Electrochemical *N*-sulfonylation of *in-situ* generated indole-based hydrazones and antimicrobial evaluation

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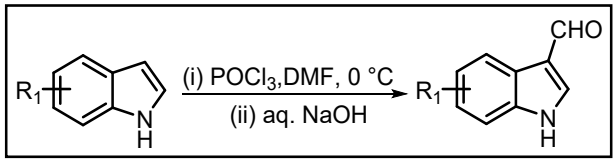
(I) General procedure for synthesis of starting materials (1 and 3)

Procedure for synthesis of 1*H*-indole-3-carbaldehydes (1)[1]

In an oven-dried round-bottom flask equipped with a magnetic stir bar, dimethylformamide (DMF) and phosphorus oxychloride ($POCl_3$) are mixed in a 5:1 molar ratio by slowly adding $POCl_3$ (0.6 mL, 8.3 mmol, 1.5 equiv.) to DMF (1.6 mL, 21.2 mmol, 5 equiv.) under continuous stirring. The flask is kept in an ice bath throughout the addition while maintaining a low temperature. After 30 minutes, indole (500 mg, 4.2 mmol, 1 equiv.) is added to the cooled reaction mixture, and the solution is stirred for an additional hour to allow the reaction to proceed. Upon completion, the reaction is quenched by the slow addition of ice-cold water, followed by the dropwise addition of an aqueous sodium hydroxide solution (11 equiv.). This

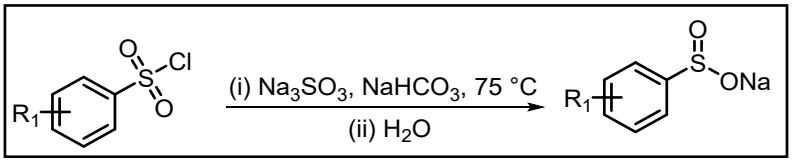
neutralization results in the formation of yellow precipitates. The solid product (**1**) is collected by filtration and thoroughly washed with cold water to remove any remaining impurities.



Scheme S1: General synthetic route for 1*H*-indole-3-carbaldehydes

Procedure for synthesis of sodium sulfinates (3)[2]

Sodium sulfinates (**3a**, **3m**, **3p,** and **3q**) were prepared by heating a mixture of sodium sulfite (600 mg, 4.8 mmol, 1.8 equiv.) and sodium carbonate (420 mg, 5 mmol, 2 equiv.) in 5 mL of water at 75 °C. After 15 minutes of stirring, sulfonyl chloride (484 mg, 2.5 mmol, 1 equiv.) was added slowly to the reaction mixture over a period of approximately 30 minutes. The reaction was then allowed to proceed for 3-4 hours. Upon cooling the mixture to room temperature, white precipitates began to form. The crude white solid was collected by filtration and used without further purification.



Scheme S2: General synthetic route for sodium sulfinates

(II) Method for crystallization

Crystallization of compound (**5t)** was achieved using the vapor diffusion method. A solution of the compound (10 mg in 1 mL of dichloromethane) was placed in a small inner glass vial. This vial was then placed inside a larger, tightly sealed container holding 4 mL of hexane. As the hexane vapor slowly diffused into the DCM solution, the solvent environment gradually changed, promoting the slow formation of single crystals over time.[3]

(III) Crystallographic data

Identification code	Ex-PM908
Empirical formula	$C_{23}H_{21}N_3O_4S_2$

Formula weight	467.55
Temperature/K	293(2)
Crystal system	triclinic
Space group	P-1
a/Å	7.5075(5)
b/Å	10.2822(5)
c/Å	15.6878(9)
α/°	72.906(5)
β/°	88.731(5)
γ/°	80.529(5)
Volume/Å^3	1141.28(12)
Z	2
ρcalcg/cm3	1.361
μ/mm^{-1}	0.268
F(000)	488.0
Crystal size/mm^3	0.02 × 0.02 × 0.02
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	6.466 to 54.158
Index ranges	-9 ≤ h ≤ 9, -12 ≤ k ≤ 13, -19 ≤ l ≤ 18
Reflections collected	14961
Independent reflections	4595 [R_{int} = 0.1534, R_{sigma} = 0.1333]
Data/restraints/parameters	4595/0/291
Goodness-of-fit on F^2	0.957
Final R indexes [I>=2σ (I)]	R_1 = 0.0676, wR_2 = 0.1555
Final R indexes [all data]	R_1 = 0.1364, wR_2 = 0.1952
Largest diff. peak/hole / e Å^{-3}	0.22/-0.39

The single-crystal X-ray diffraction data for compound 5t were obtained at 293 K using a Rigaku Oxford Diffraction, 2017 with Mo-Kα radiation (λ = 0.71073 Å) as the X-ray source. The crystal structure was determined using the intrinsic phasing method implemented in the SHELXT, and further refinement was performed with SHELXL employing least-squares minimization techniques. All computational procedures were carried out using the Olex2 interface. The crystallographic information has been deposited with the Cambridge

Crystallographic Data Centre under deposition number CCDC=2471164. These data are available free of charge via the CCDC website at www.ccdc.cam.ac.uk or by contacting the centre at 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44 (0)1223 336 033; Email: deposit@ccdc.cam.ac.uk.

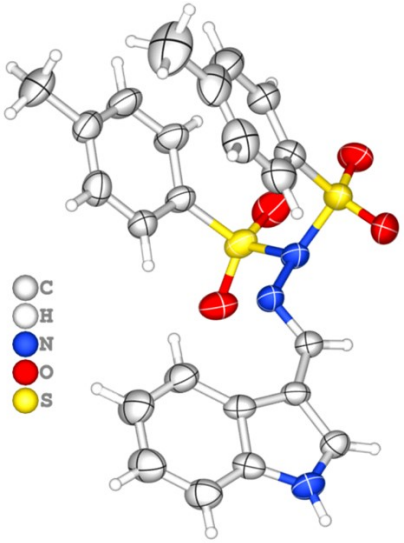
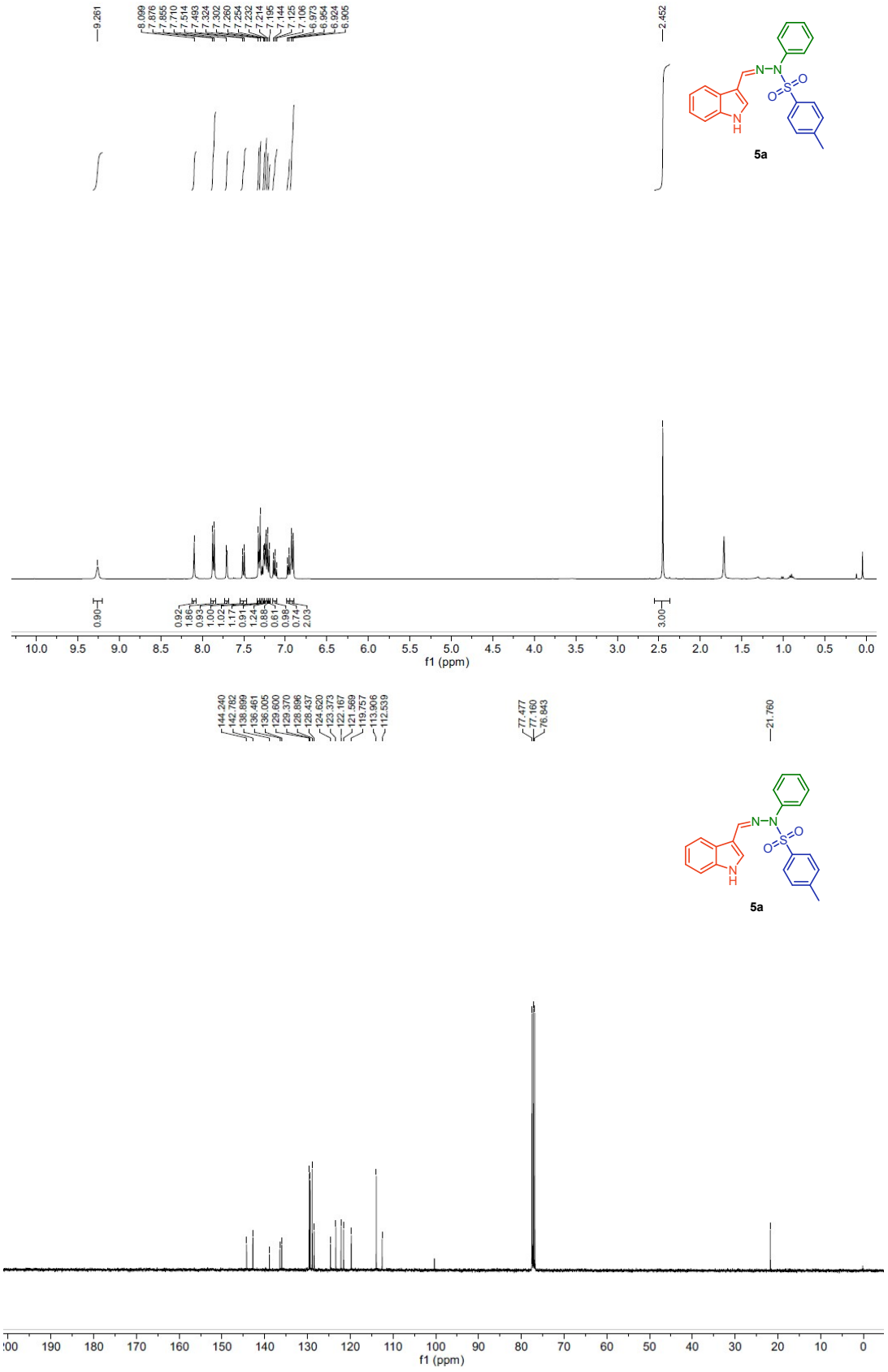


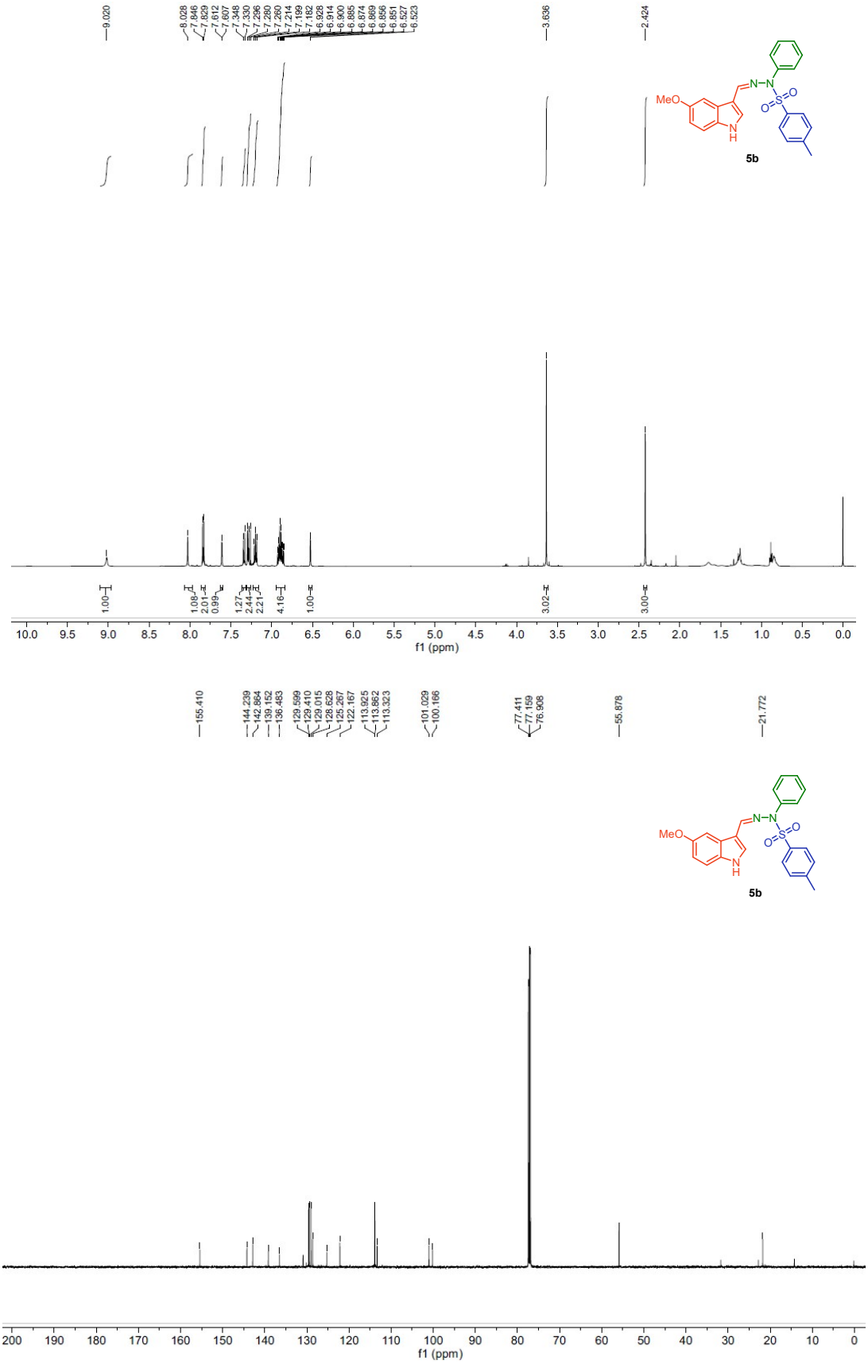
Figure S1: X-ray crystal structure of **5t** (CCDC 2471164)

(IV) ^{1}H and ^{13}C NMR spectra of synthesized compounds

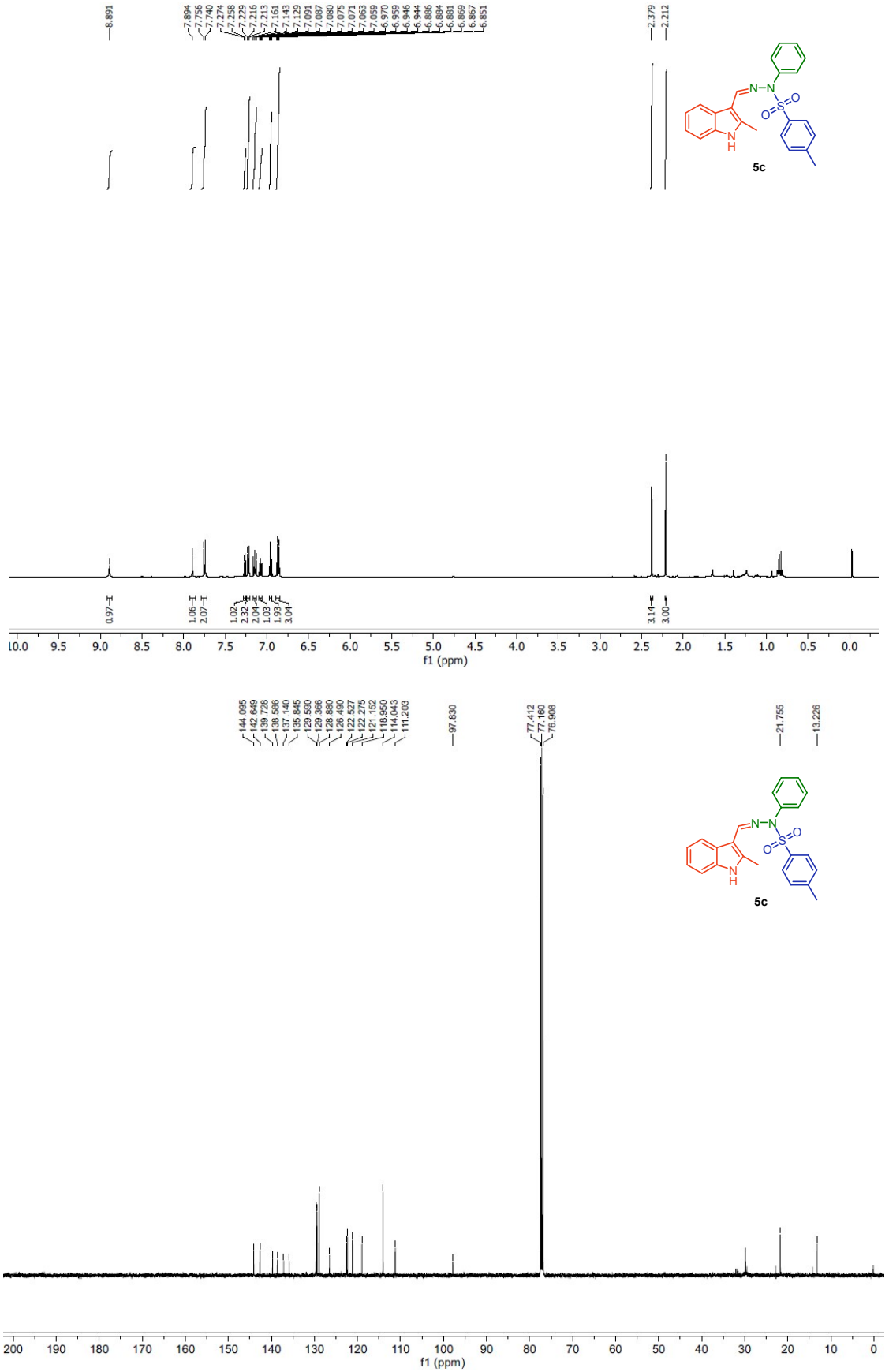
^{1}H NMR (400 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of (**5a**)



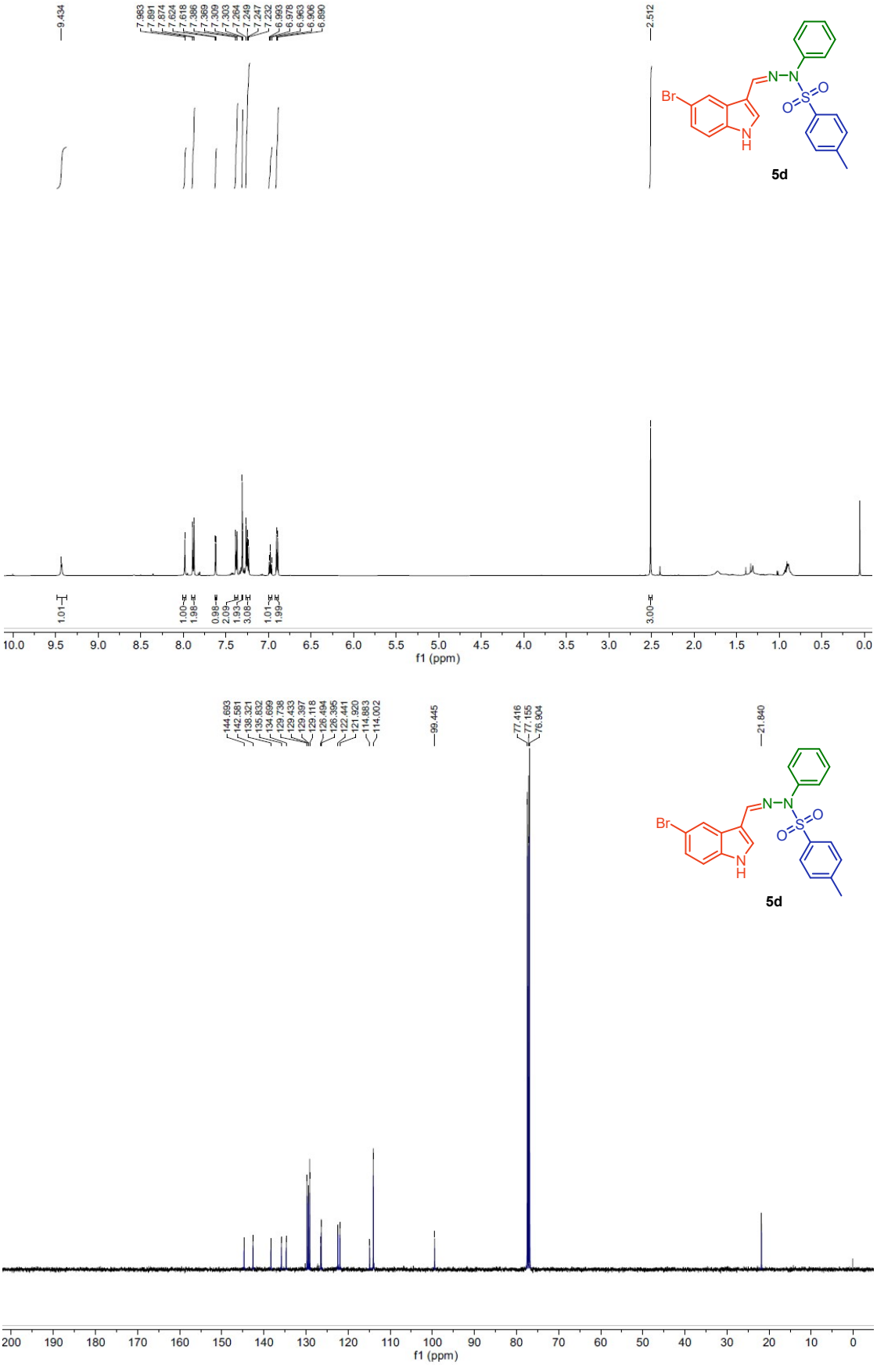
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5b**)



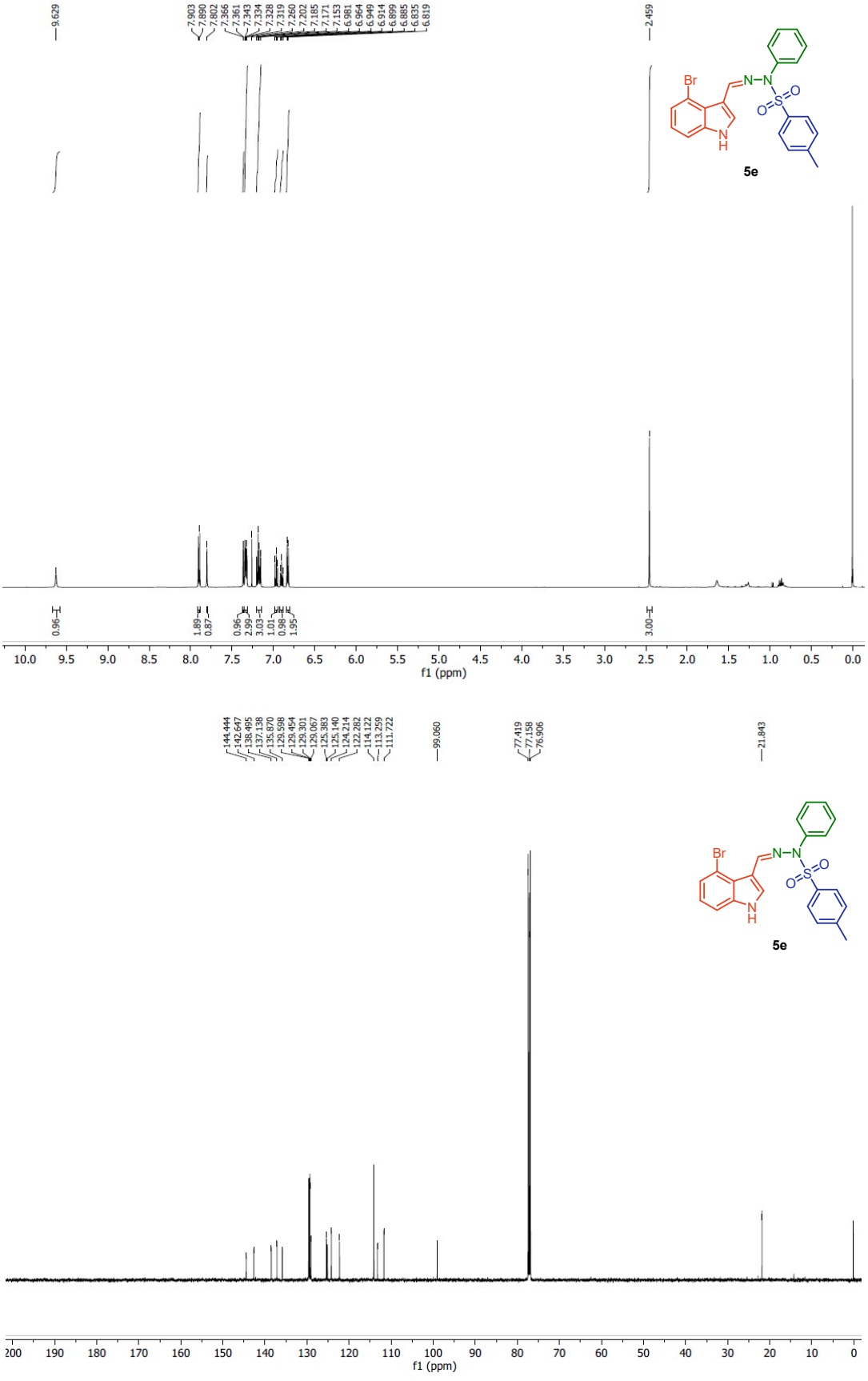
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5c**)



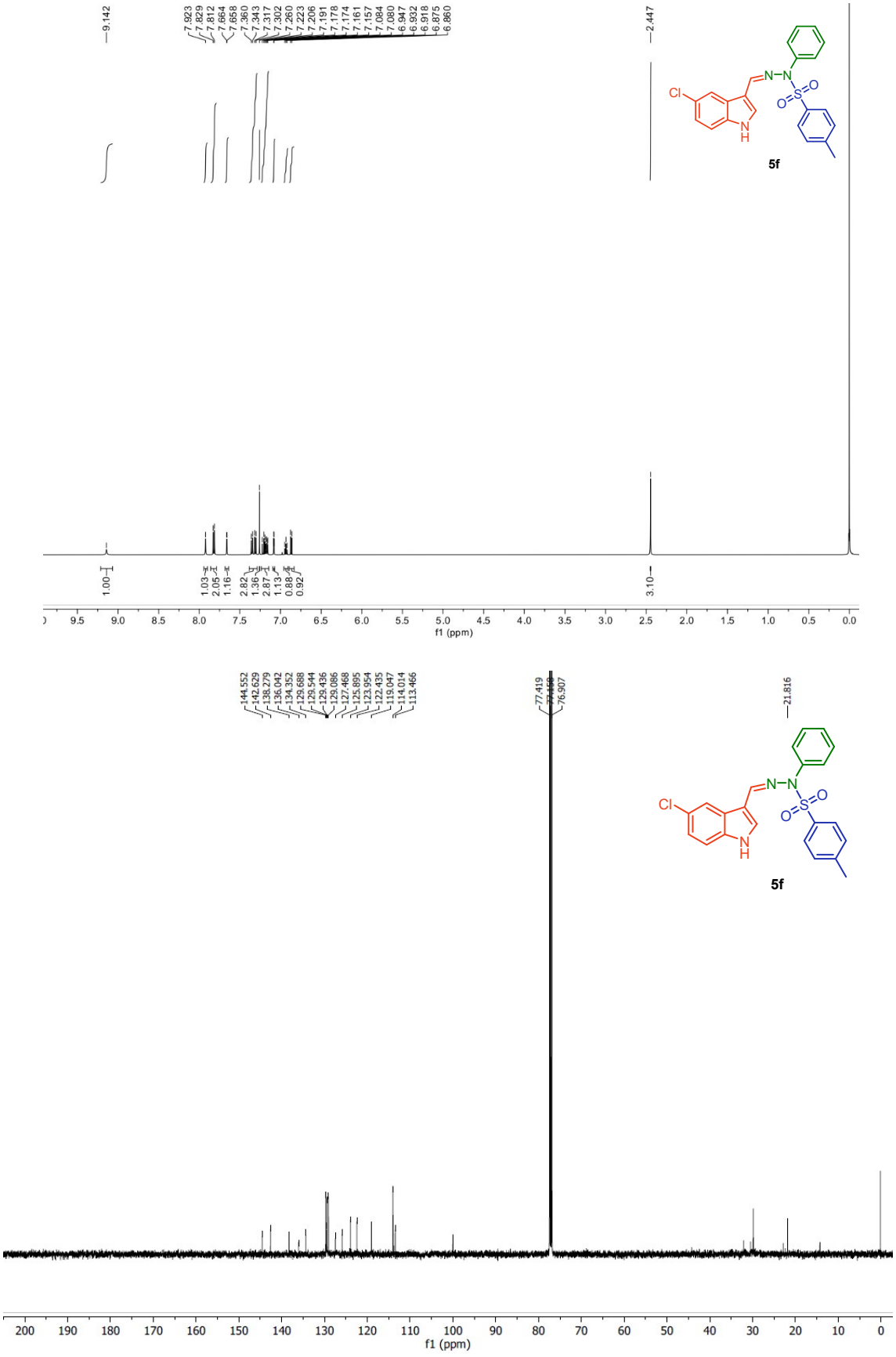
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5d**)



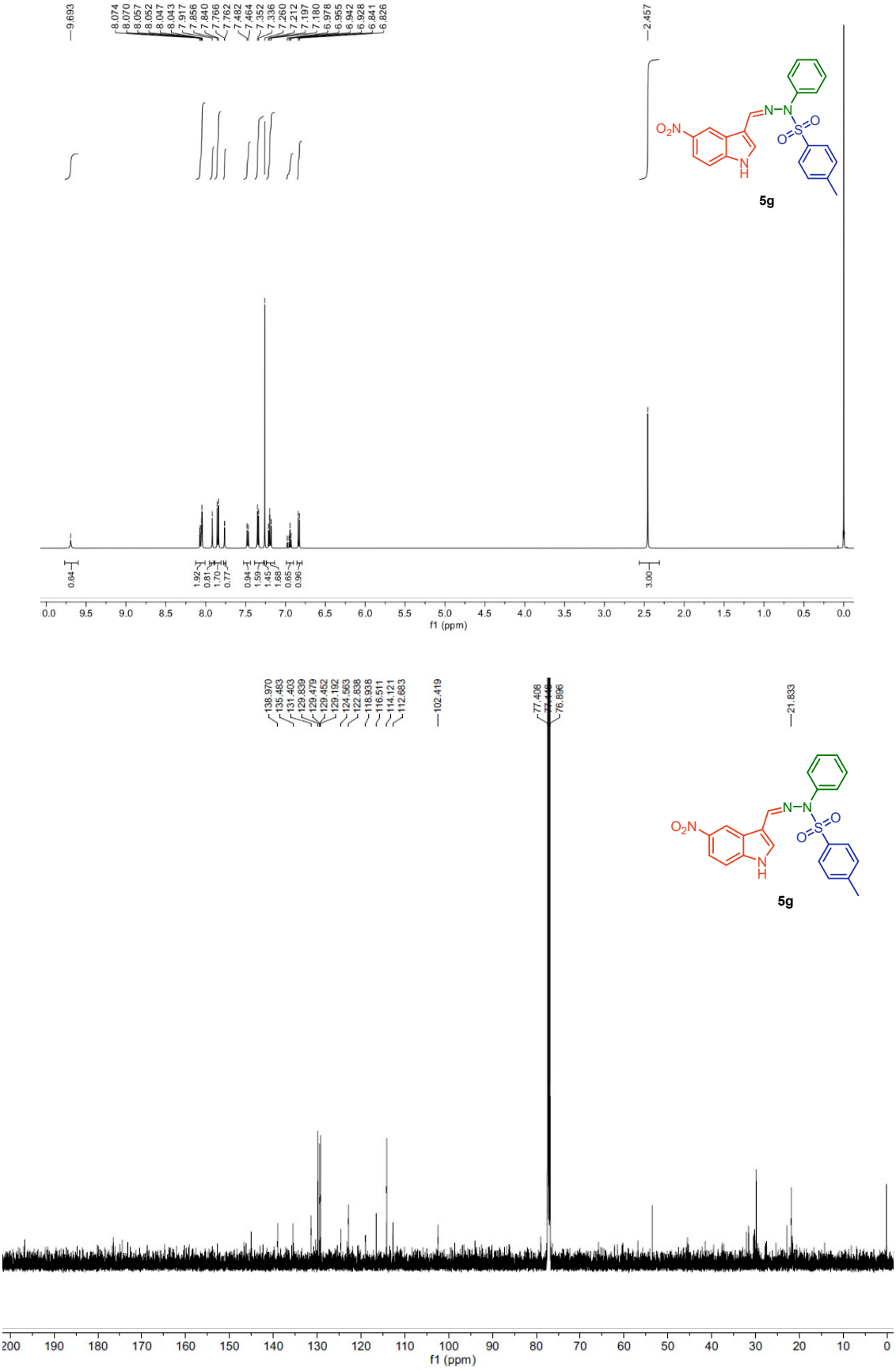
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5e**)



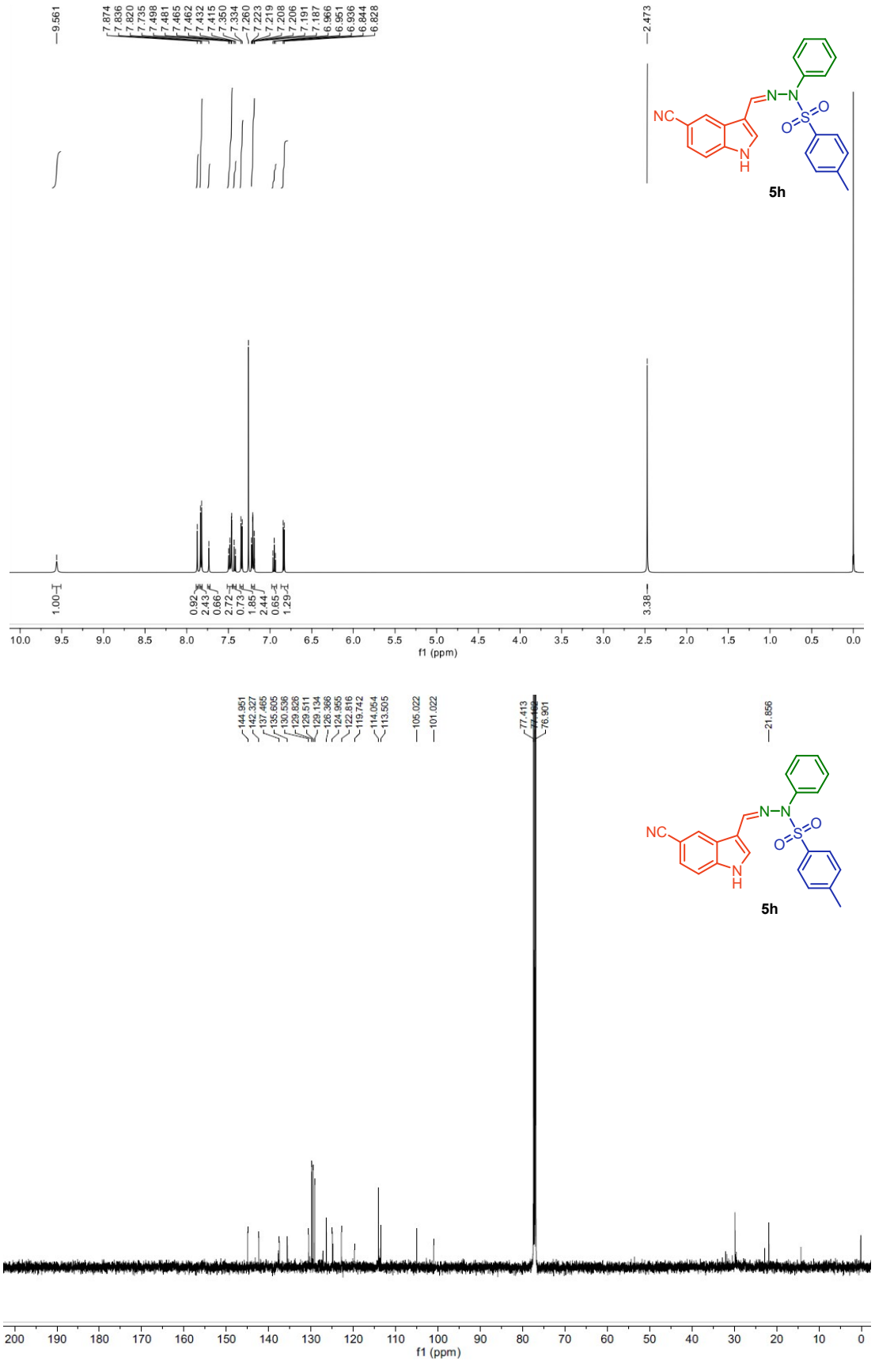
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5f**)



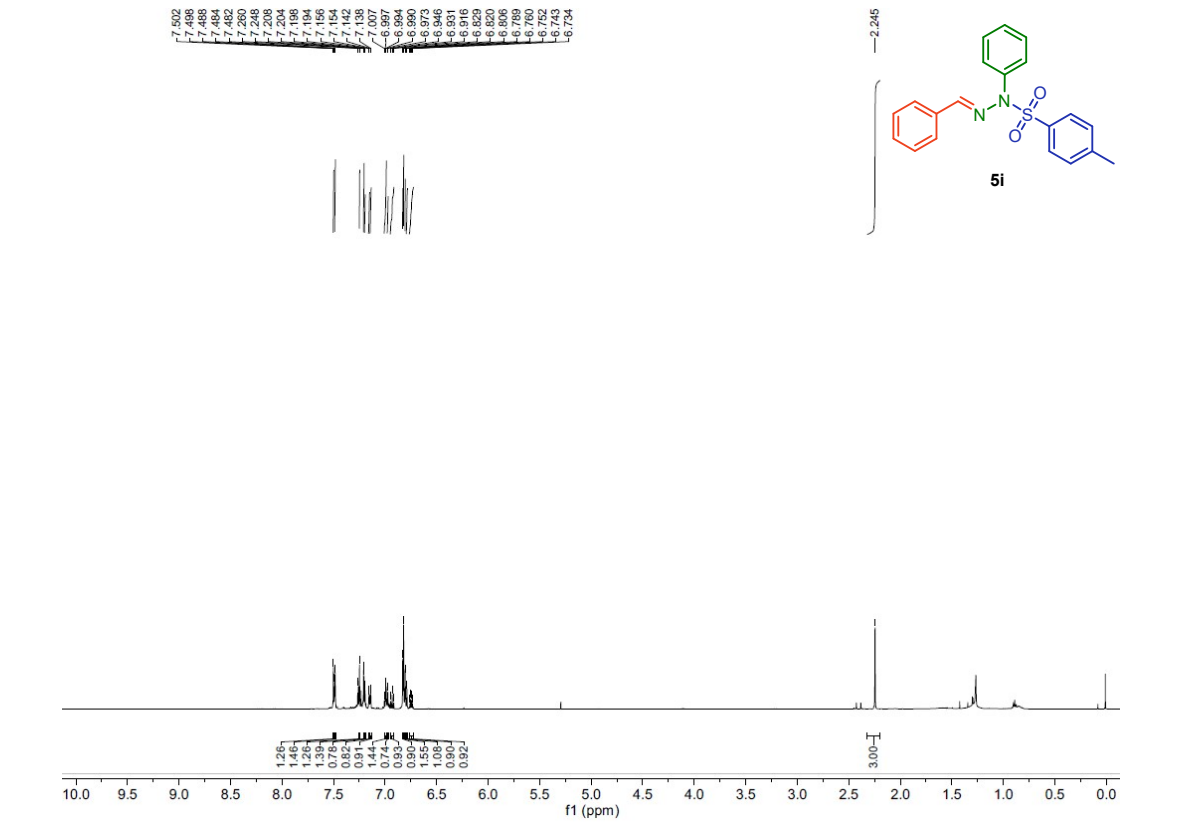
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5g**)



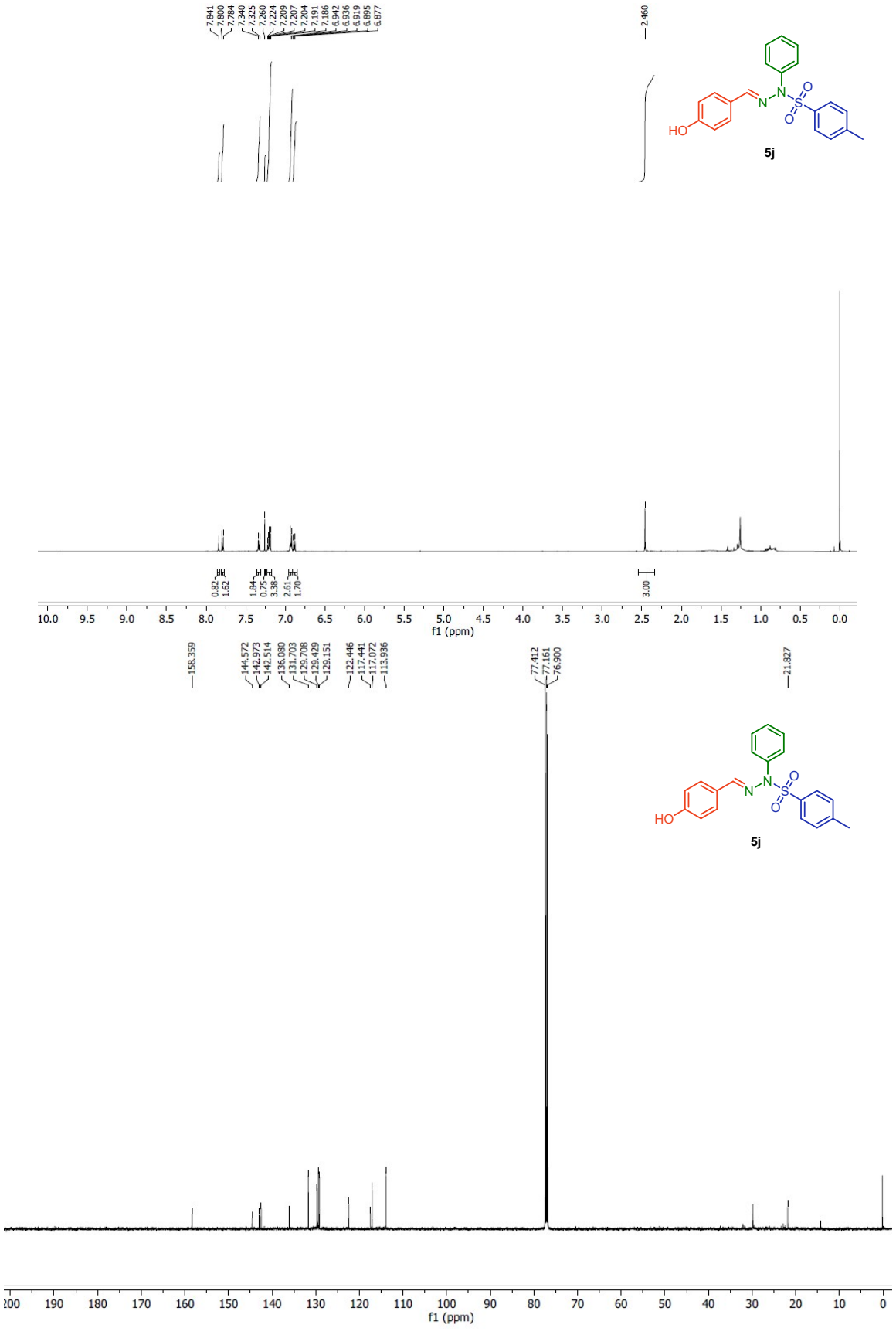
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5h**)



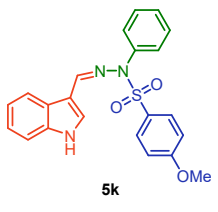
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5i**)

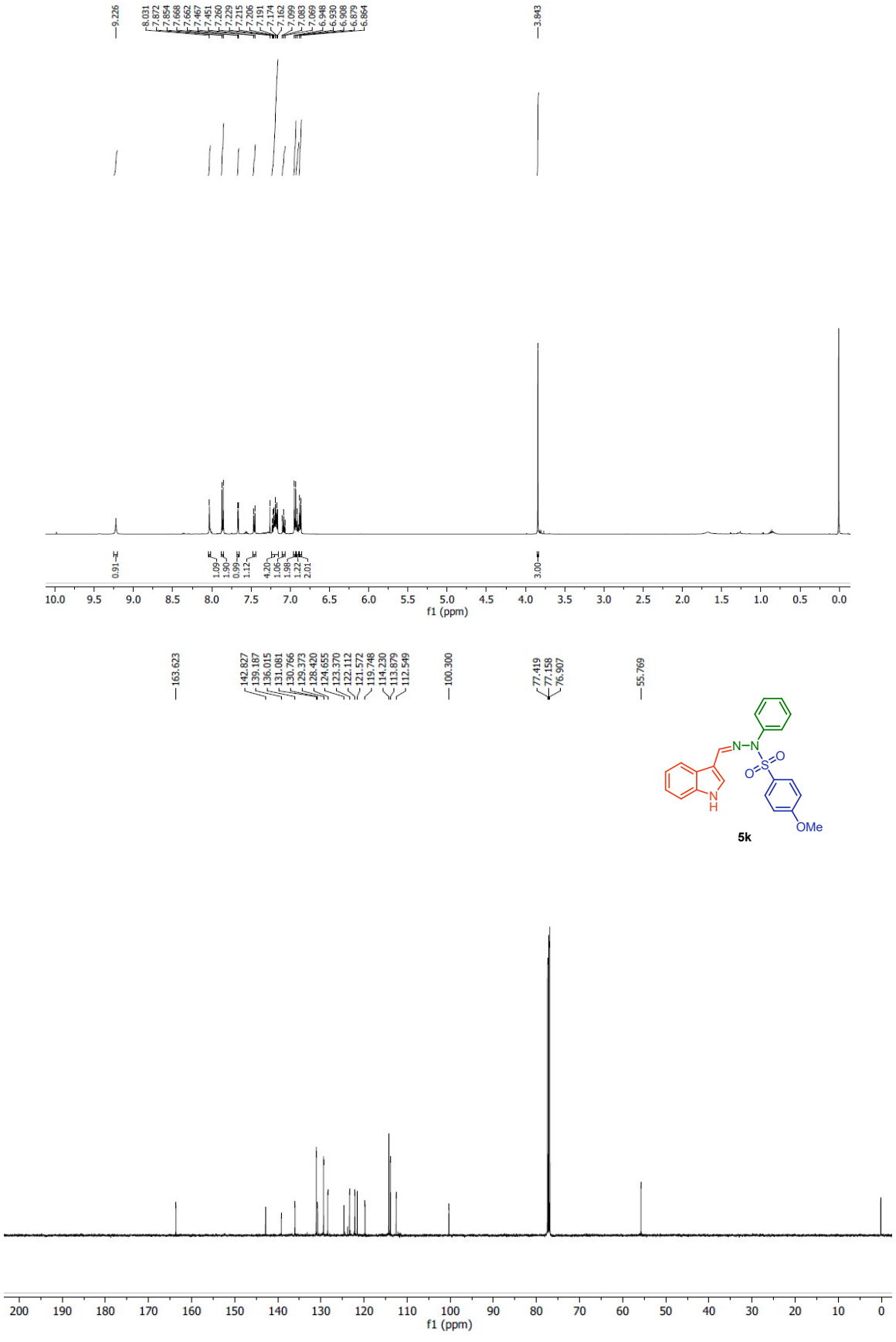


^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5j**)

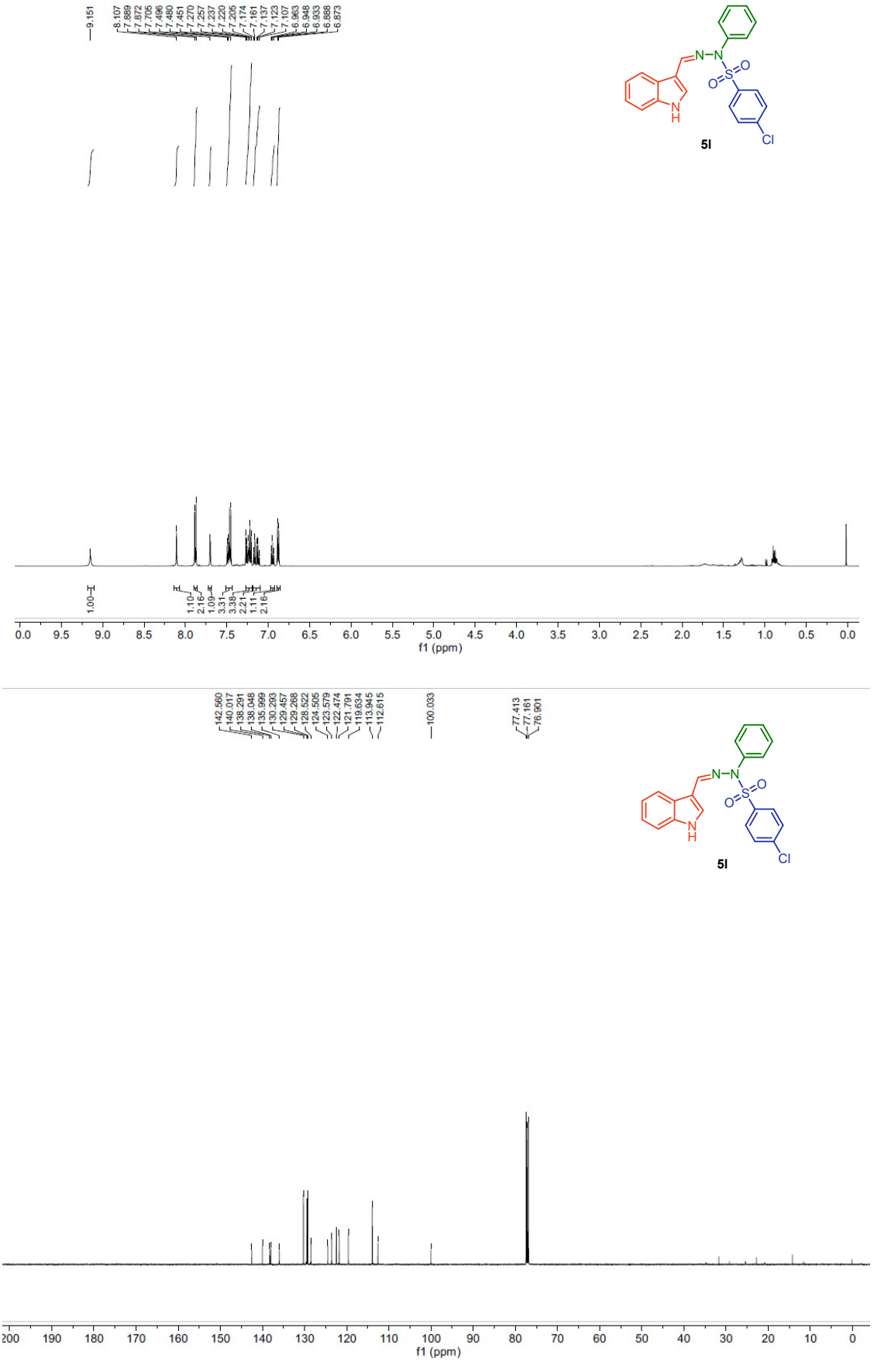


^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5k**)

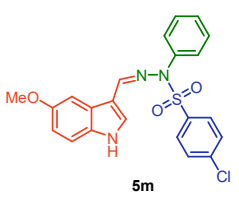


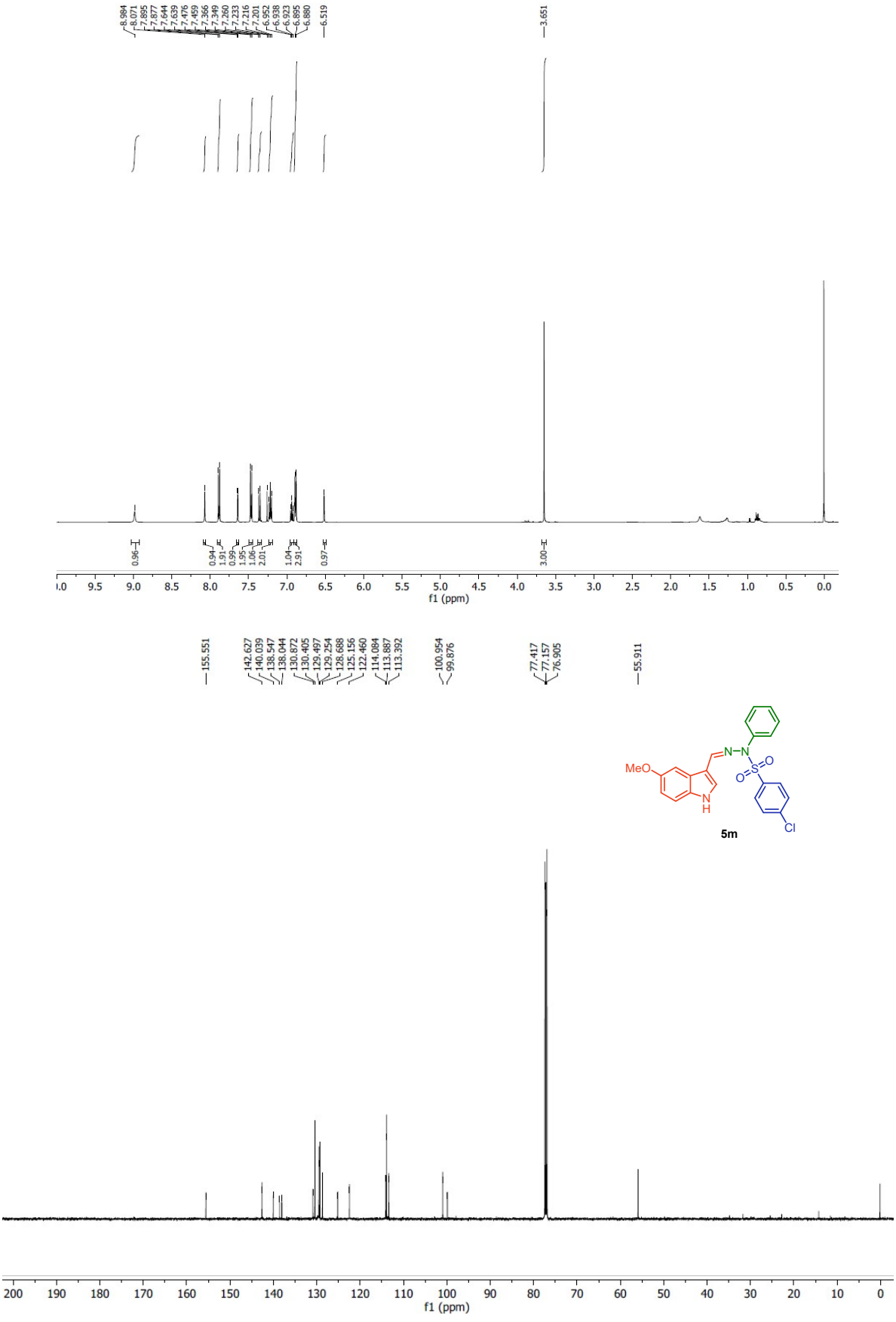


^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5l**)

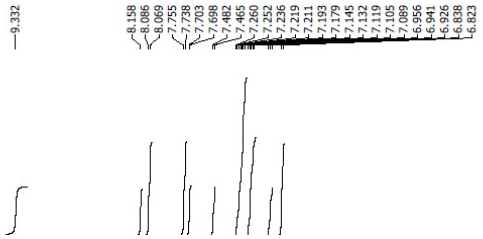


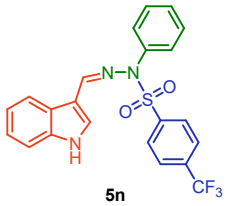
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) of (**5m**)





^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5n**)





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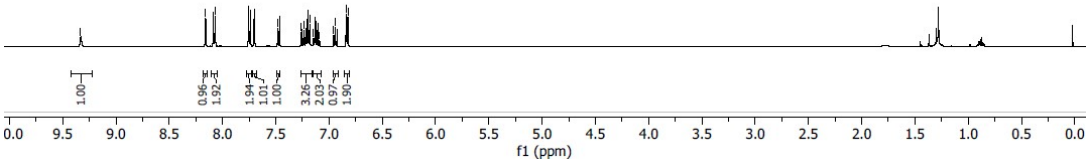

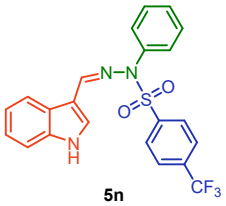

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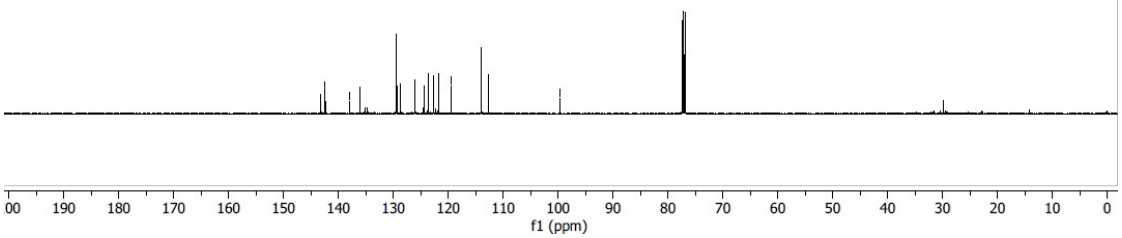
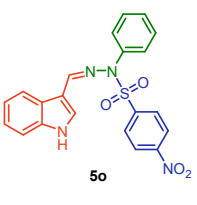


^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5o**)



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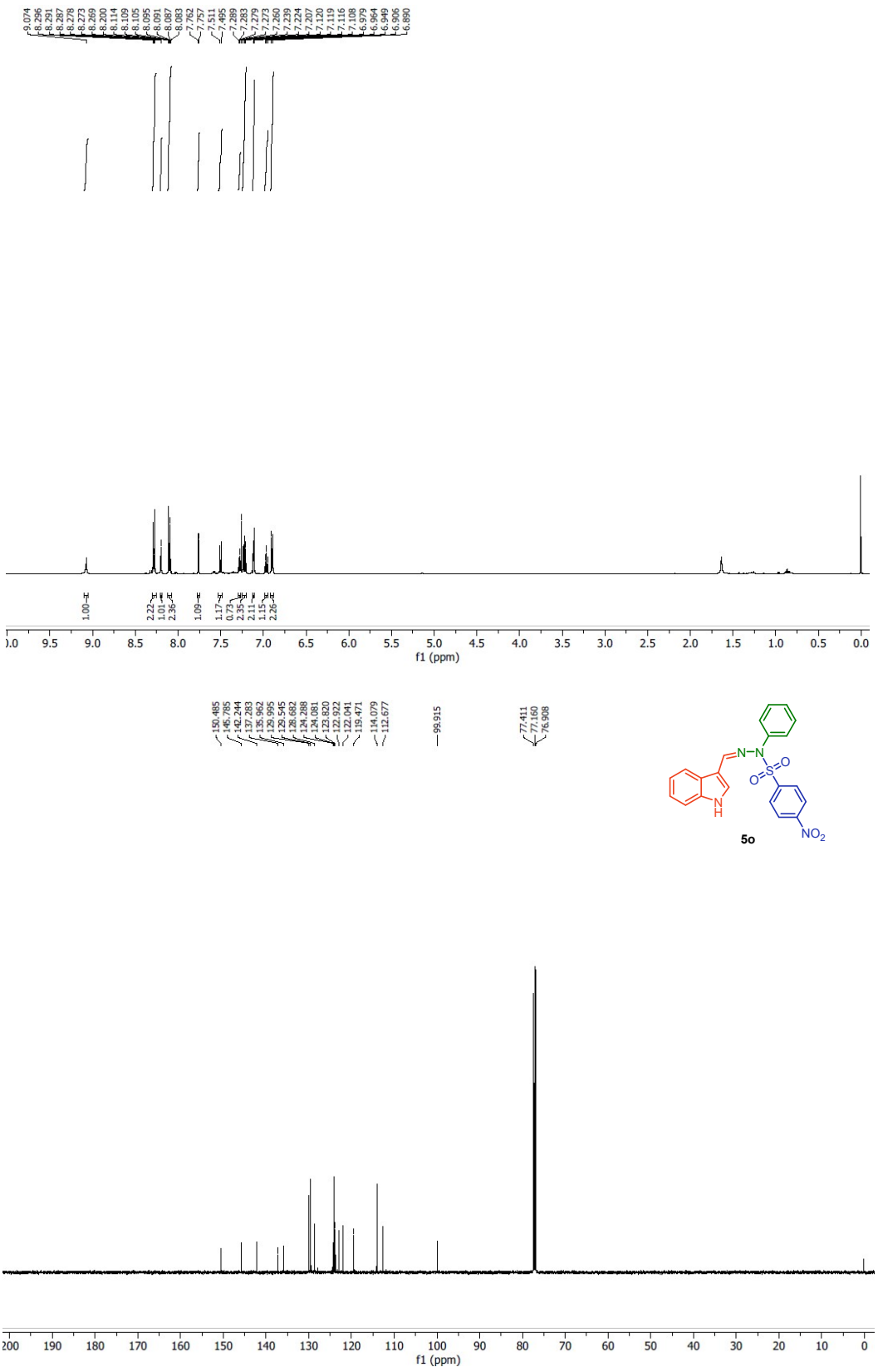
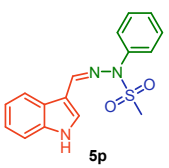
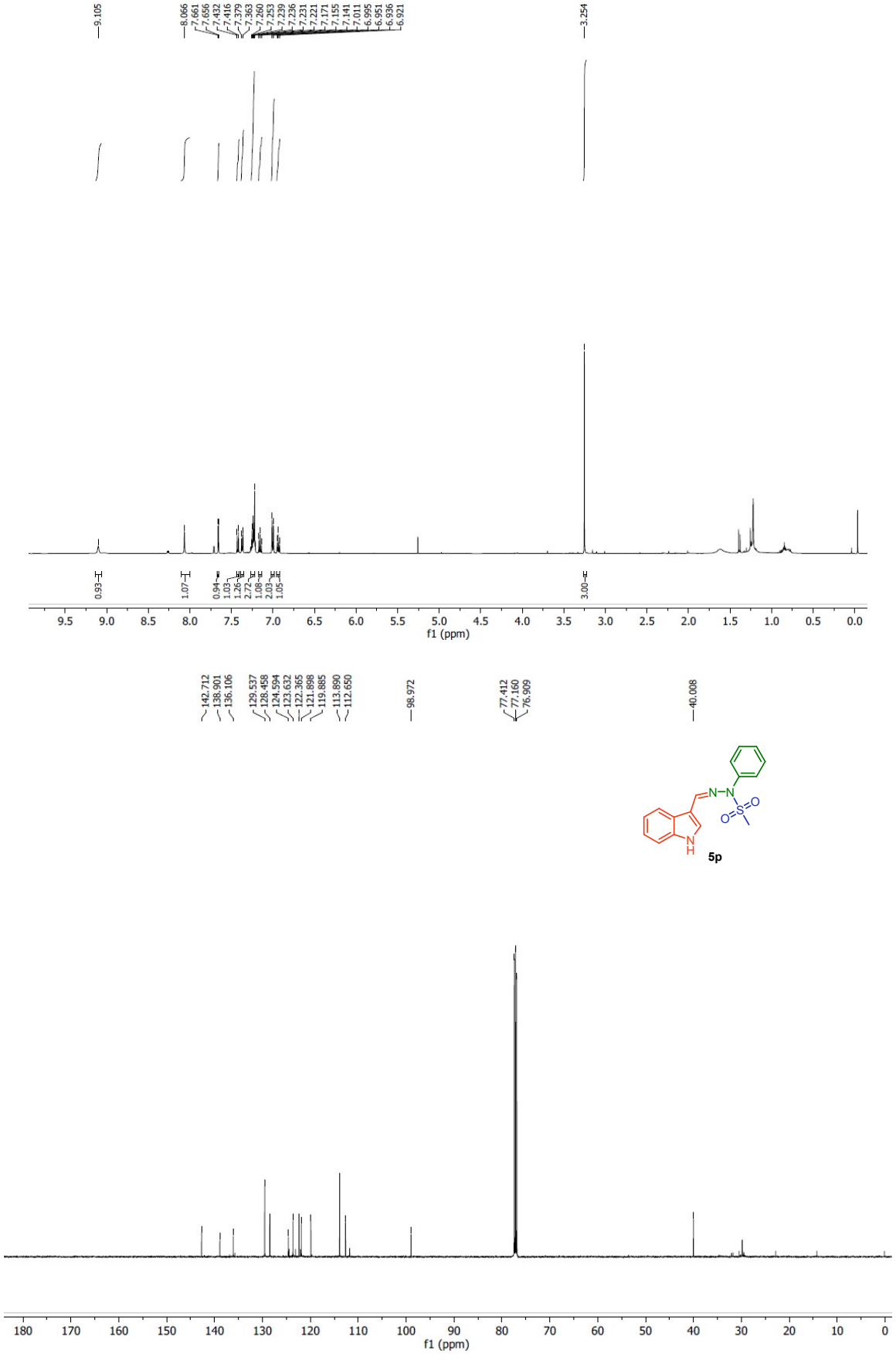
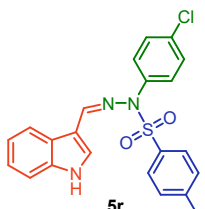


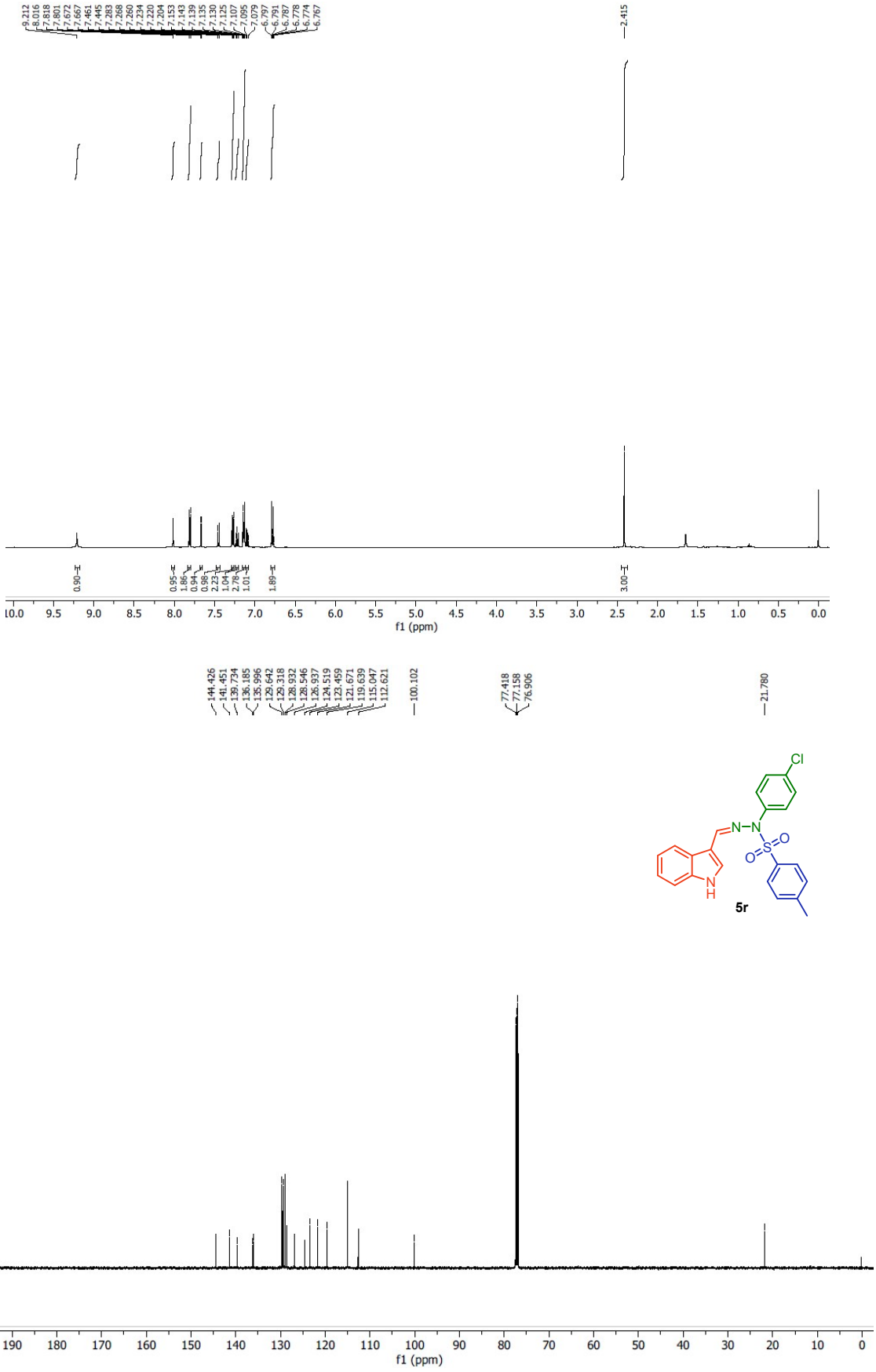
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5p**)



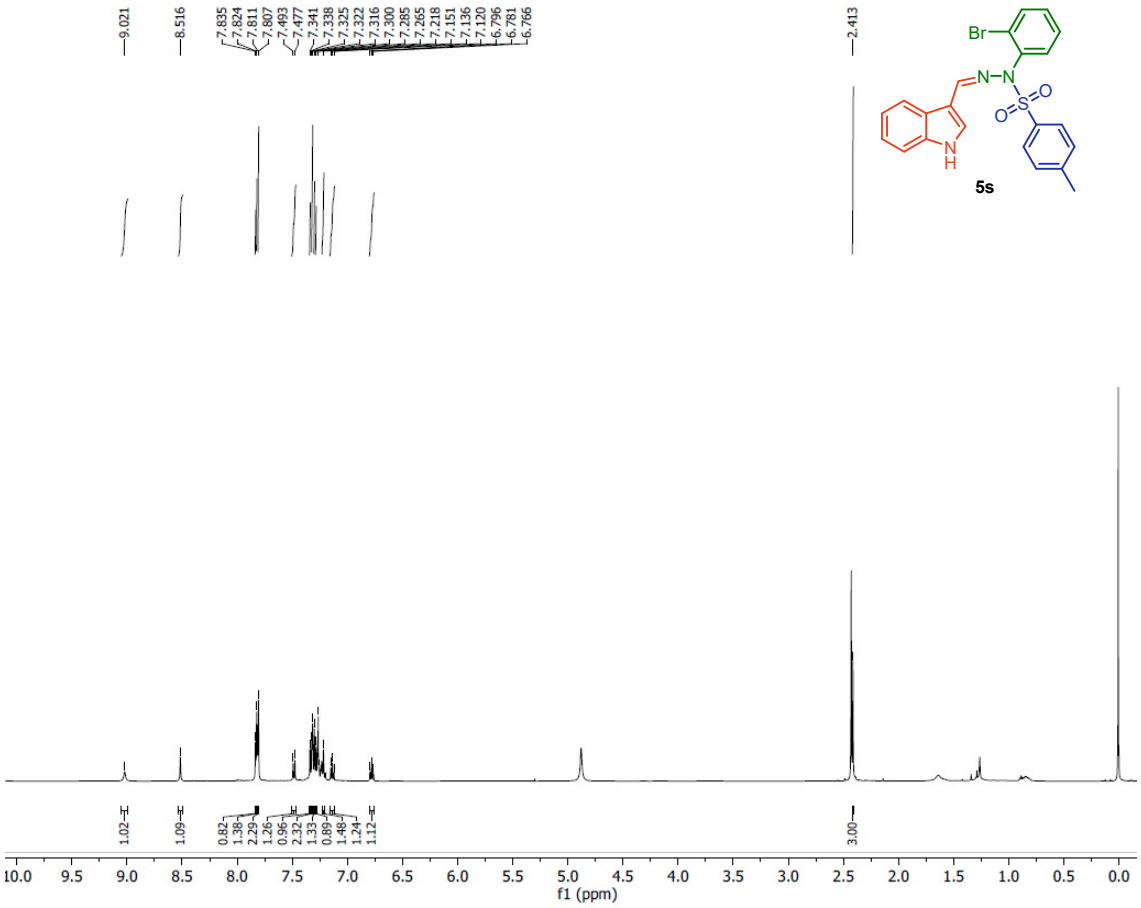


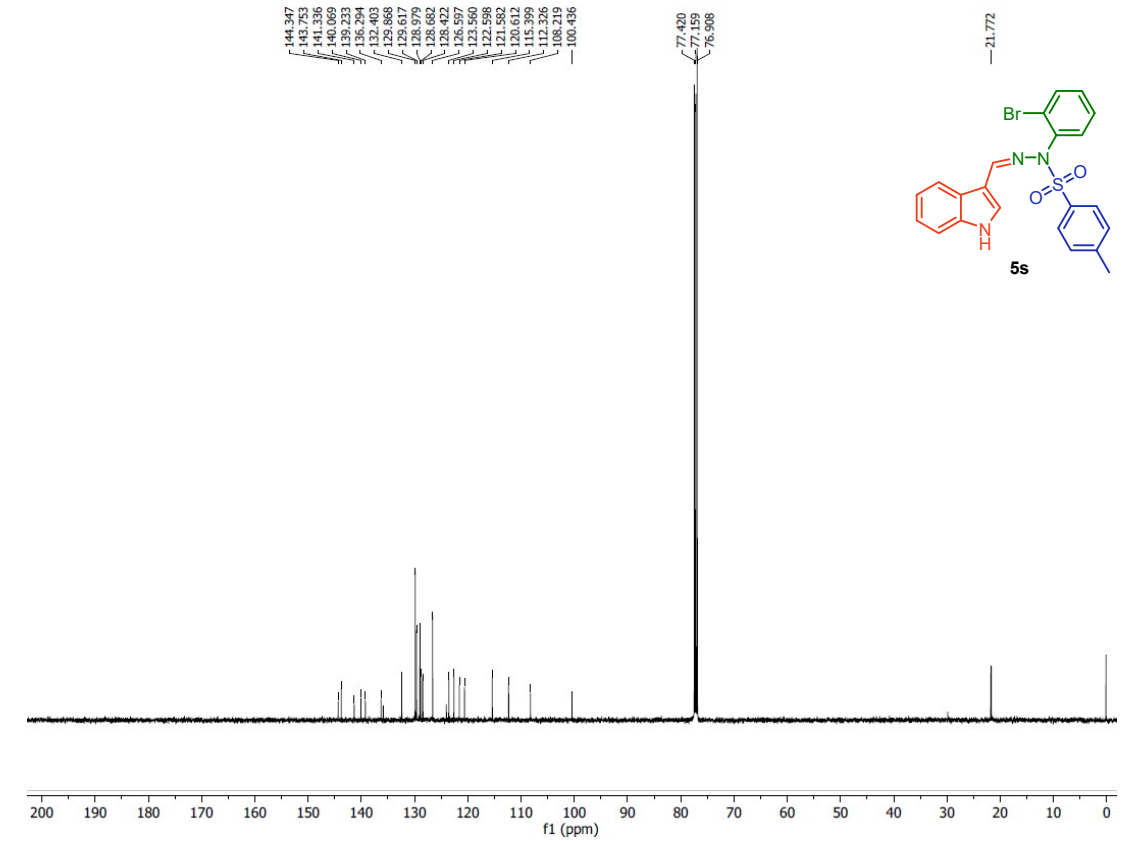
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) of (**5r**)



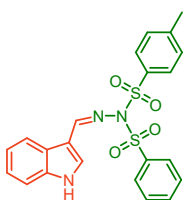


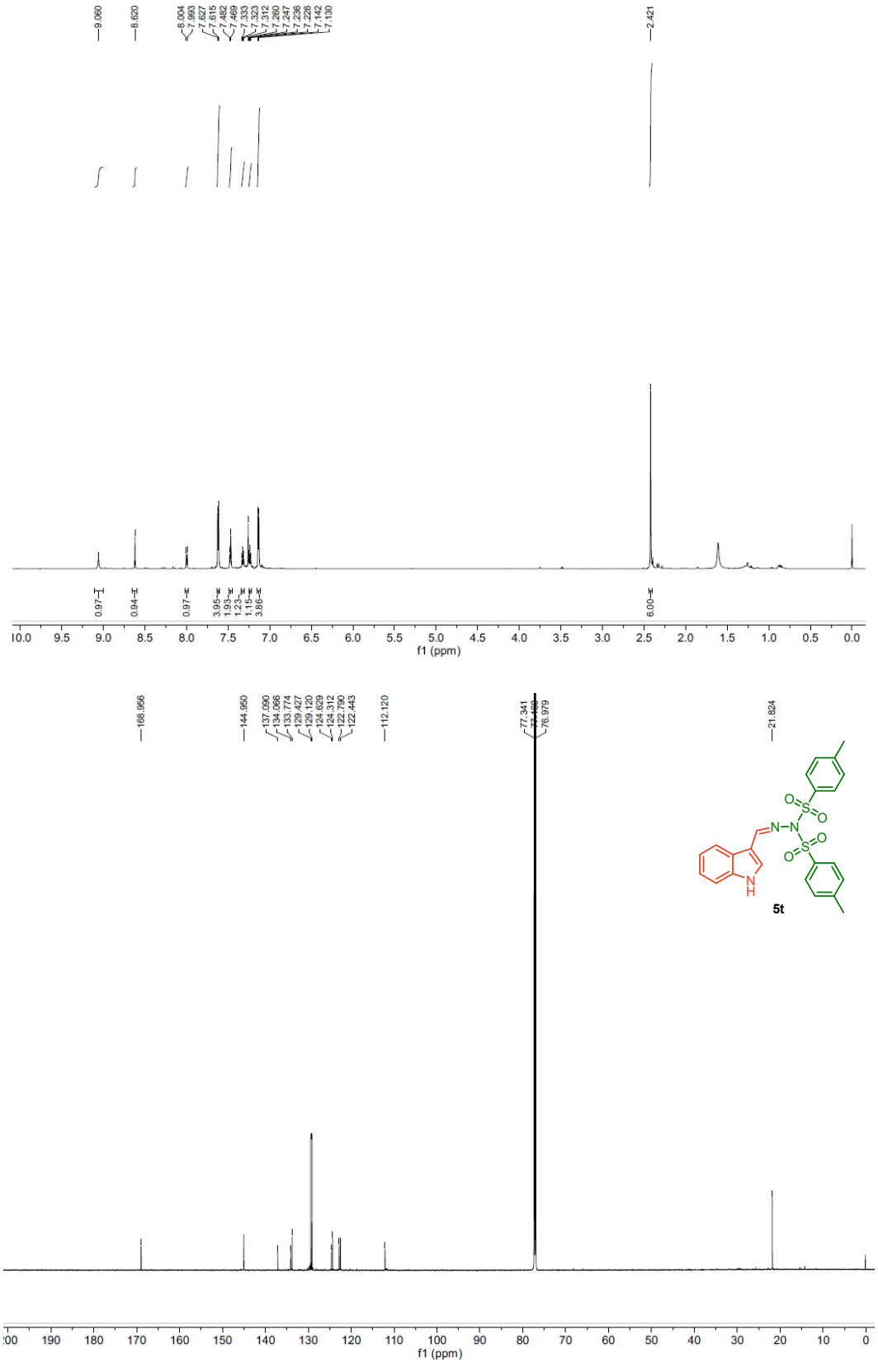
^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5s**)



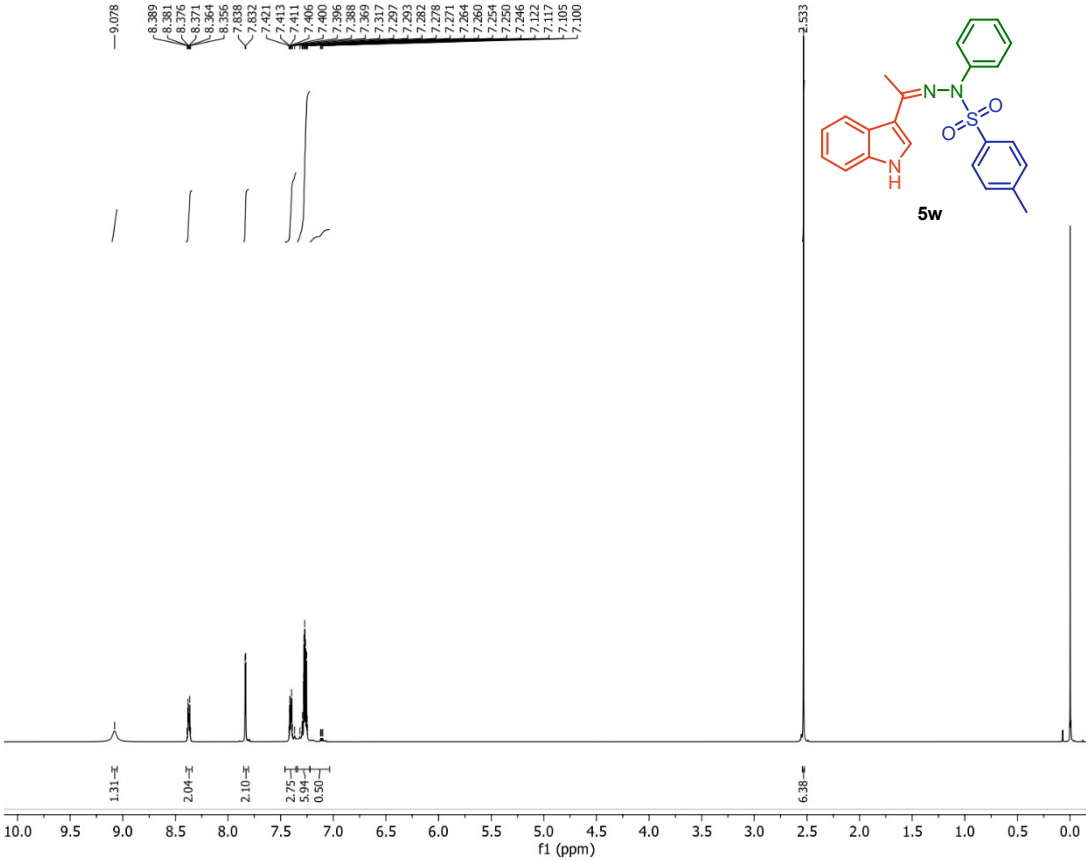


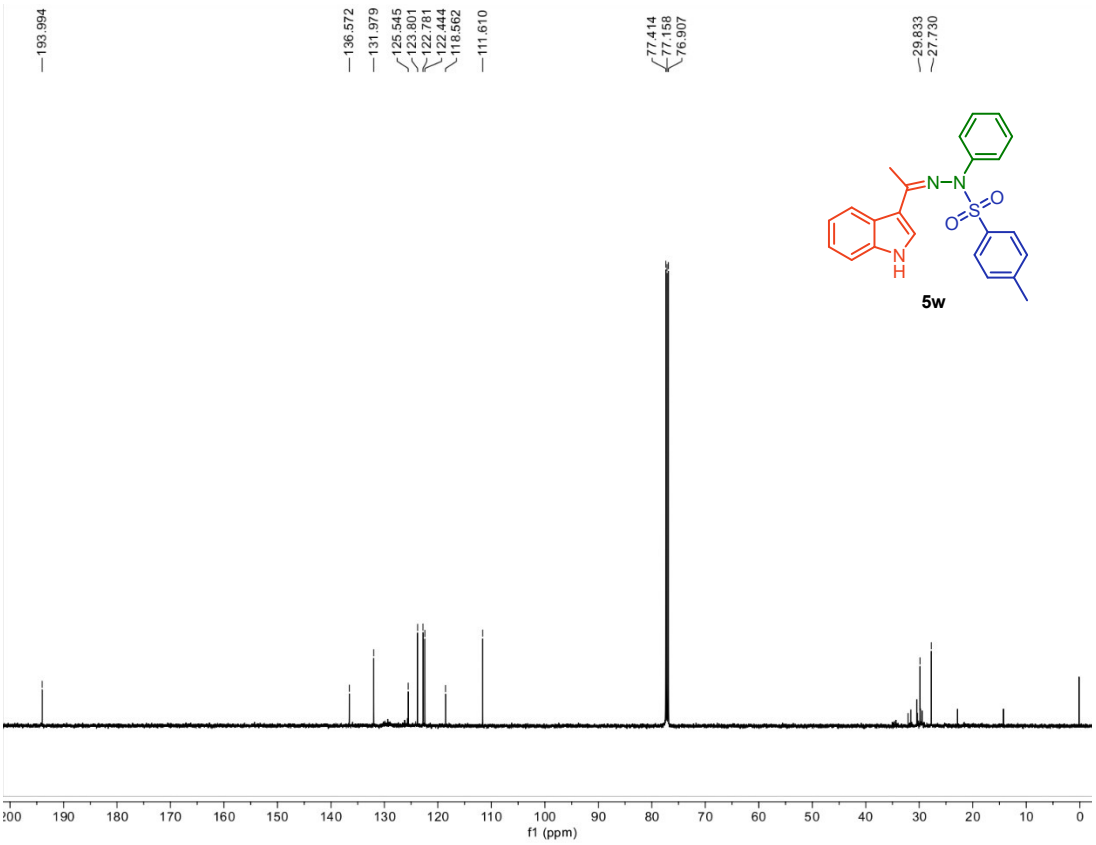
^{1}H NMR (700 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$) of (**5t**)





^{1}H NMR (500 MHz, $CDCl_3$) and $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of (**5w**)





(V) HRMS data of model reaction

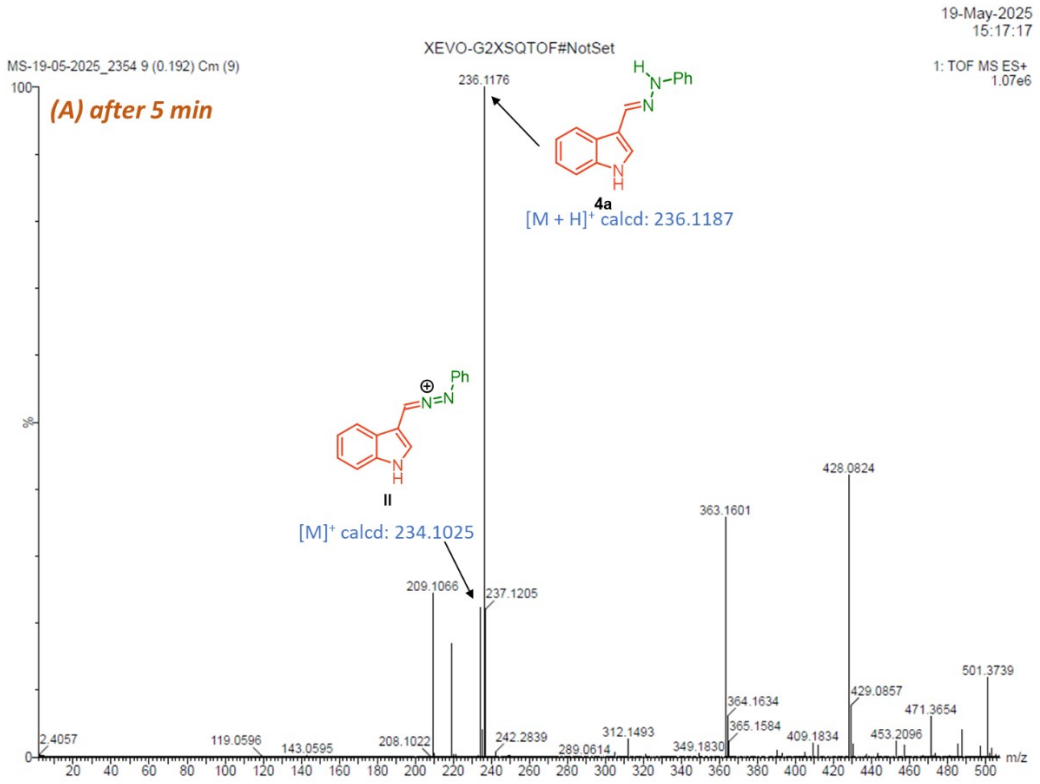


Figure S2: HRMS spectrum of the model reaction mixture recorded after 5 minutes

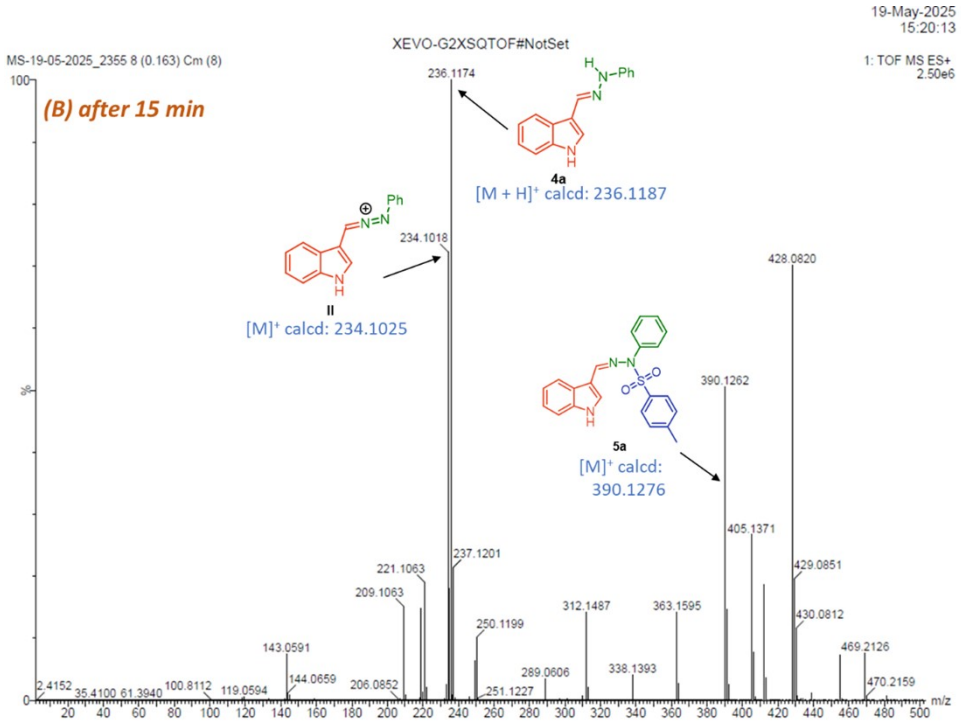


Figure S3: HRMS spectrum of the model reaction after 15 minutes

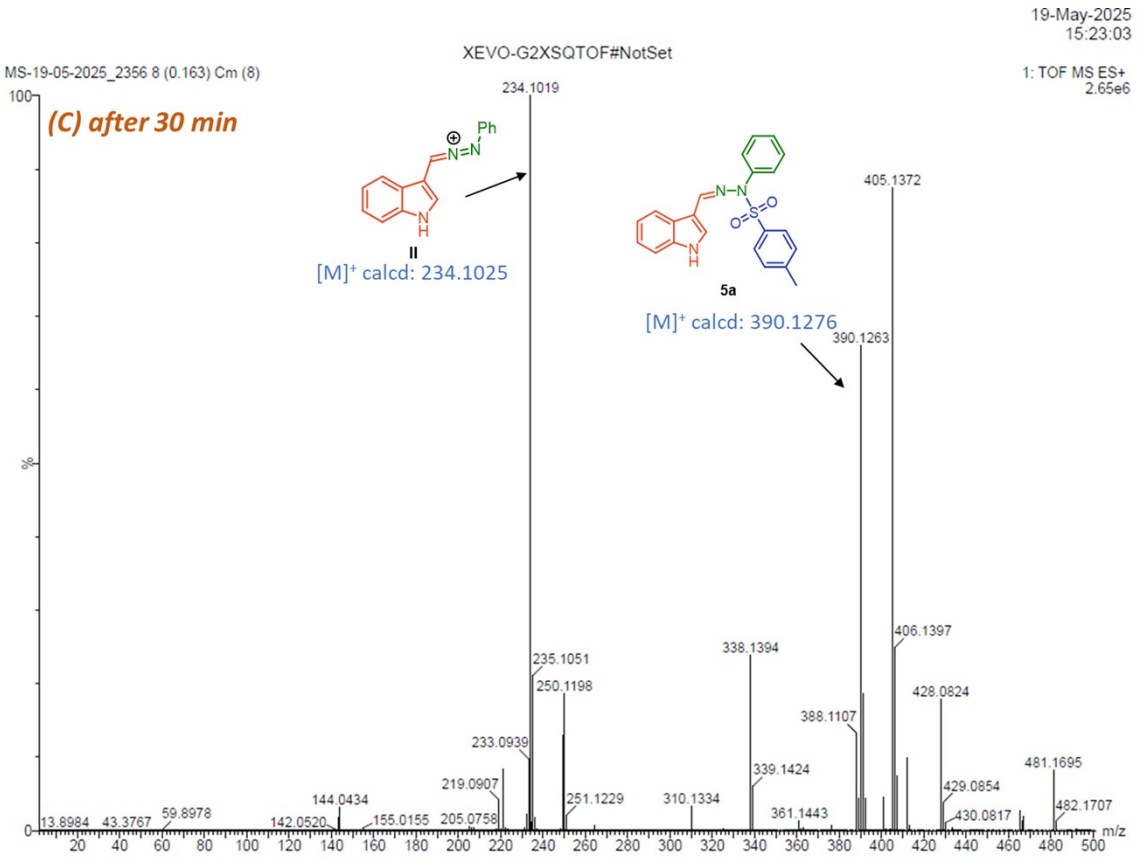


Figure S4: HRMS spectrum of the model reaction mixture recorded after 15 minutes

(VI) References

1. P. N. James and H. R. Snyder, *Org. Synth.* 1959, ***39***, 30.
2. B. Sarkar, P. Ghosh and A. Hajra, *Org. Lett.*, 2023, **25**, 3440–3444.
3. Spingler, B.; Schnidrig, S.; Todorova, T.; Wild, F. *CrystEngComm*, 2012, **14**, 751–757.