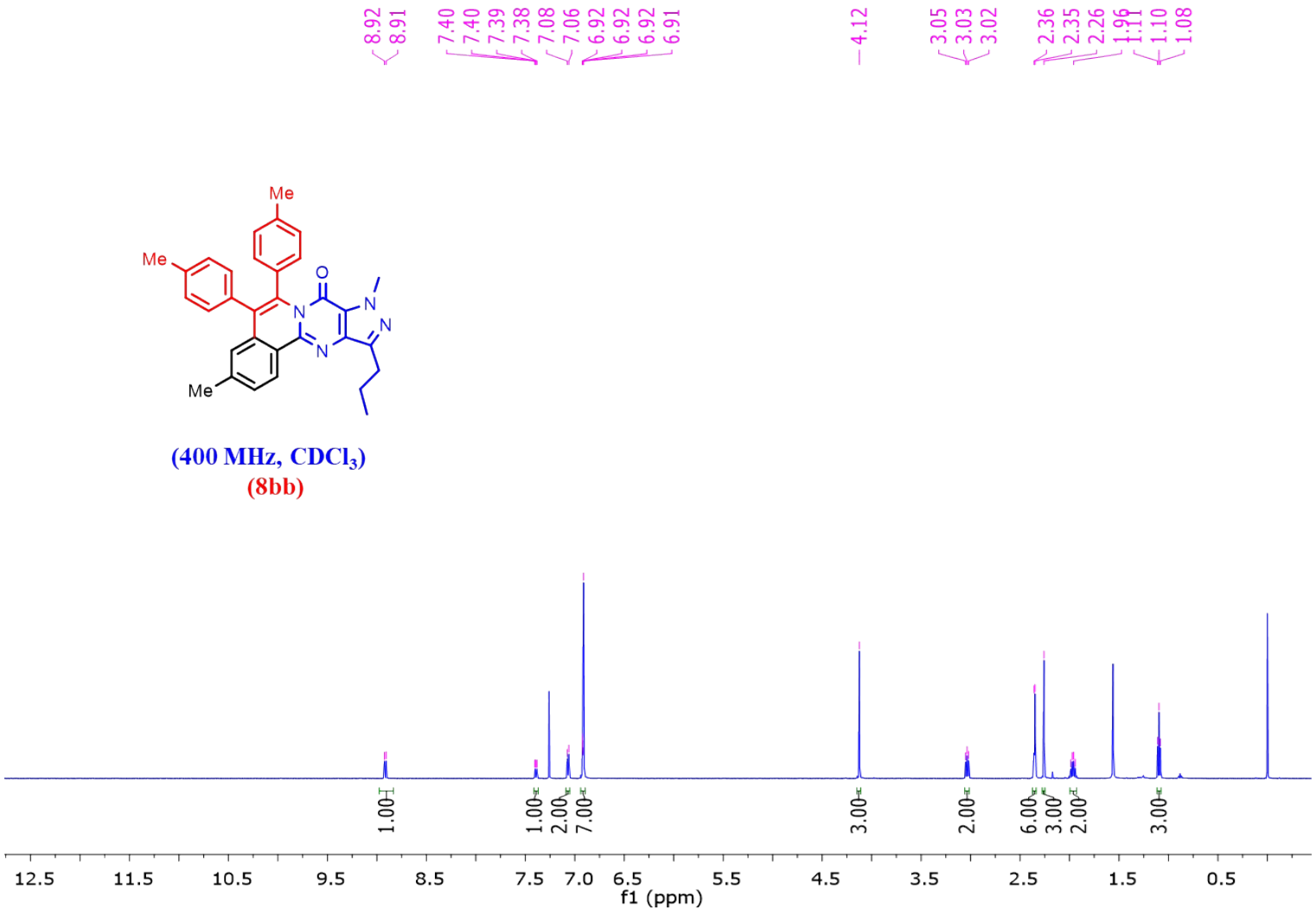


Fig. S148. ^{1}H NMR spectra of 3,5,9-Trimethyl-6-phenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8bb)** in $CDCl_3$.

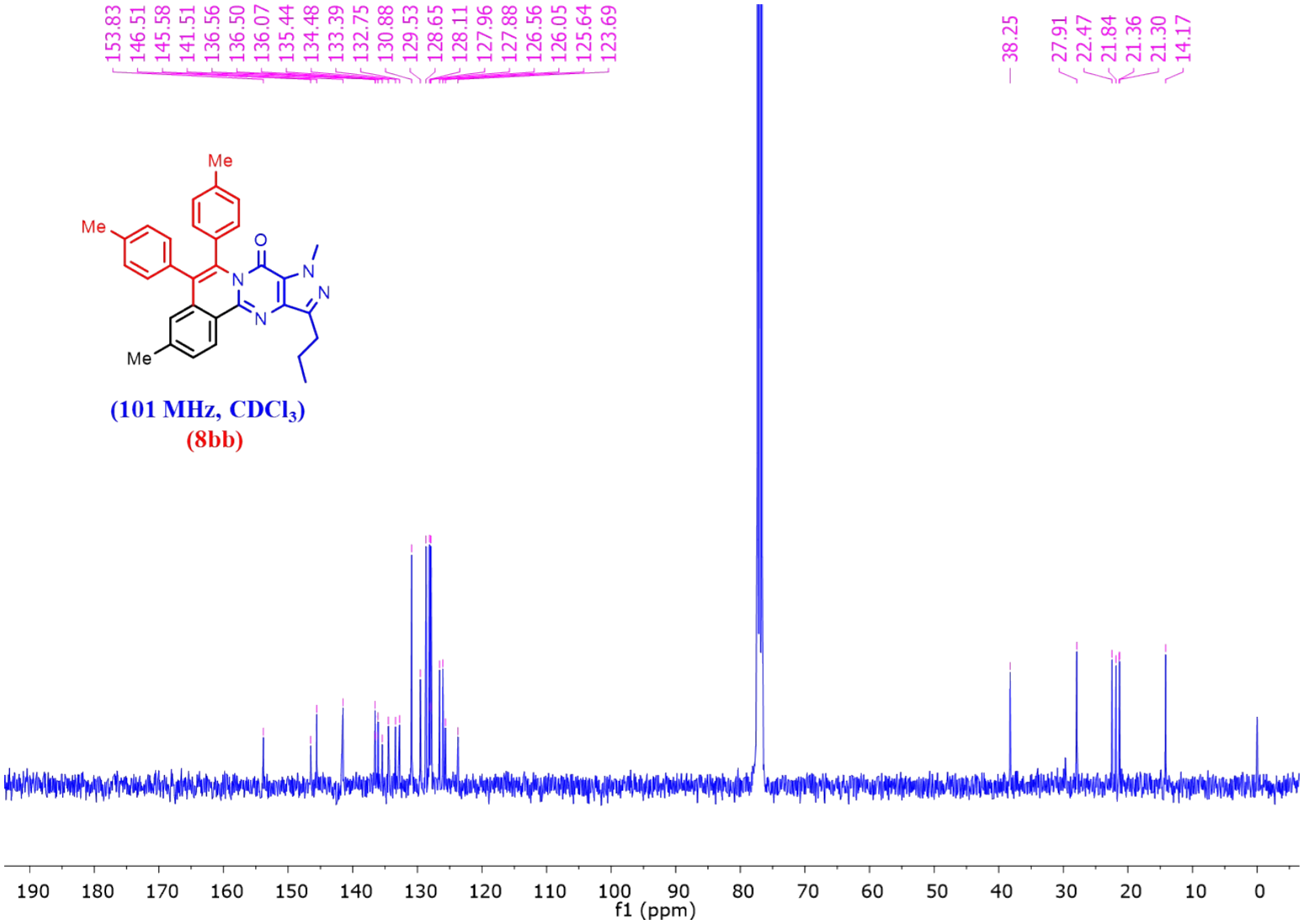


Fig. S149. ^{13}C NMR spectra of 3,5,9-Trimethyl-6-phenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8bb)** in $CDCl_3$.

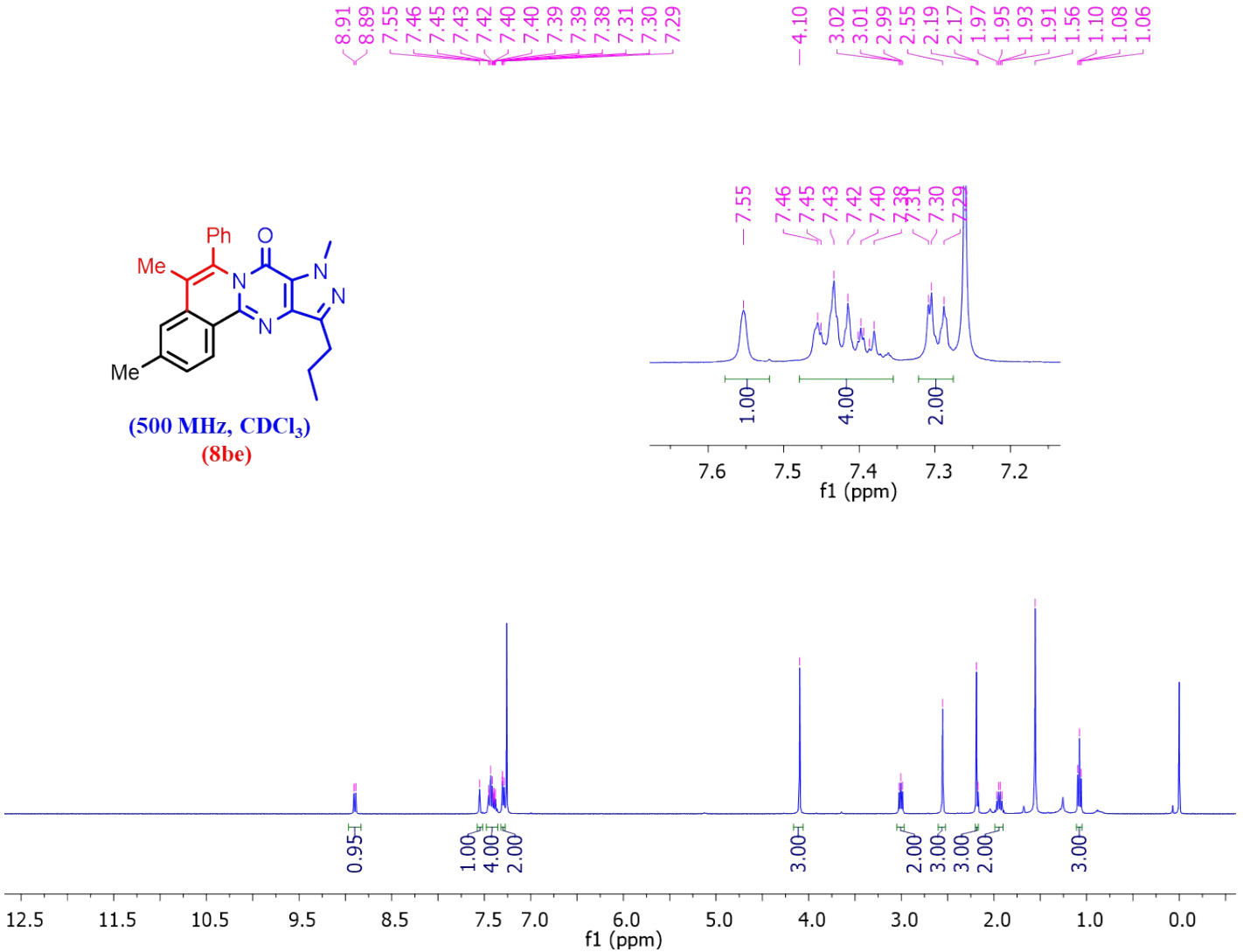


Fig. S150. ^{1}H NMR spectra of 3,9-Dimethyl-11-propyl-5,6-di-p-tolylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8be)** in $CDCl_3$.

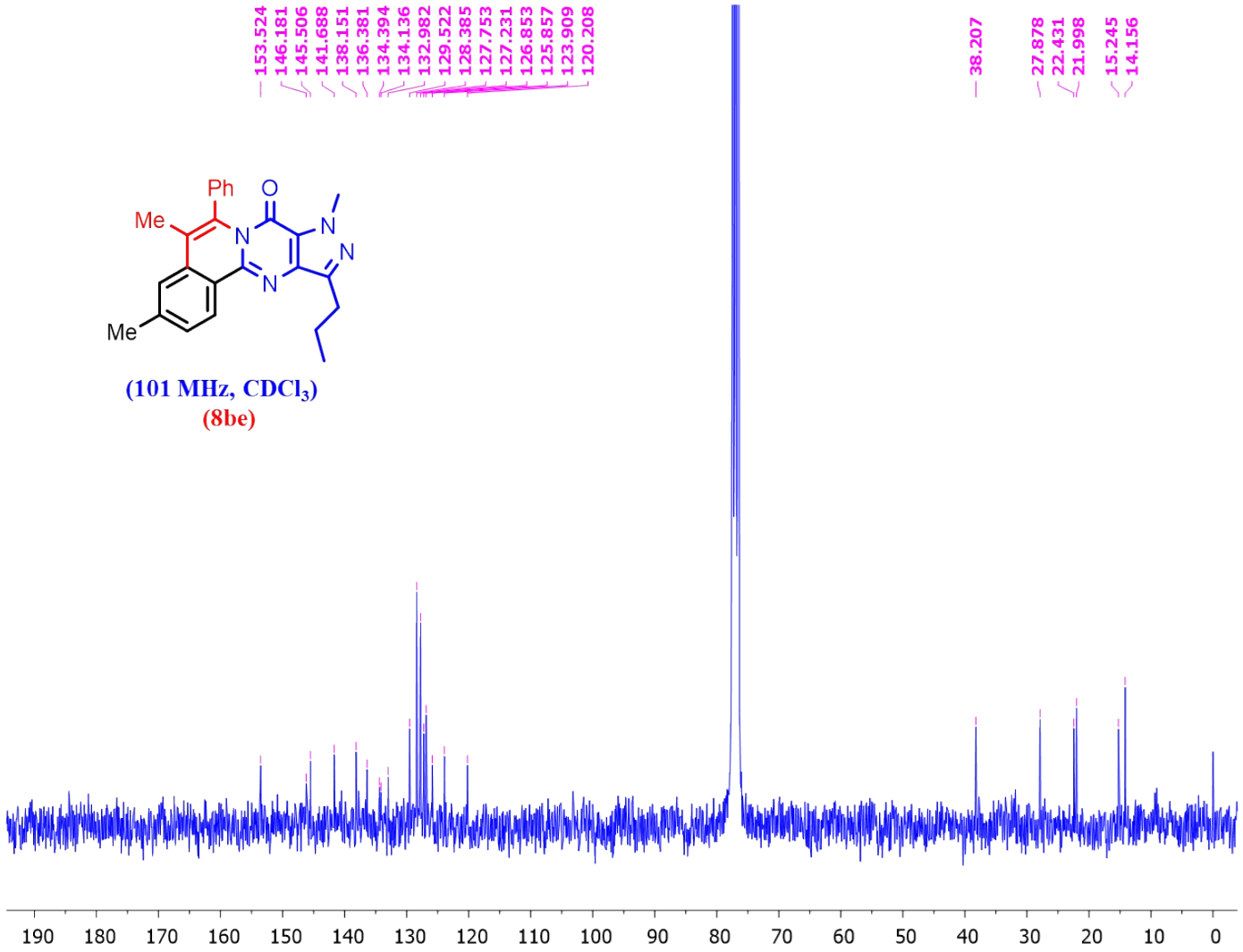


Fig. S151. ^{13}C NMR spectra of 3,9-Dimethyl-11-propyl-5,6-di-p-tolylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8be)** in $CDCl_3$.

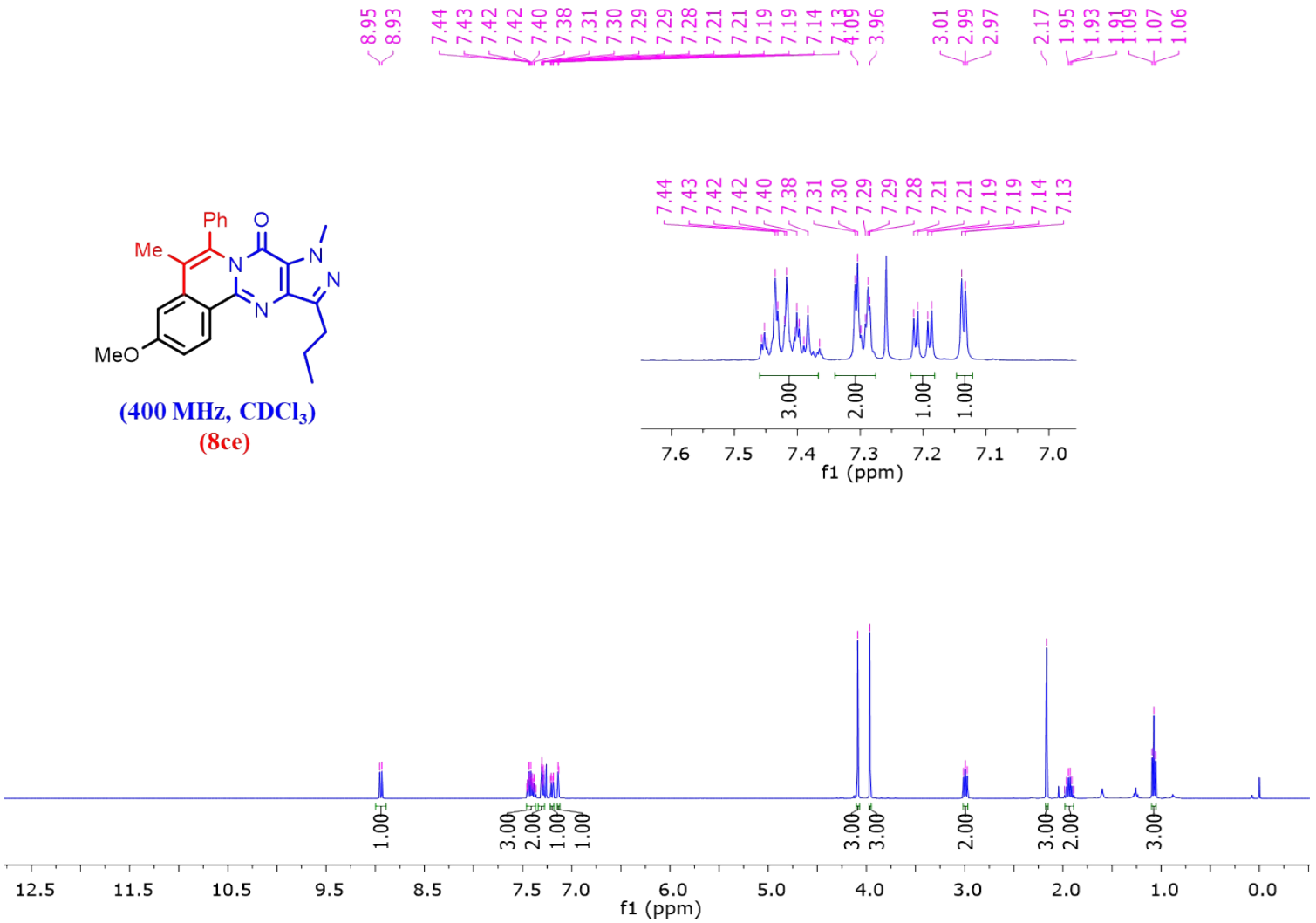


Fig. S152. ^{1}H NMR spectra of 3-Methoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ce)** in $CDCl_3$.

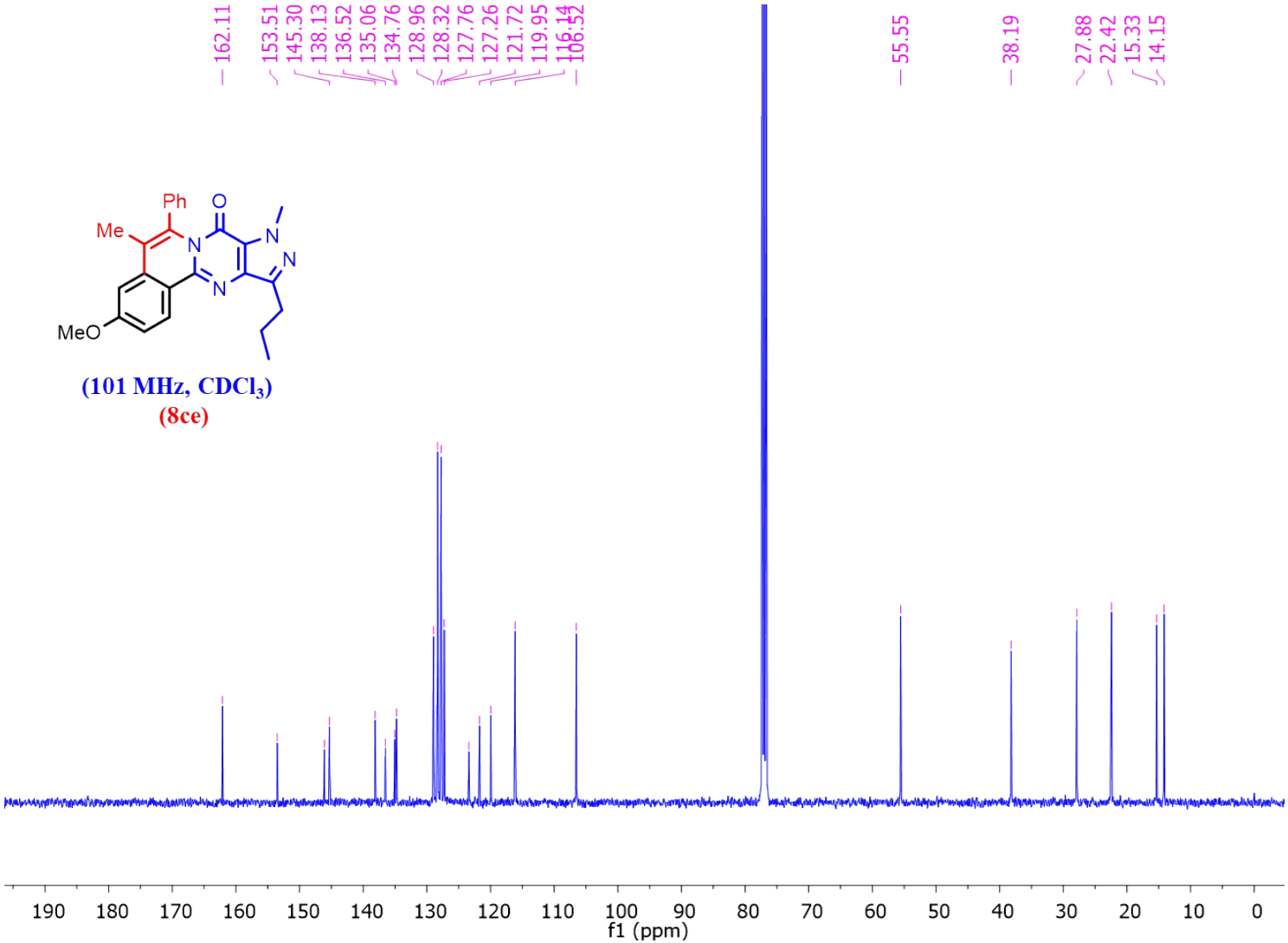


Fig. S153. ^{13}C NMR spectra of 3-Methoxy-9-methyl-5,6-diphenyl-11-propylpyrazolo[4',3':4,5]pyrimido[2,1-a]isoquinolin-8(9H)-one **(8ce)** in $CDCl_3$.