Supplementary Material

Synthesis of novel imidazopyridine-oxadiazole molecular hybrids by a regioselective sulfenylation of imidazo[1,2-*a*]pyridines with 1,3,4-oxadiazole-2-thiols using I_2-$FeCl_3$ catalytic system and O_2/air as co-oxidant

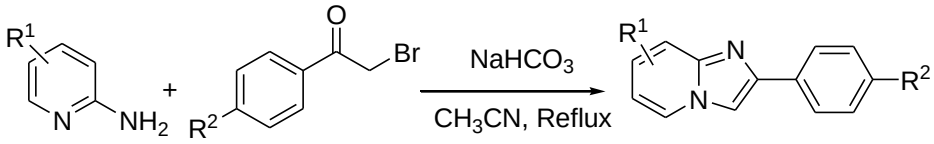
Kartik Dutta,[a,b] Nisha Kushwah,[c] Amey P. Wadawale,[c] and Sunil K. Ghosh*[a,b]

[a]*Bio-Organic Division, Bhabha Atomic Research Centre, Trombay, Mumbai 400085*
[b]*Homi Bhabha National Institute, Anushaktinagar, Mumbai 400094*
[c]*Chemistry Division, Bhabha Atomic Research Centre, Trombay, Mumbai-400085, India*
Email: ghsunil@barc.gov.in

Table of Contents

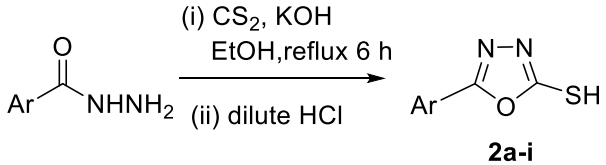
1. General procedure for synthesis imidazo[1,2-a]pyridine derivatives 1a-h

Following the reported procedure,[1] sodium bicarbonate (1.6 g, 20 mmol) was added to a stirred solution of 2-bromoacetophenone derivatives (10 mmol) and 2-aminopyridine derivatives (10 mmol) in 50 mL of acetonitrile and the mixture was refluxed for 2 h. After completion of reaction as monitored by TLC, the reaction mixture was diluted with water and extracted with ethyl acetate. The organic phase was then dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude product was purified by silica gel column chromatography using petroleum ether and ethyl acetate as the eluent to afford pure **1a-h**. Spectroscopic data for **1a**,**f**[2]; **1b-e**[3] and **1g**,**h**[4] were similar as reported.



2. General procedure for synthesis 2a-i

Following the reported procedure,[5] a vigorously stirred solution of appropriately substituted carboxy benzohydrazide (10 mmol) in 30 mL absolute ethanol was basified with potassium hydroxide (10 mmol) until a solid precipitate came out. Carbon disulphide (15 mmol) was added to the mixture and refluxed for 6 h. After completion of the reaction as verified by TLC, ethanol was removed under vacuum. Then sticky mass was diluted with cold water and acidified with 0.5 M HCL to maintain pH = 3-4. The precipitated crude product was filtered, washed with water and air dried. Recrystallization from ethanol gave pure **2a-i** in 68-75% yield. Spectroscopic data for **2a,c**[5] and **2e-h**[5] were similar as reported.



	Ar
2a	4-$OMeC_6H_4$
2b	Ph
2c	Me
2d	3,4,5-$OMeC_6H_2$
2e	4-OHC_6H_4
2f	4-FC_6H_4
2g	4-ClC_6H_4
2h	4-BrC_6H_4
2i	4-$NO_2C_6H_4$

Scheme S1 synthesis of 1,3,4-oxadiazole-2-thiols **2a-i**

3. Characterization data for 2b, 2d and 2i

5-phenyl-1,3,4-oxadiazole-2-thiol (2b) White solid (1.3 g, 75% yield); mp 202.2 – 221.9 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 7.86 (d, J = 6.9 Hz, 2 H), 7.62–7.55 (m, 3 H); ^{13}C NMR (75

MHz, DMSO-d_6) δ (ppm) 177.8, 160.9, 132.7, 129.9, 126.5, 122.9; Elemental Anal. Calcd. for $C_8H_6N_2OS$ C, 53.92; H, 3.39; N, 15.72; S, 17.99%. Found C, 54.25; H, 3.52; N, 15.69; S, 18.24%.

5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole-2-thiol (2d) White solid (1.9 g, 71% yield); mp 185.6- 186.9 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 7.09 (s, 2 H), 3.85 (s, 6 H), 3.73 (s, 3.09); NMR (75 MHz, DMSO-d_6) δ (ppm) 177.7, 160.8, 153.9, 141.2, 117.9, 103.8, 60.7, 56.6; Elemental Anal. Calcd. for $C_{11}H_{12}N_2O_4S$ C, 49.25; H, 4.51; N, 10.44; S, 11.95%. Found C, 49.25; H, 4.37; N, 10.31; S, 12.26%.

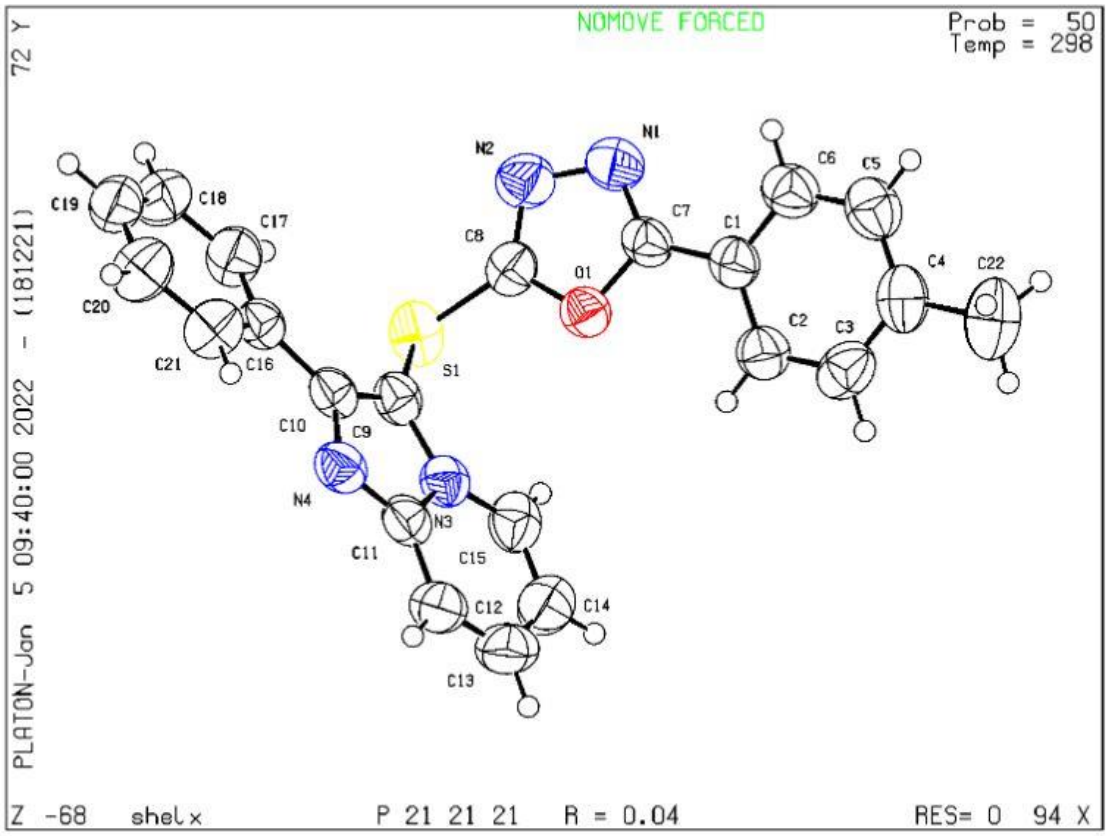
5-(4-nitrophenyl)-1,3,4-oxadiazole-2-thiol (2i) Yellow solid (1.5 g, 68% yield); mp 190.1-191.9 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 8.37 (d *J* = 8.7 Hz 2 H), 8.10 (d *J* = 8.7 Hz 2 H); NMR (75 MHz, DMSO-d_6) δ (ppm) 178.1, 159.3, 149.6, 128.5, 127.9, 125.0; Elemental Anal. Calcd. for $C_8H_5N_3O_3S$ C, 43.05; H, 2.26; N, 18.83; S, 14.36%. Found C, 43.18; H, 2.54; N, 18.70; S, 14.67%.

3. X-ray crystallographic Characterization of compound 3c

Table S1. Crystal data and structure refinement for **3c**

CCDC number 2184609	
Empirical formula	$C_{22}H_{16}N_4OS$
Formula weight	384.45
Temperature [K]	298(2)
Crystal system	orthorhombic
Space group (number)	$P2_12_12_1$ (19)
a [Å]	8.3230(3)
b [Å]	10.8098(3)
c [Å]	20.8096(6)
α [Å]	90
β [Å]	90
γ [Å]	90
Volume [Å^3]	1872.24(10)
Z	4
ρ_{calc} [g/cm^3]	1.364

μ [mm^{-1}]	1.699
F(000)	800
Crystal size [mm^3]	0.150×0.050×0.050
Crystal colour	colorless
Crystal shape	needle
Radiation	Cu K_α (λ=1.54184 Å)
2Θ range [°]	9.22 to 153.70 (0.79 Å)
Index ranges	-9 ≤ h ≤ 10 -13 ≤ k ≤ 13 -24 ≤ l ≤ 26
Reflections collected	29635
Independent reflections	3791 R_{int} = 0.1362 R_{sigma} = 0.0653
Completeness to θ = 67.684°	99.9 %
Data / Restraints / Parameters	3791/0/256
Goodness-of-fit on F^2	1.008
Final *R* indexes [I≥2σ(I)]	R_1 = 0.0432 wR_2 = 0.1008
Final *R* indexes [all data]	R_1 = 0.0629 wR_2 = 0.1150
Largest peak/hole [eÅ^3]	0.15/-0.23
Flack X parameter	-0.02(3)
Extinction coefficient	0.0021(5)


NOMOVE FORCED
Prob = 50
Temp = 298
PLATON-Jan 5 09:40:00 2022 - (181221)
72 Y
Z -68 shelx
P 21 21 21 R = 0.04
RES= 0 94 X
N1
N2
C1
C2
C3
C4
C5
C6
C7
C8
O1
S1
C9
C10
C11
C12
C13
C14
C15
C16
C17
C18
C19
C20
C21
C22
N3
N4

4. ^{1}H & ^{13}C NMR Spectra

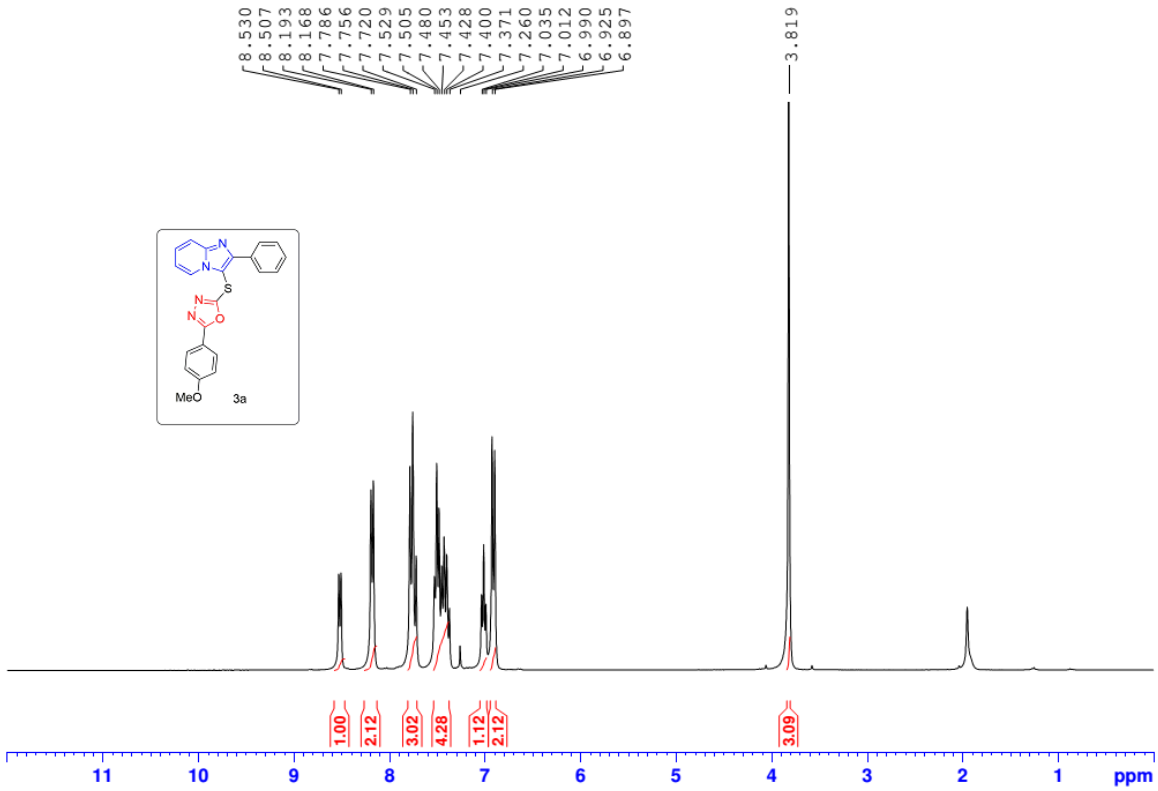


Figure S1. ^{1}H NMR spectrum of **3a**

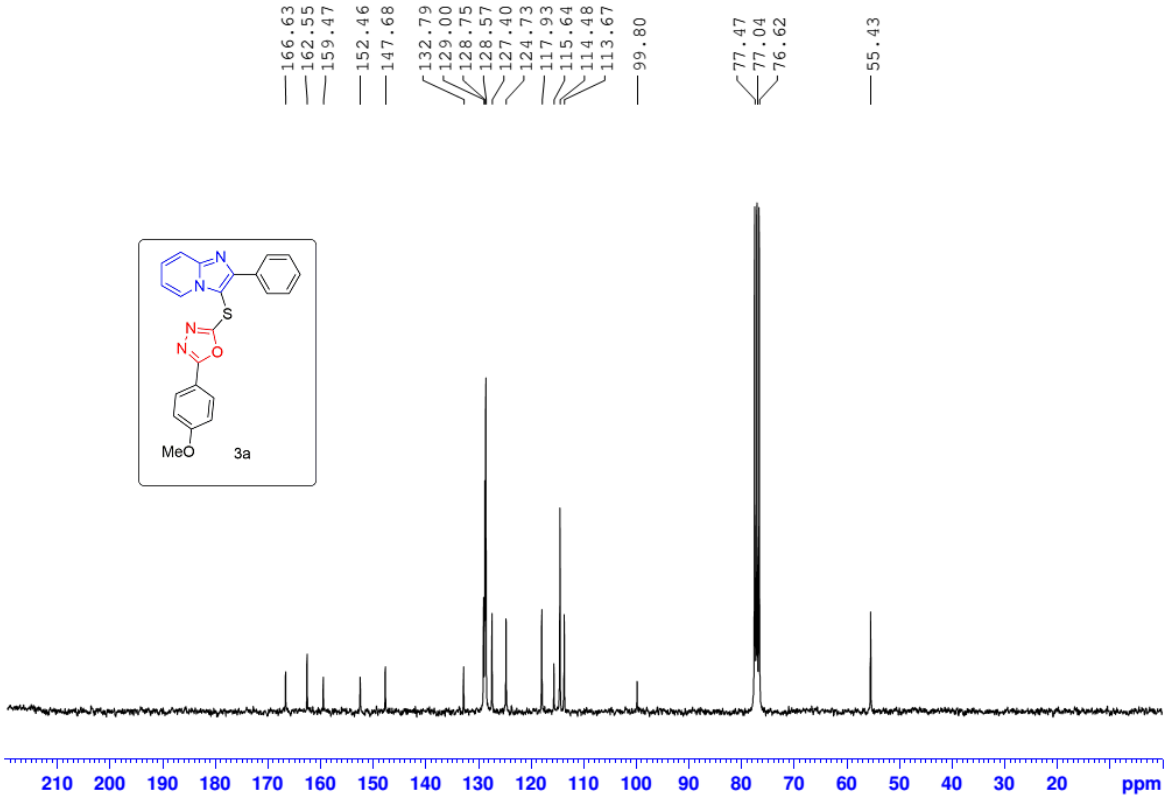


Figure S2. ^{13}C NMR spectrum of **3a**

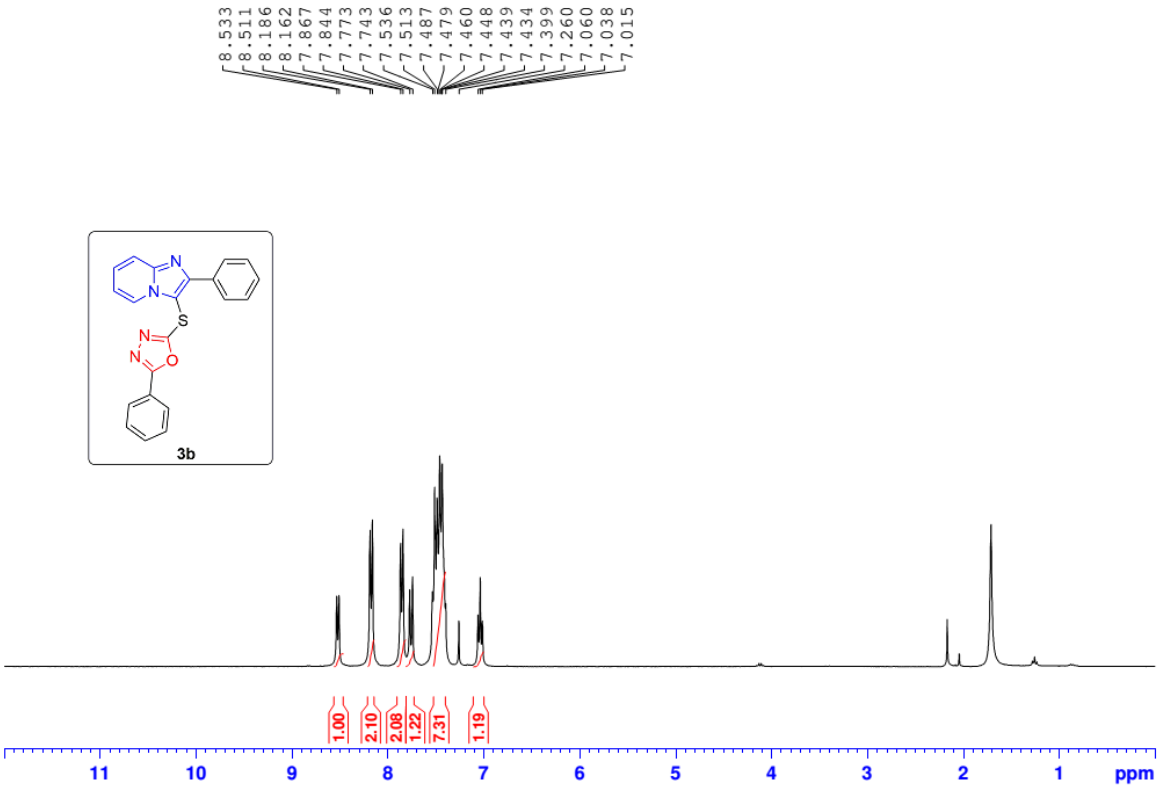


Figure S3. ^{1}H NMR spectrum of **3b**

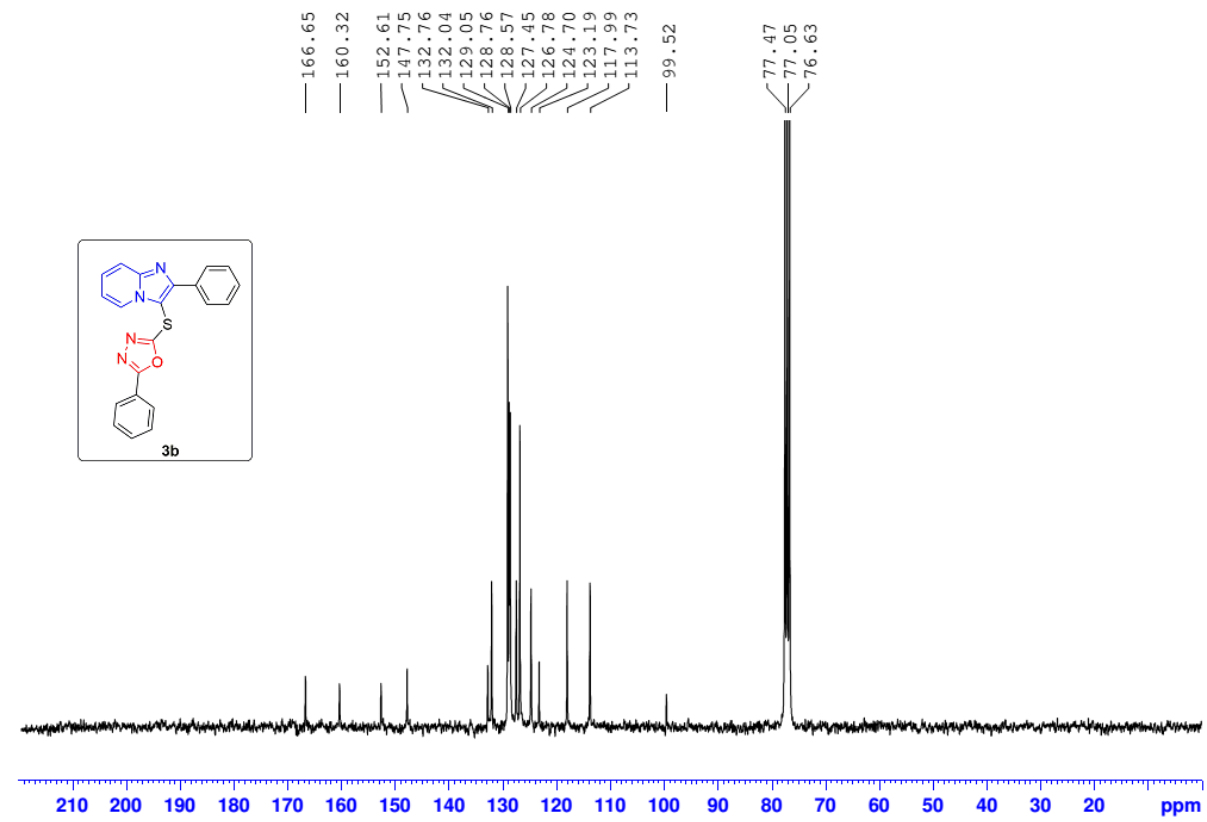


Figure S4. ^{13}C NMR spectrum of **3b**

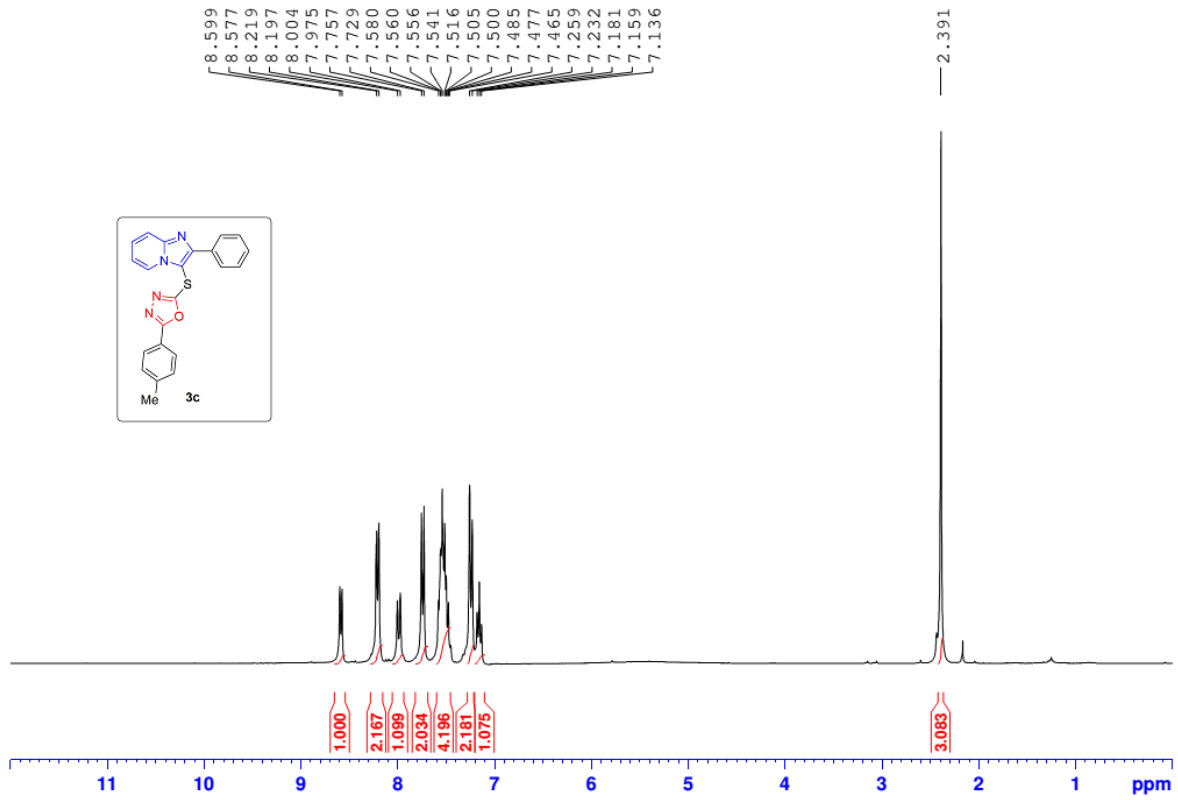


Figure S5. ^{1}H NMR spectrum of **3c**

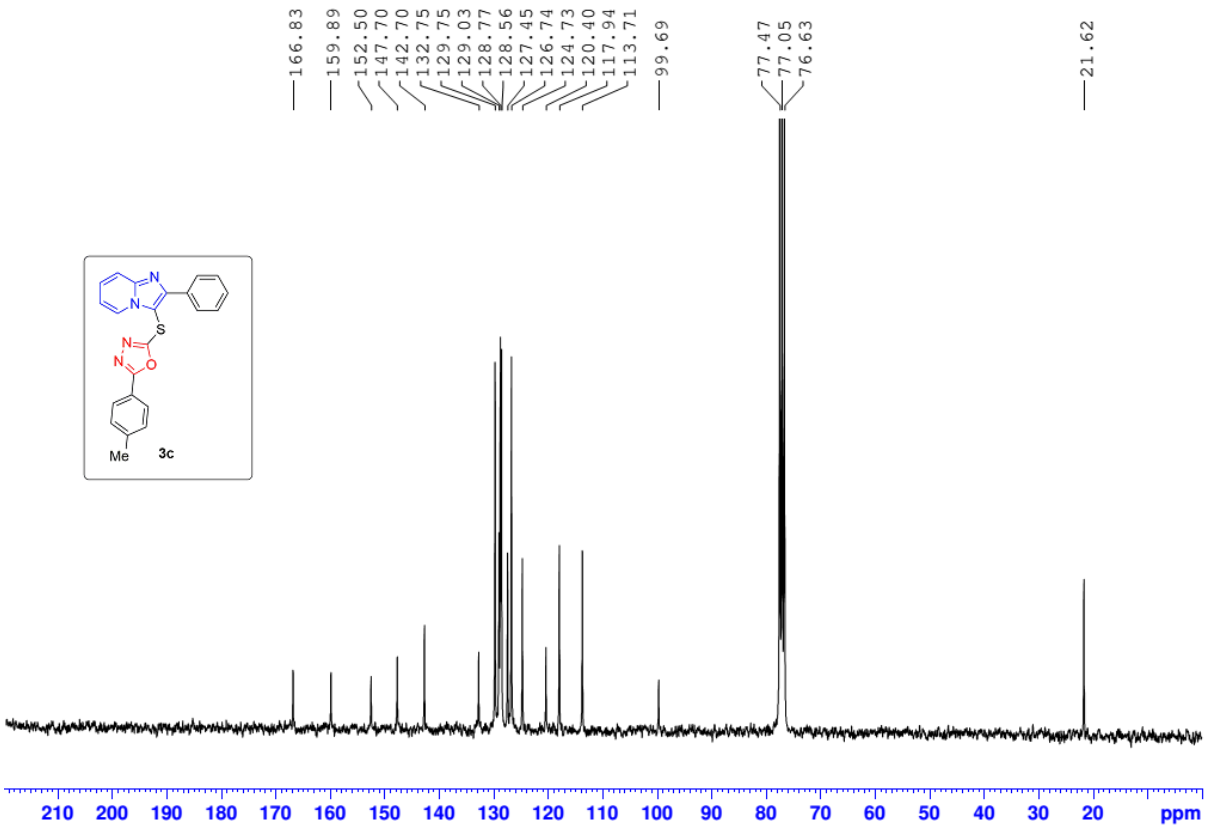


Figure S6. ^{13}C NMR spectrum of **3c**

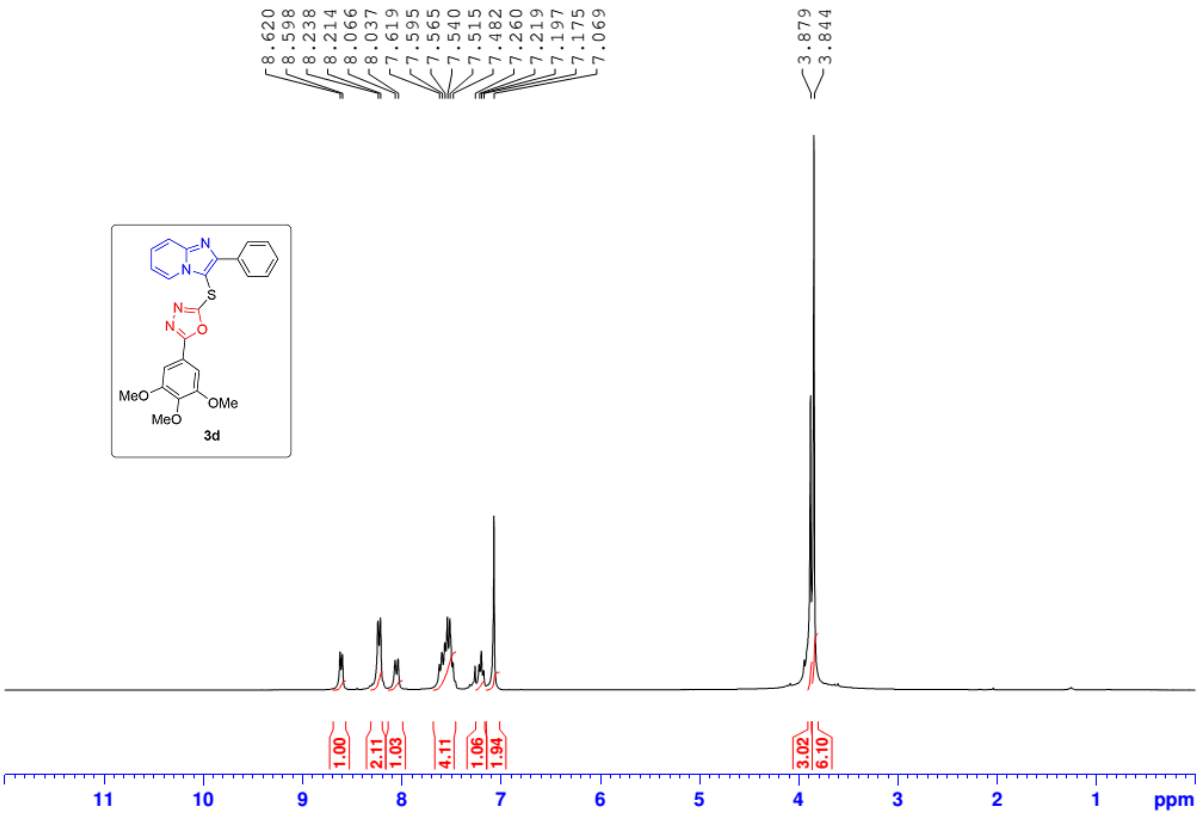


Figure S7. ^{1}H NMR spectrum of **3d**

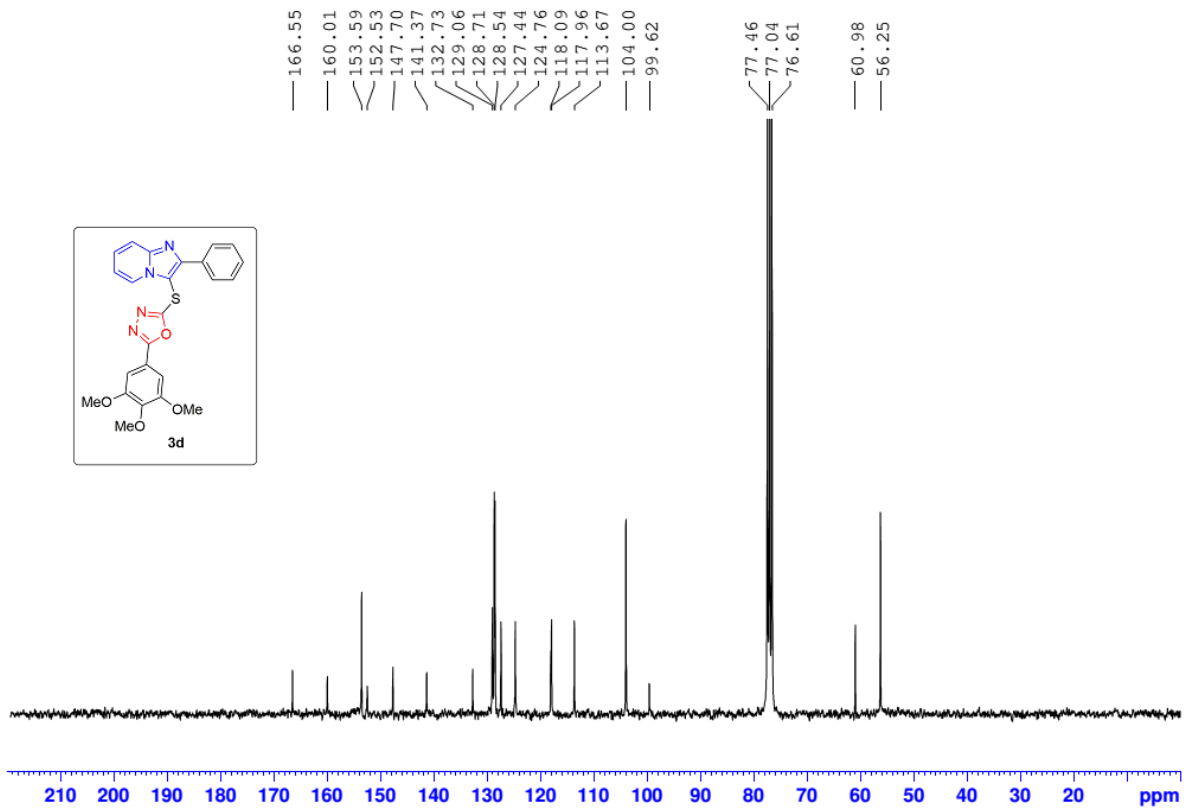


Figure S8. ^{13}C NMR spectrum of **3d**

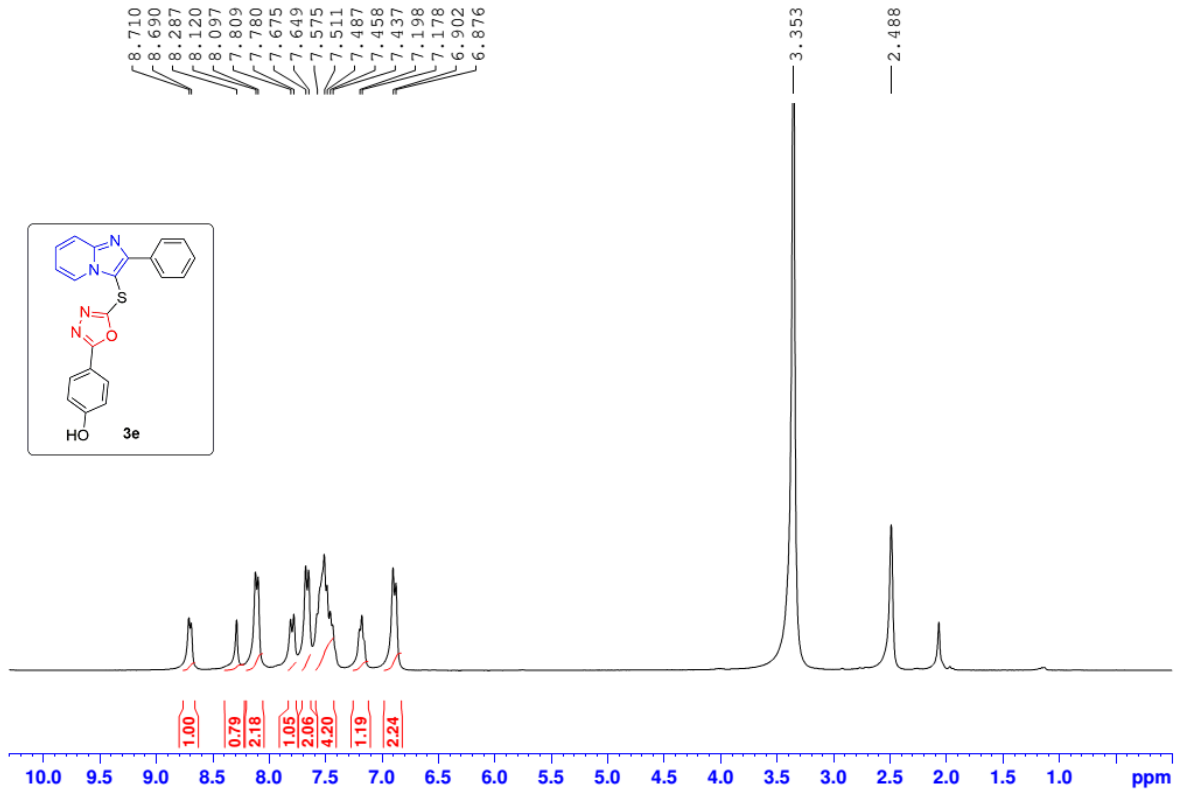


Figure S9. ^{1}H NMR spectrum of **3e**

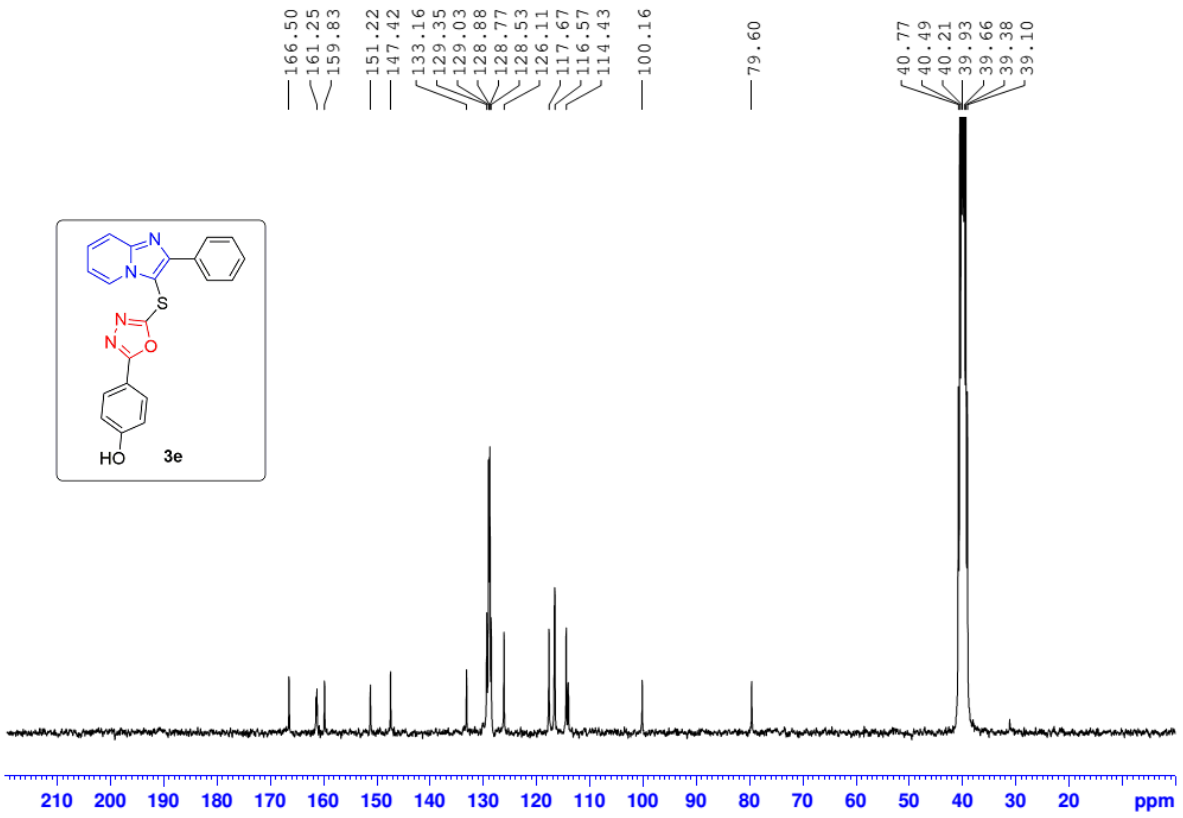


Figure S10. ^{13}C NMR spectrum of **3e**

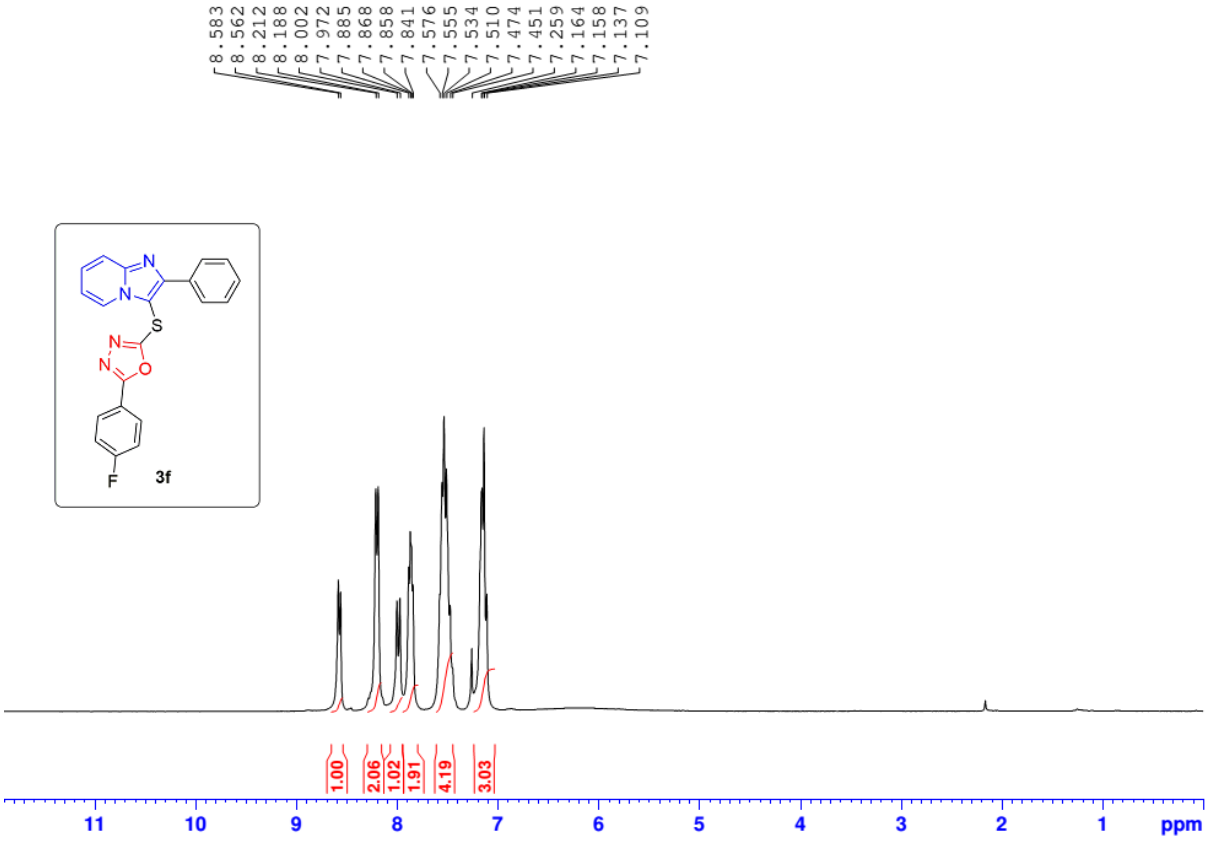


Figure S11. ^{1}H NMR spectrum of **3f**

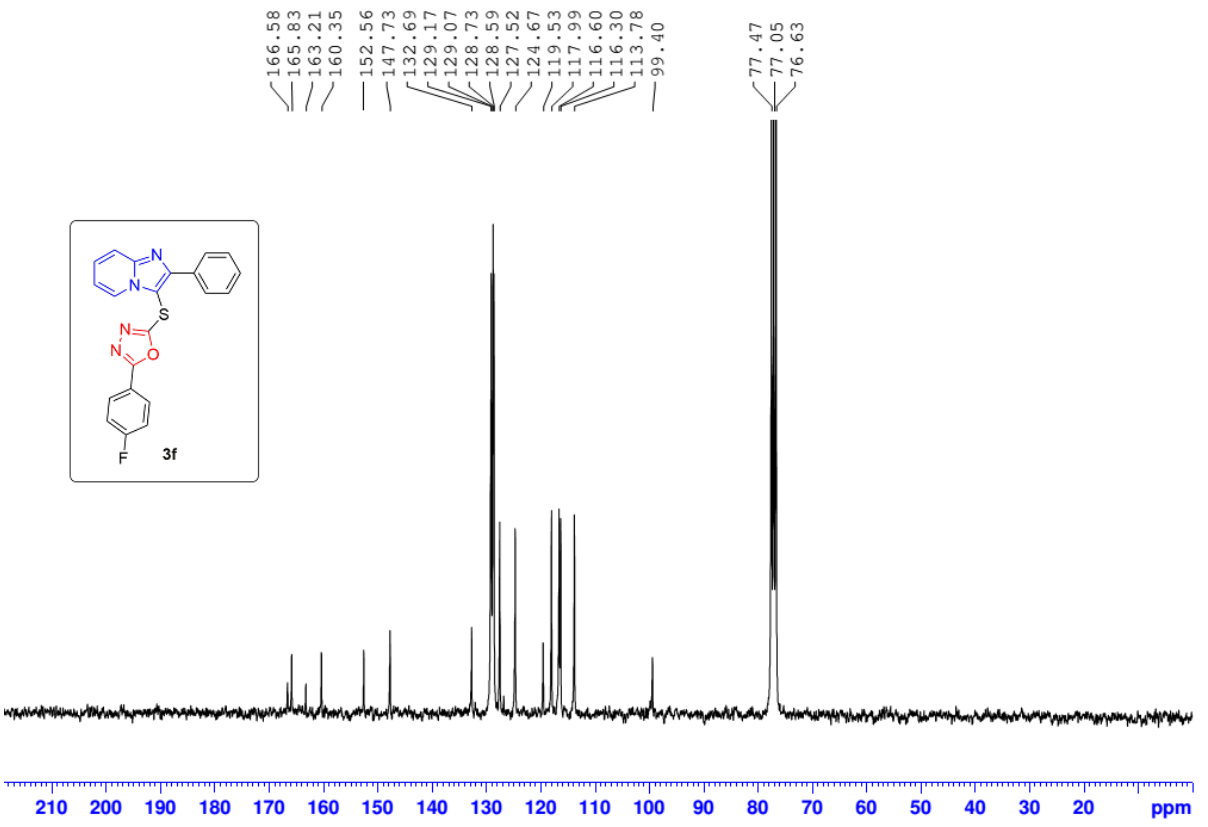


Figure S12. ^{13}C NMR spectrum of **3f**

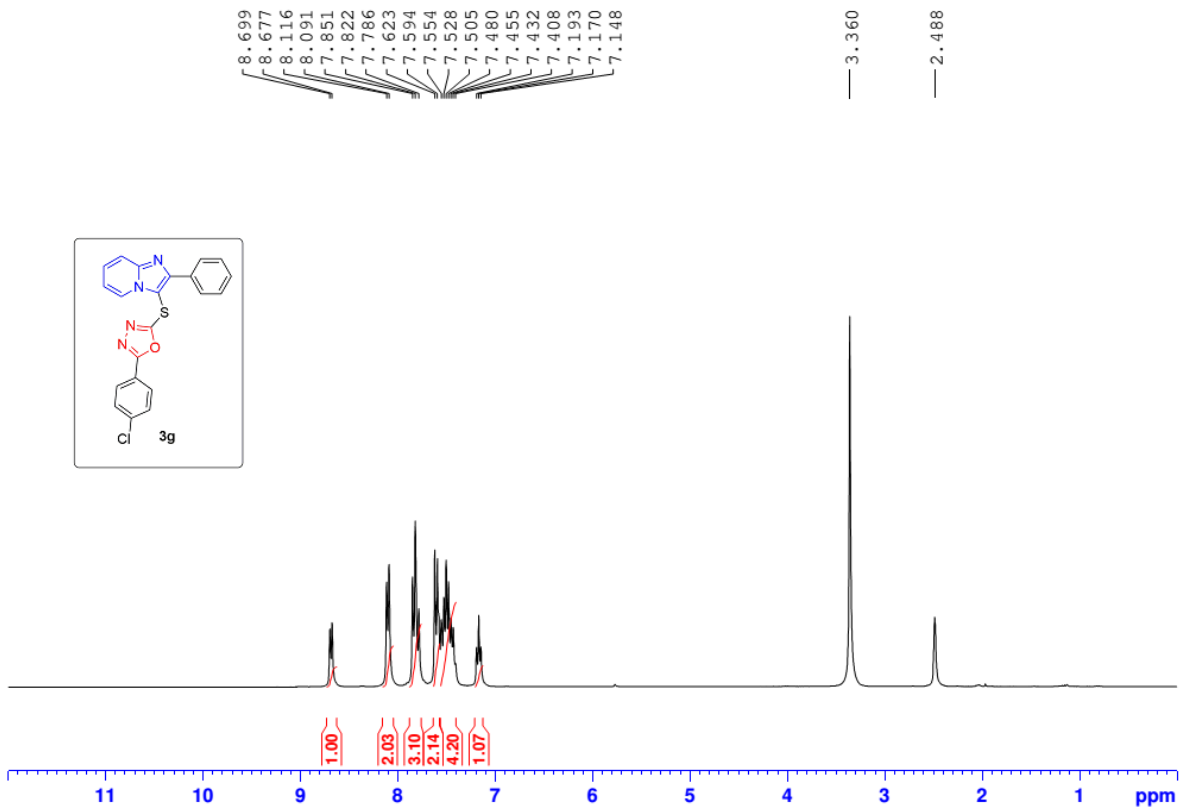


Figure S13. ^{1}H NMR spectrum of **3g**

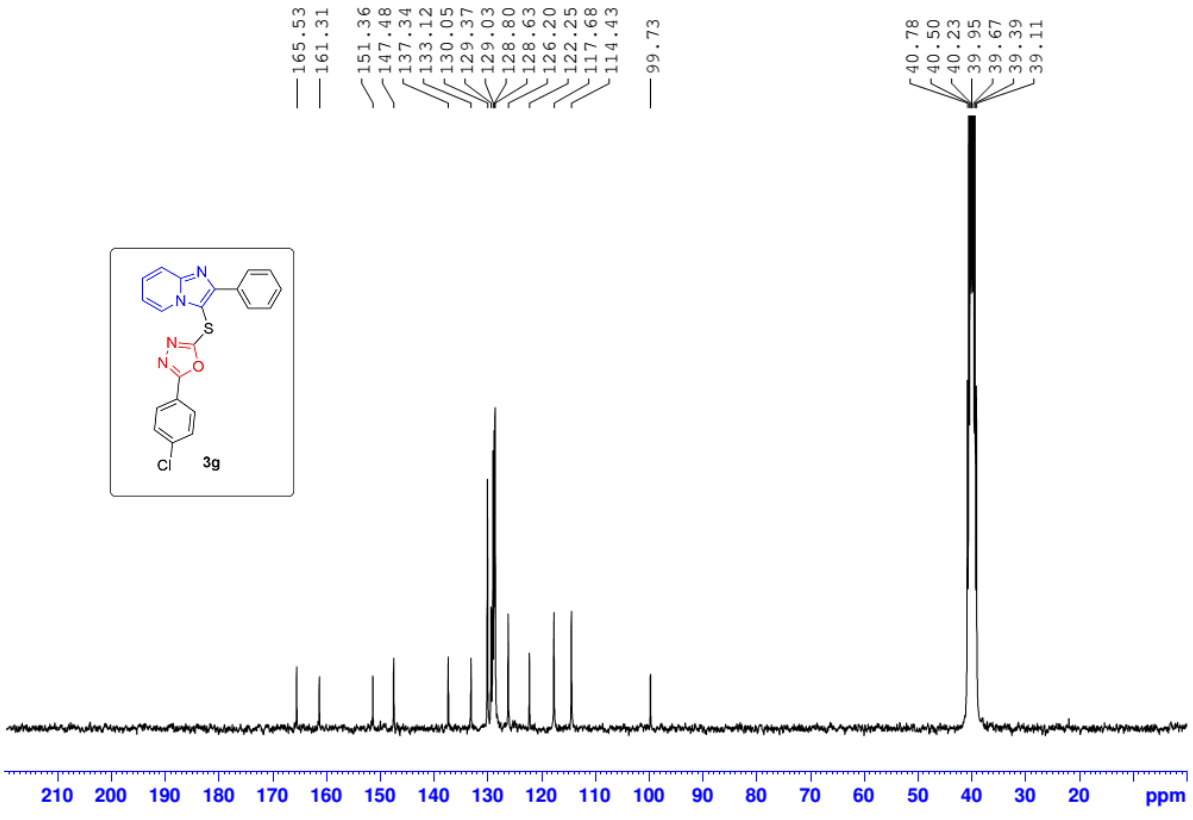


Figure S14. ^{13}C NMR spectrum of **3g**

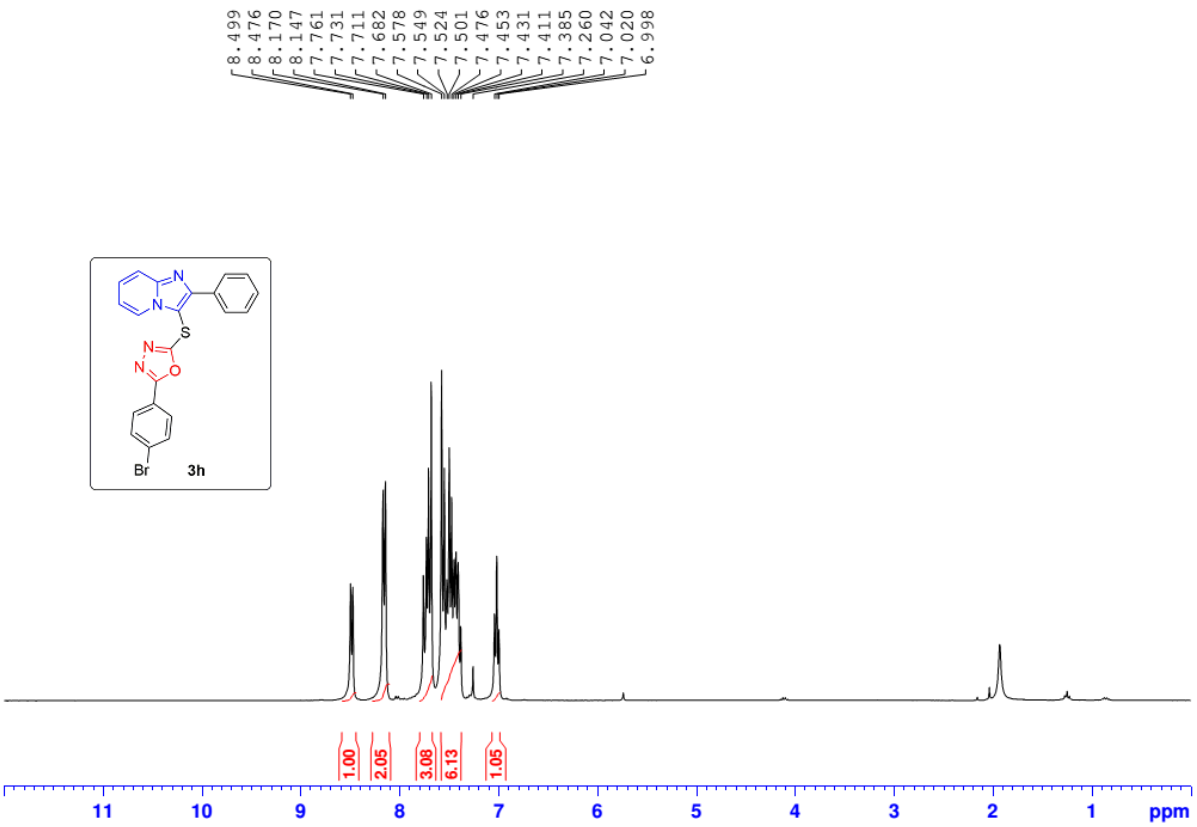


Figure S15. ^{1}H NMR spectrum of **3h**

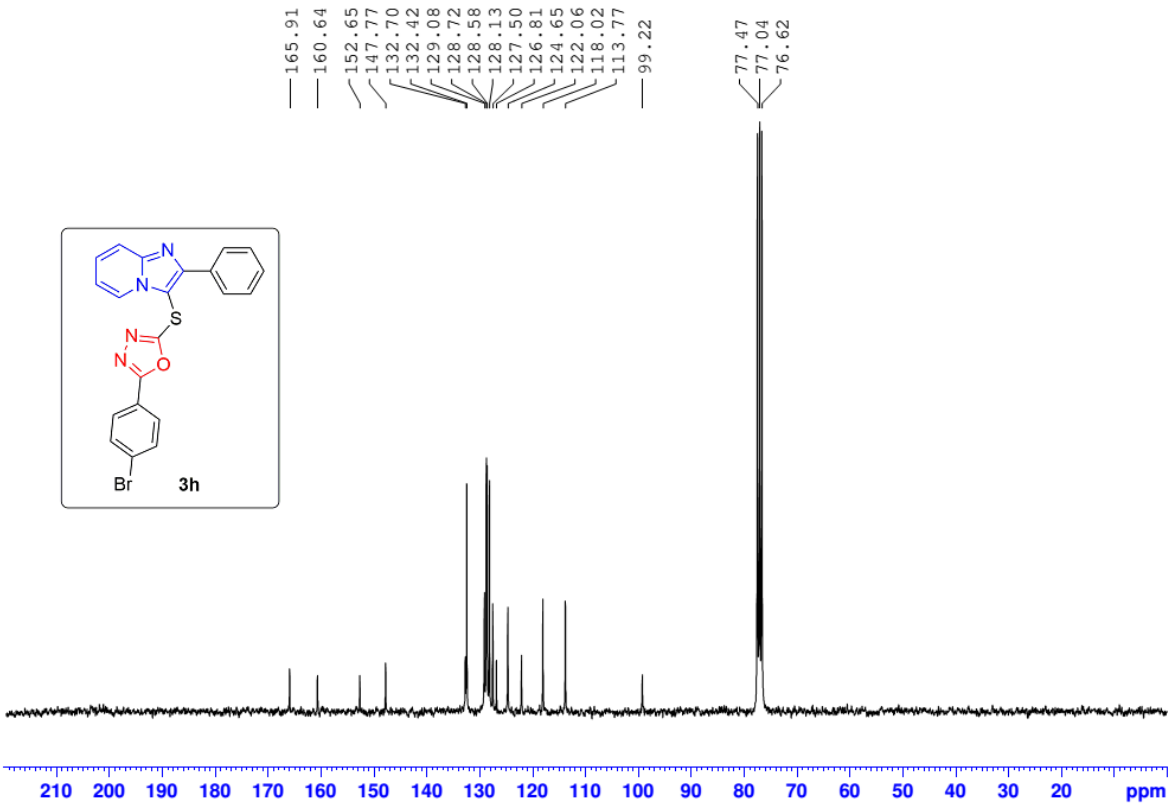


Figure S16. ^{13}C NMR spectrum of **3h**

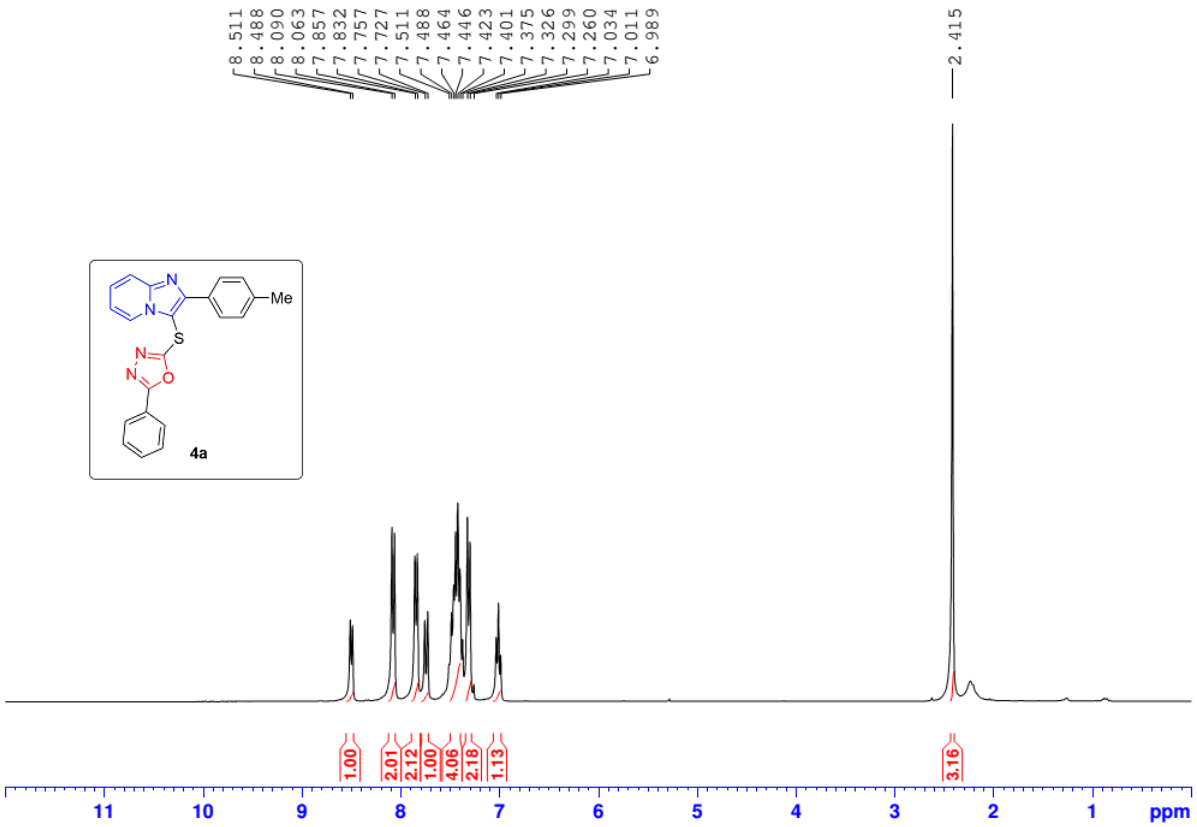


Figure S17. ^{1}H NMR spectrum of **4a**

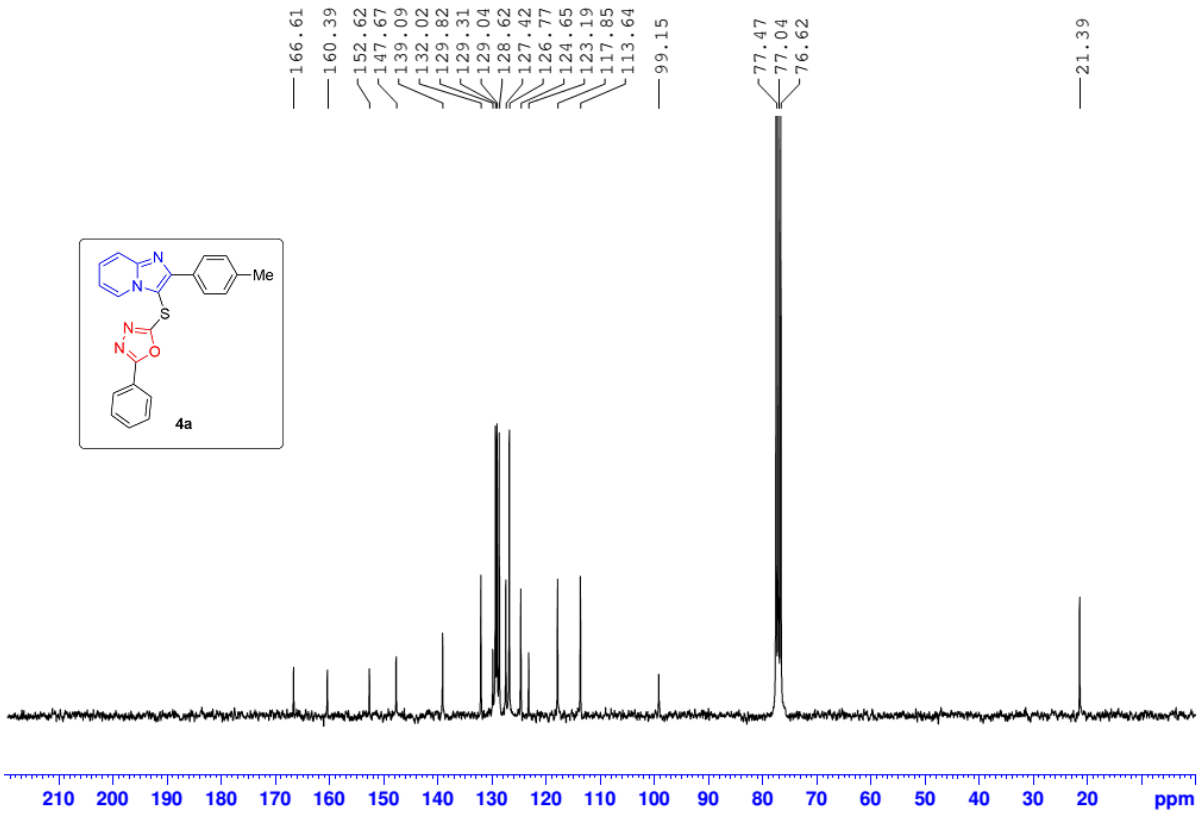


Figure S18. ^{13}C NMR spectrum of **4a**

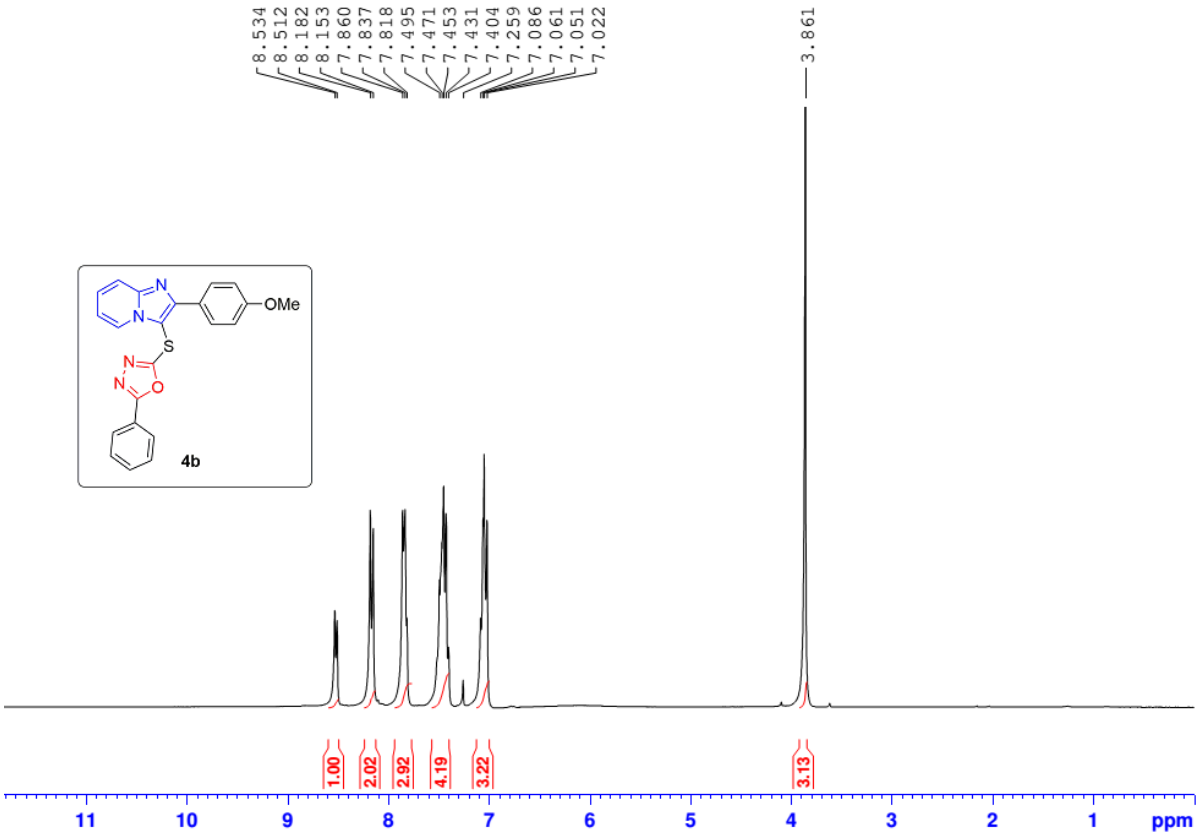


Figure S19. ^{1}H NMR spectrum of **4b**

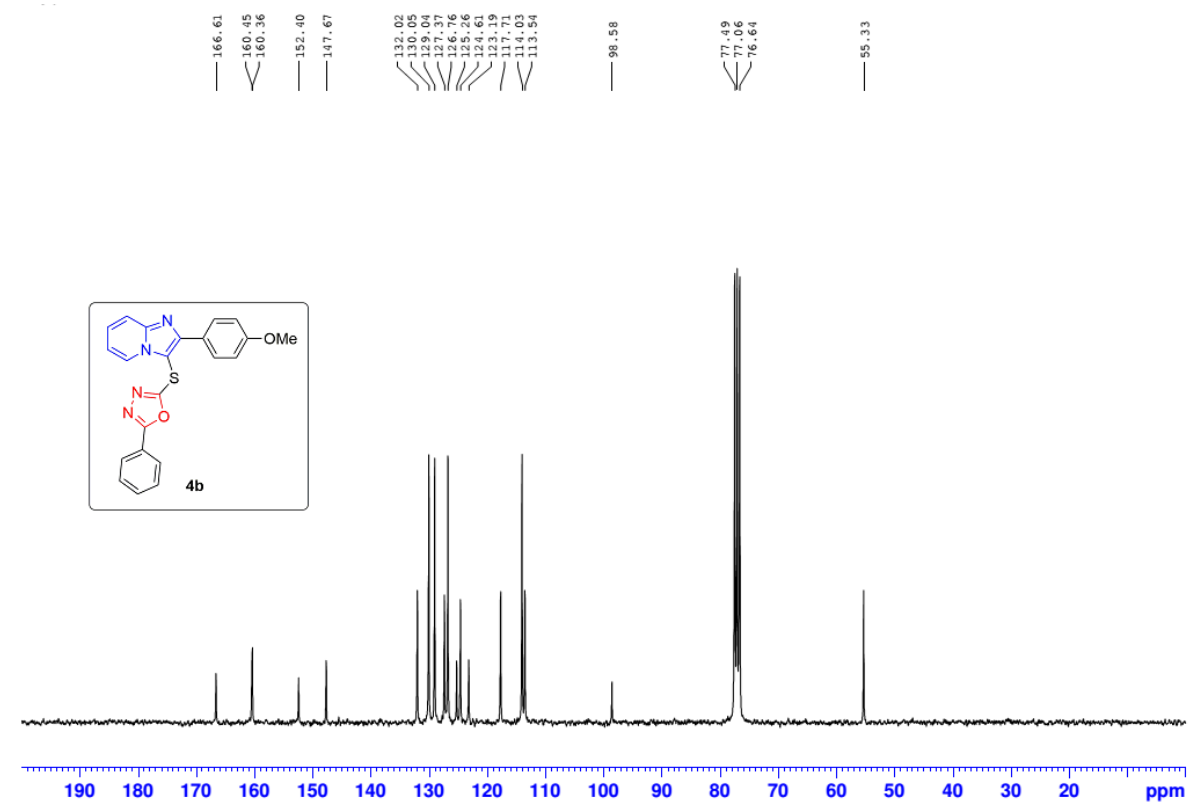


Figure S20. ^{13}C NMR spectrum of **4b**

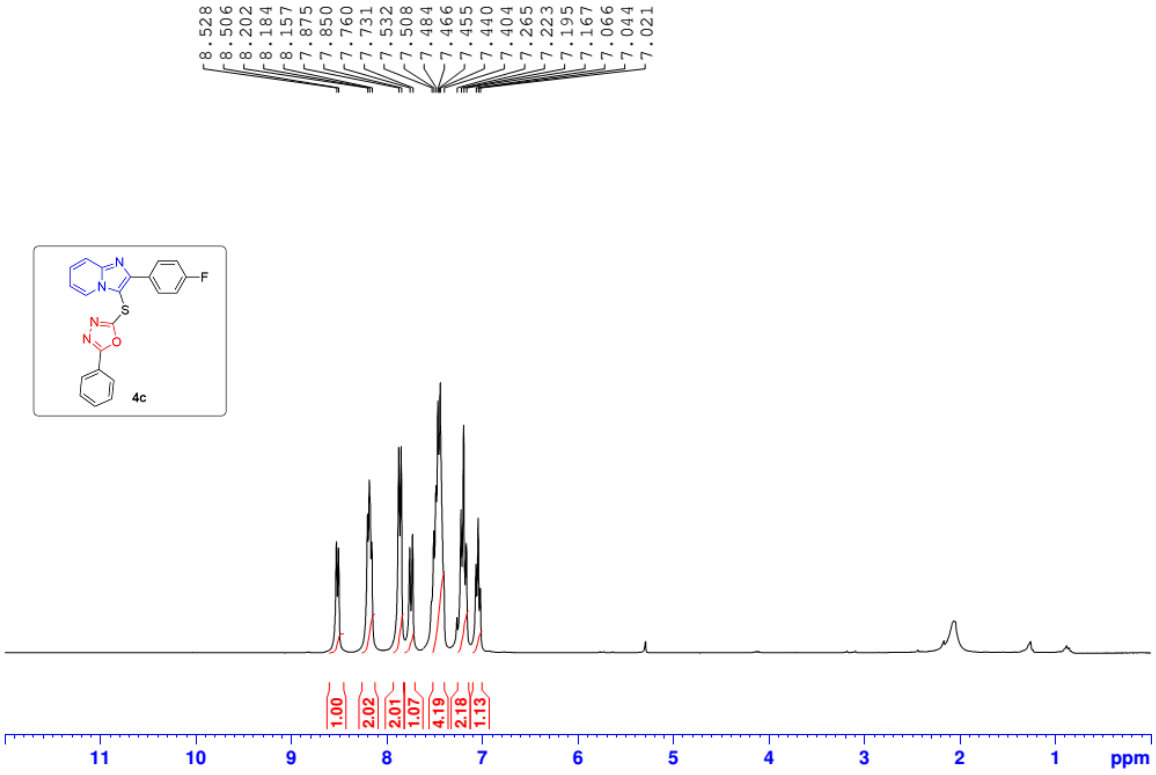


Figure S21. ^{1}H NMR spectrum of **4c**

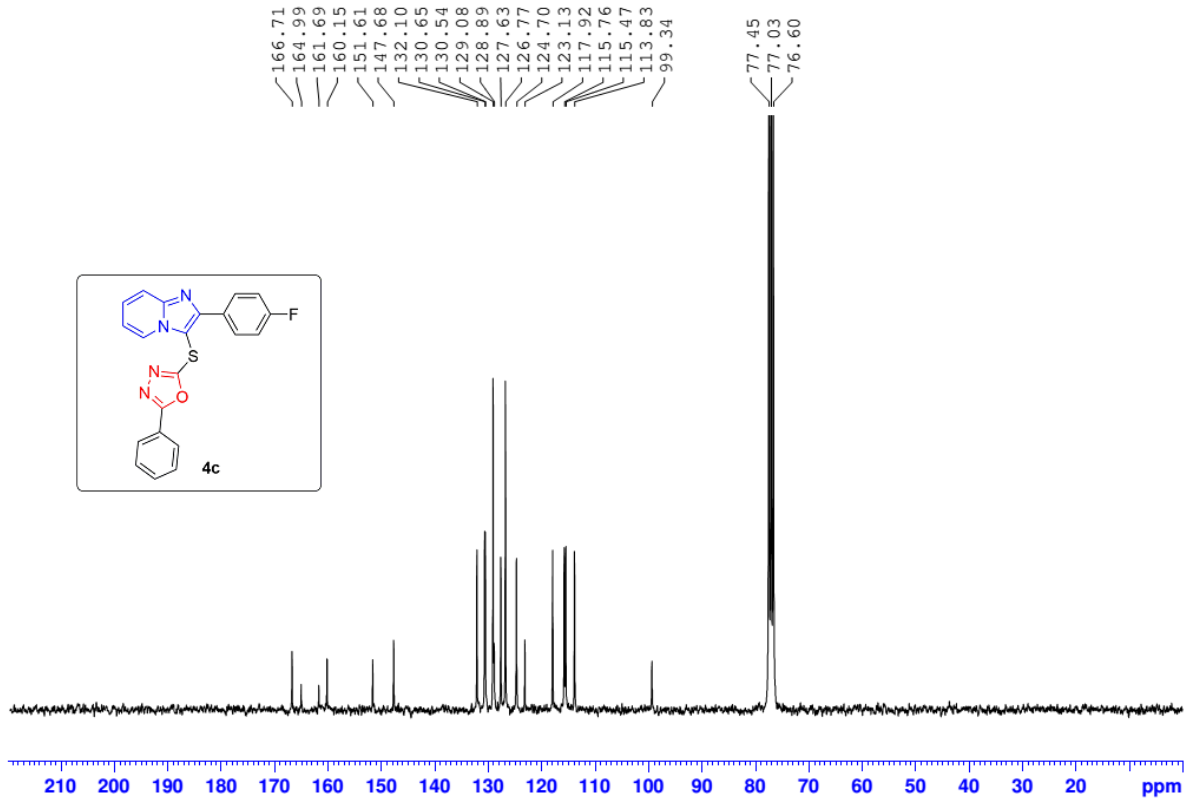


Figure S22. ^{13}C NMR spectrum of **4c**

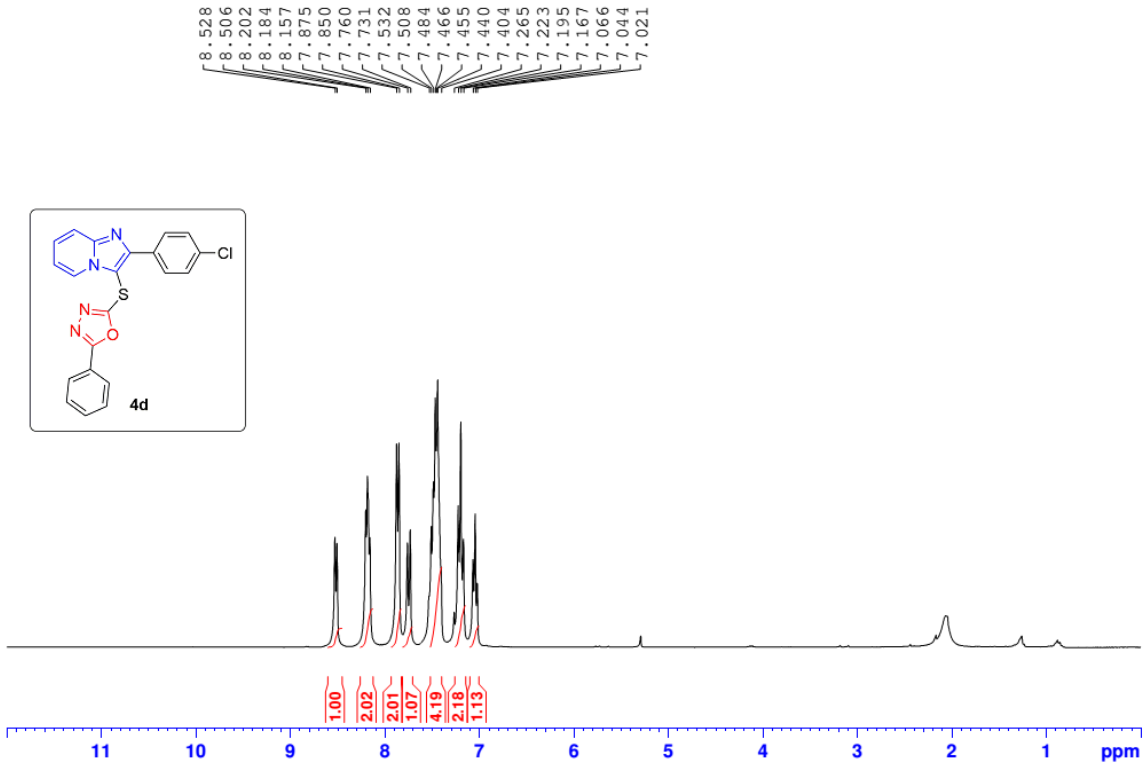


Figure S23. ^{1}H NMR spectrum of **4d**

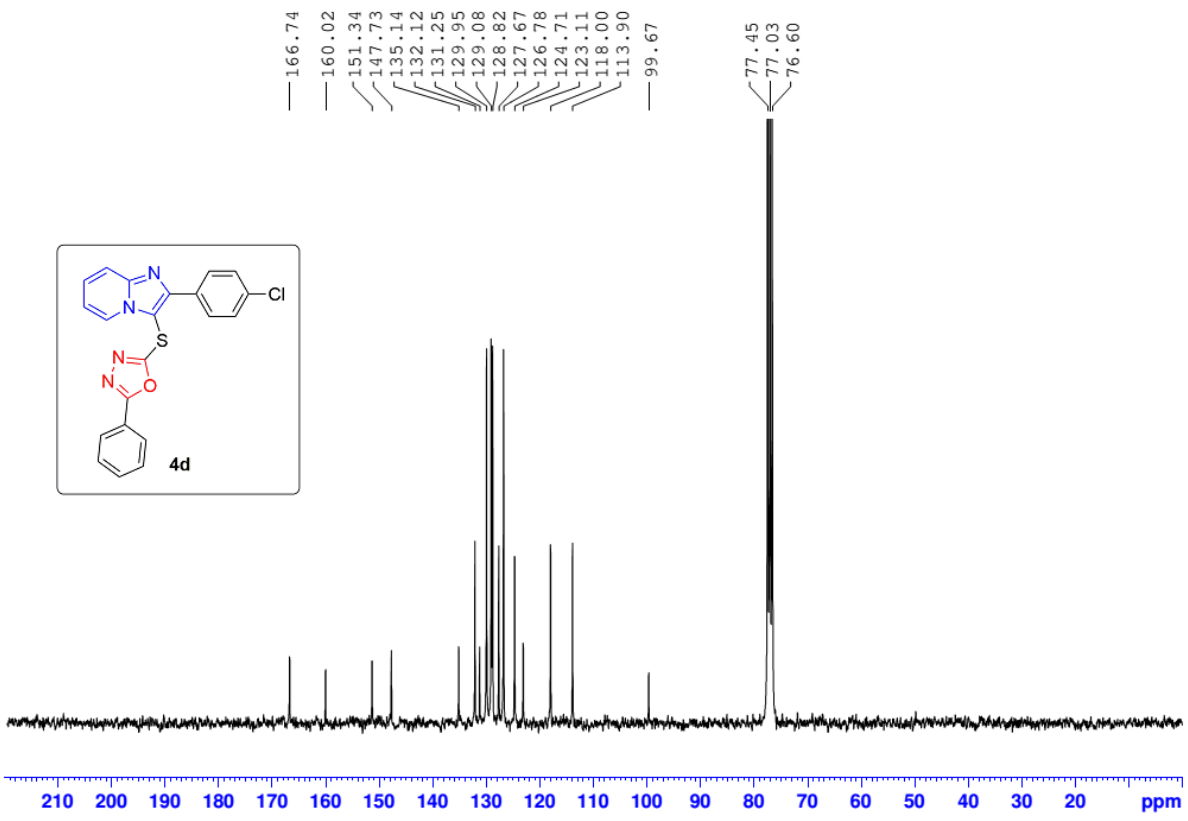


Figure S24. ^{13}C NMR spectrum of **4d**

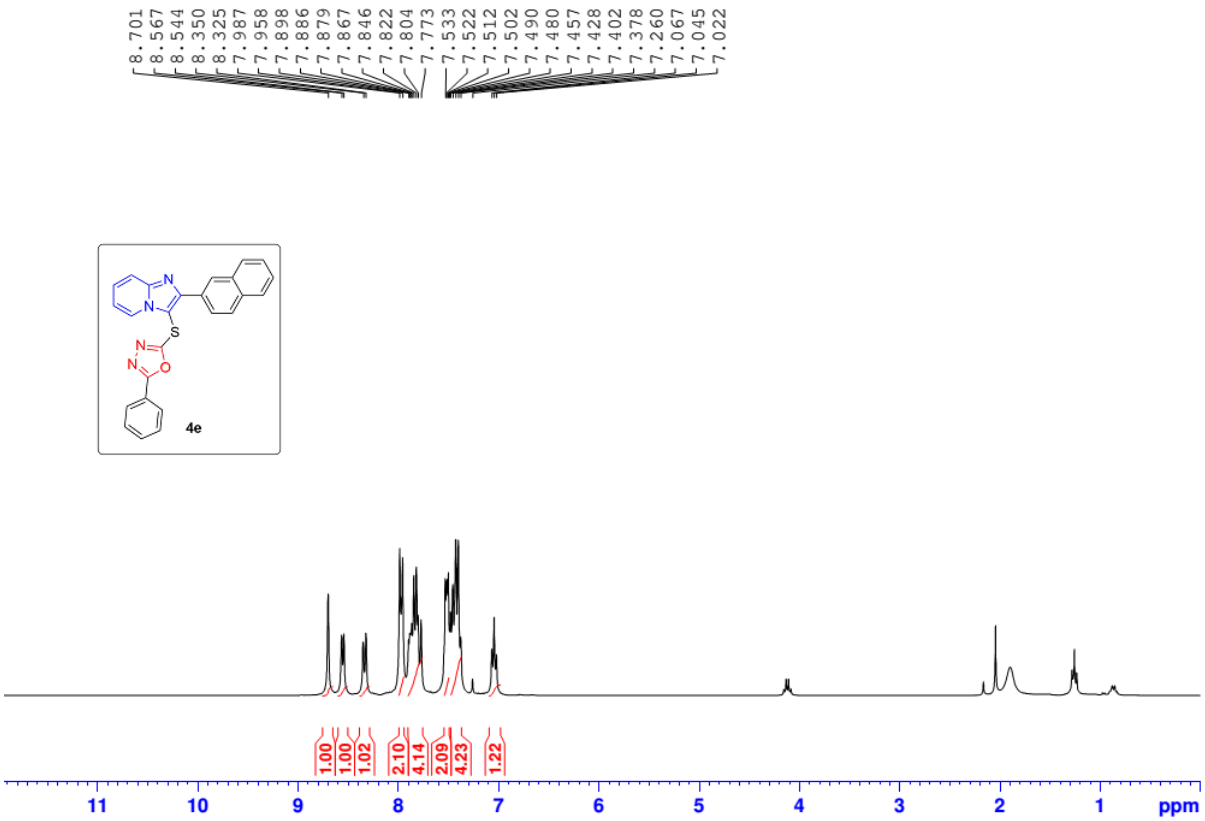


Figure S25. ^{1}H NMR spectrum of **4e**

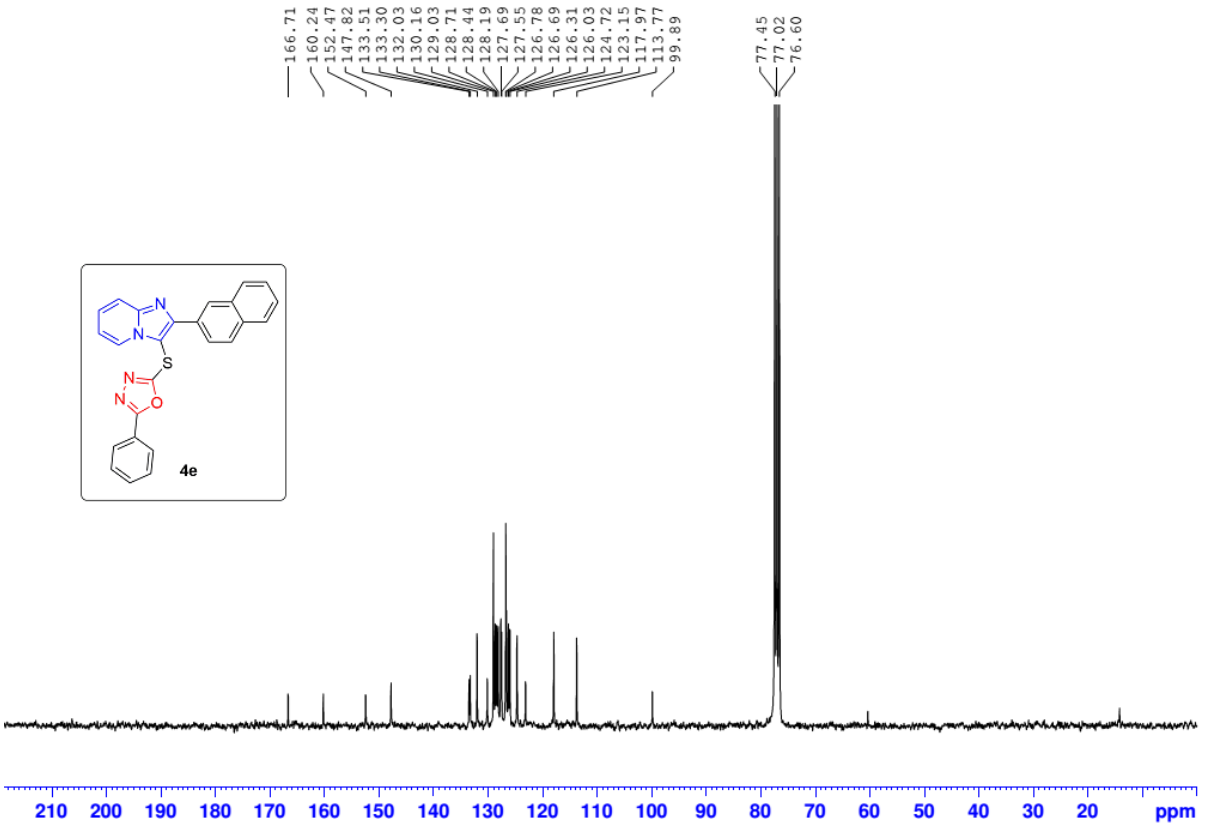


Figure S26. ^{13}C NMR spectrum of **4e**

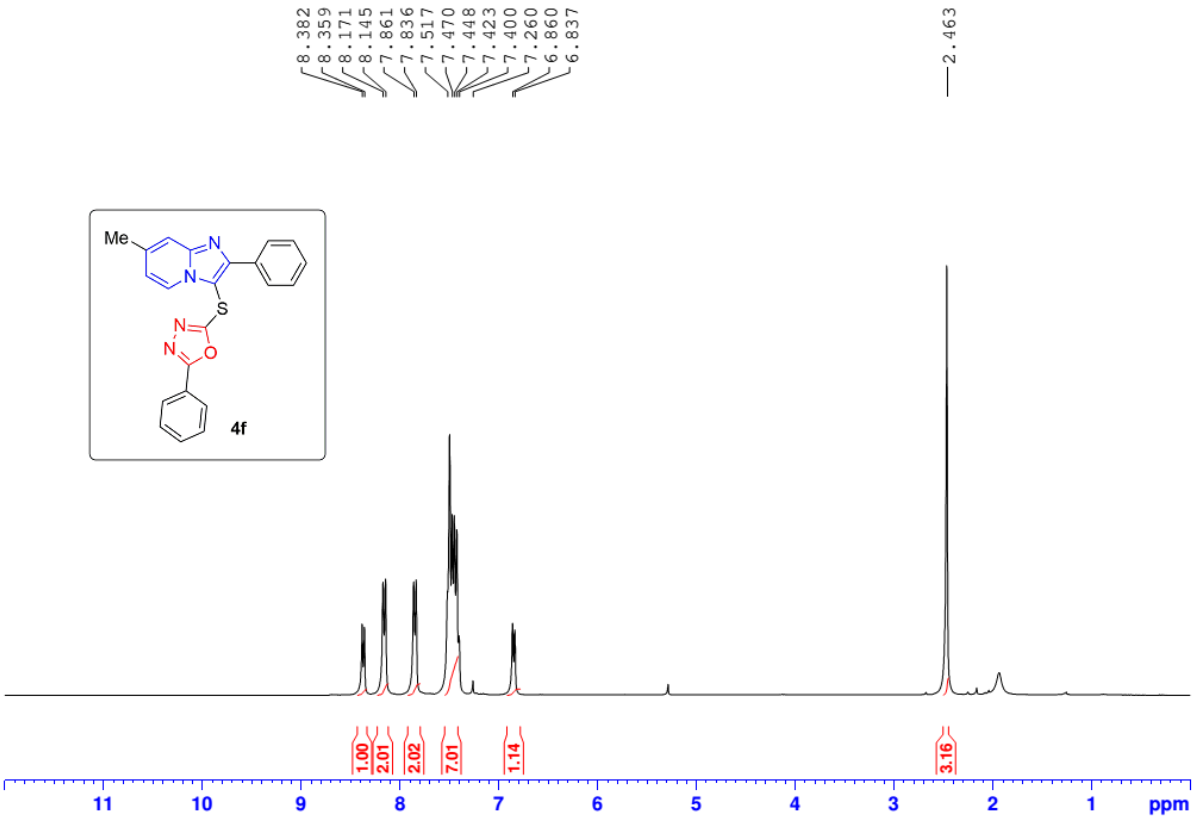


Figure S27. ^{1}H NMR spectrum of **4f**

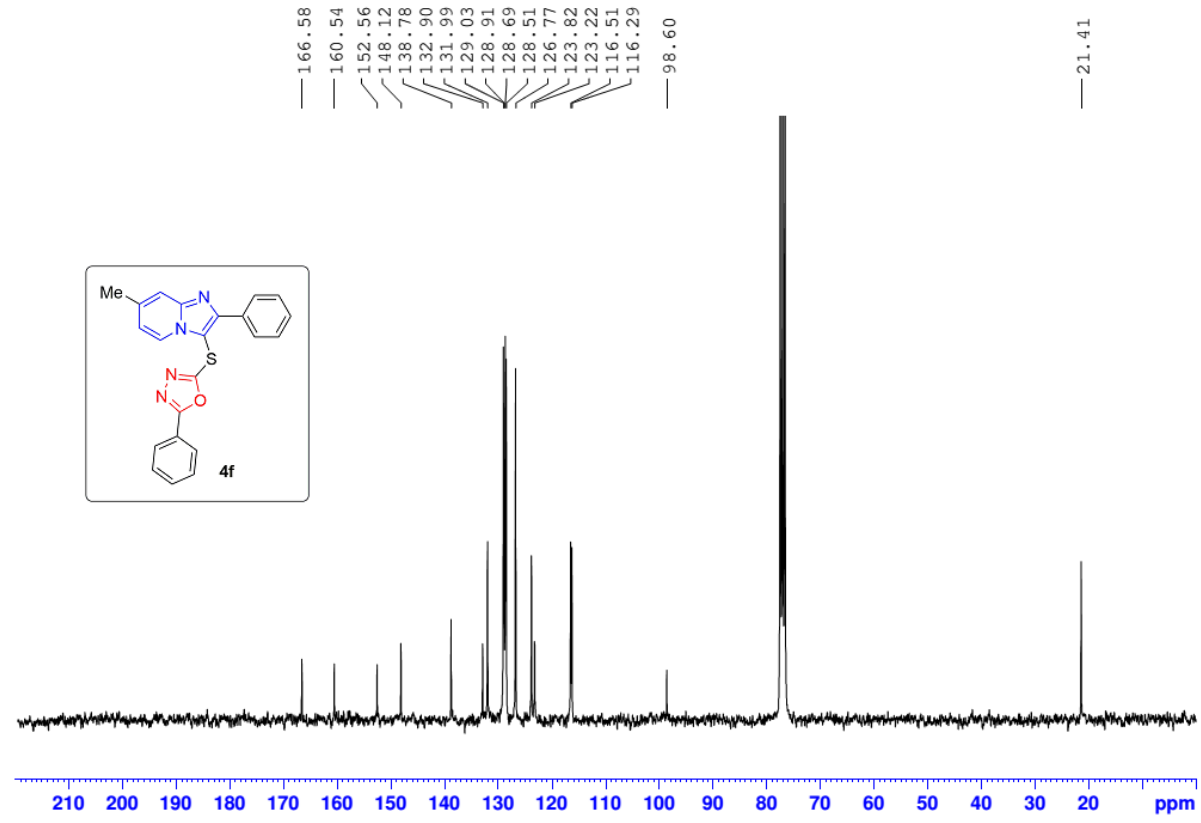


Figure S28. ^{13}C NMR spectrum of **4f**

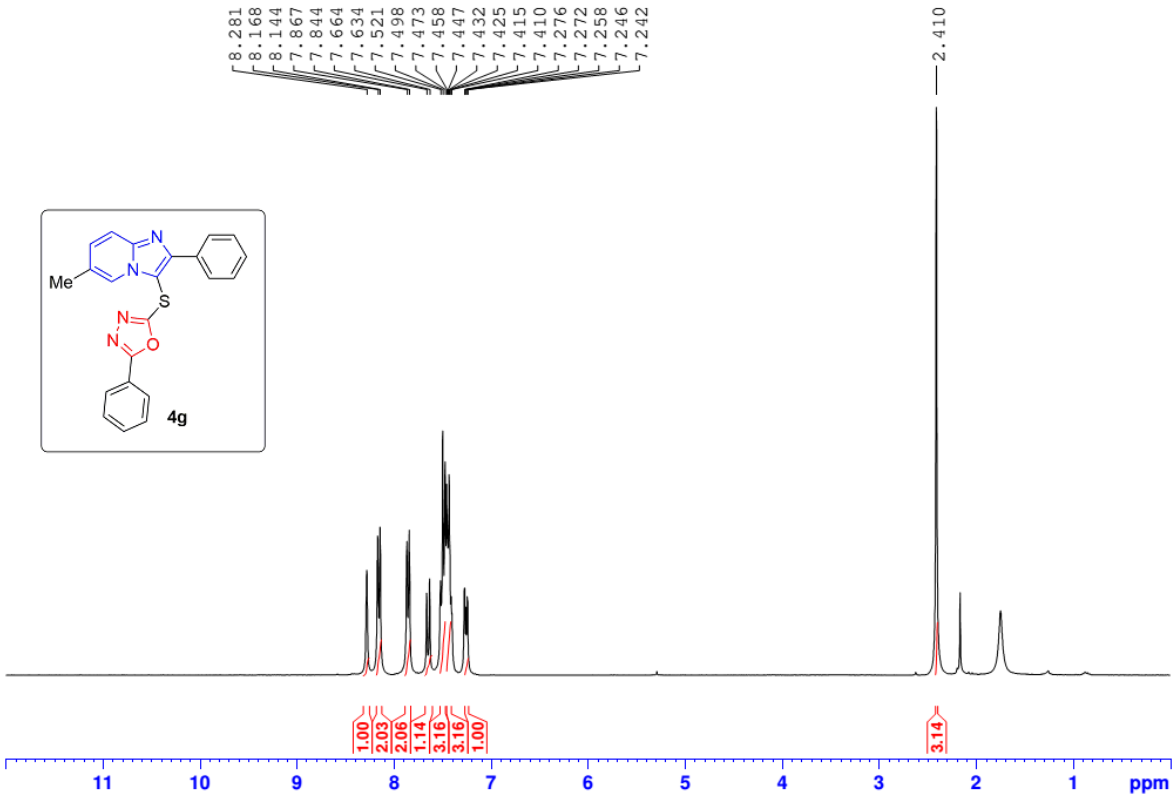


Figure S29. ^{1}H NMR spectrum of **4g**

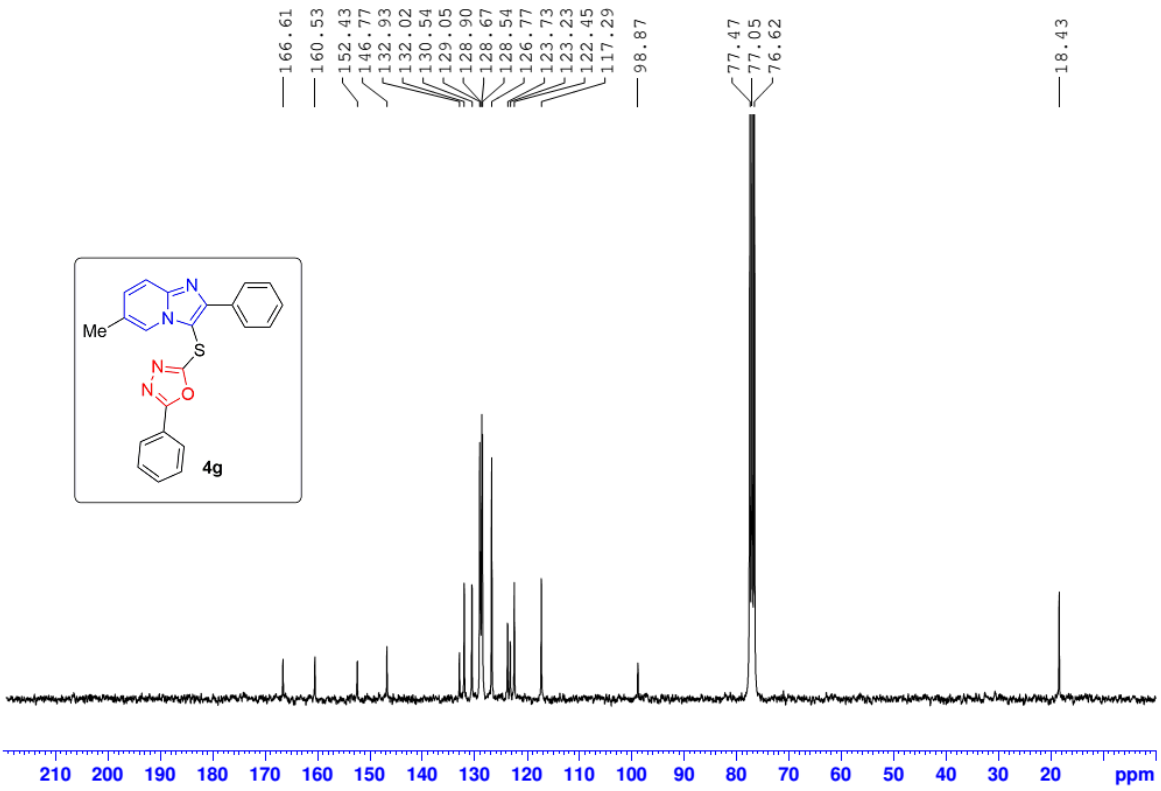


Figure S30. ^{13}C NMR spectrum of **4g**

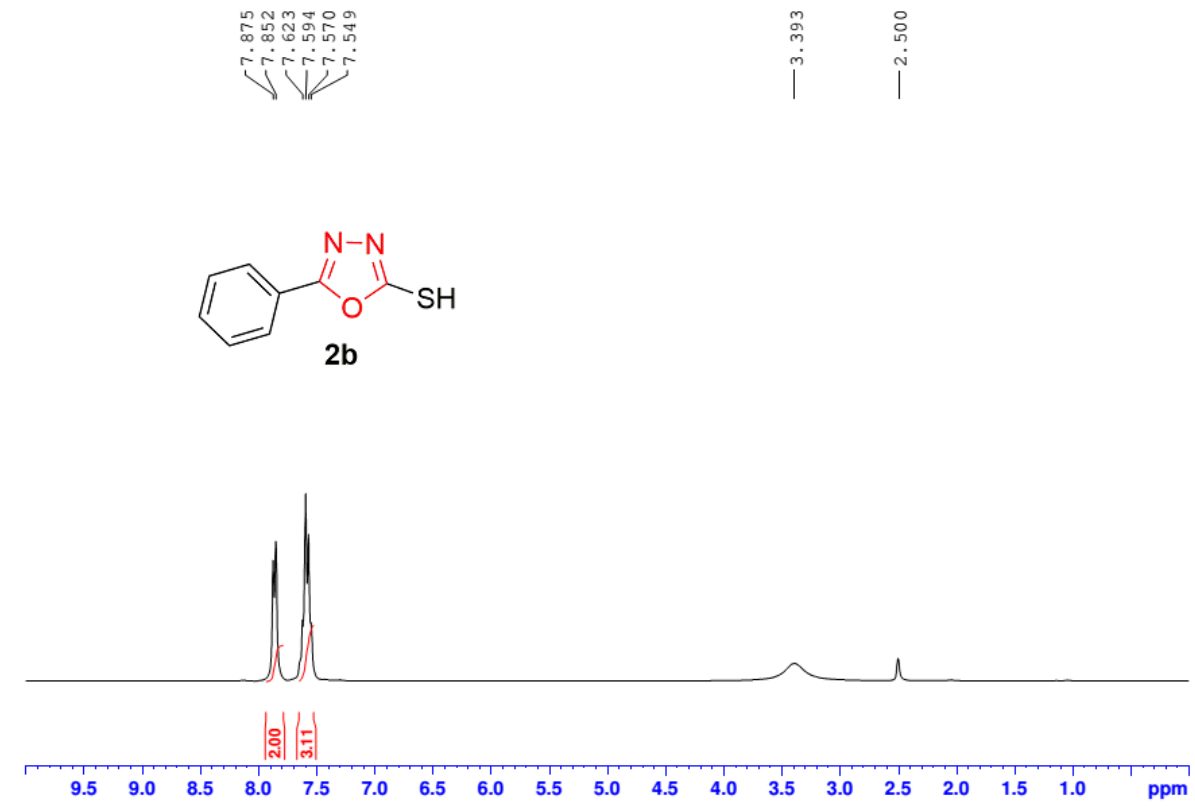


Figure S31. ^{1}H NMR spectrum of **2b**

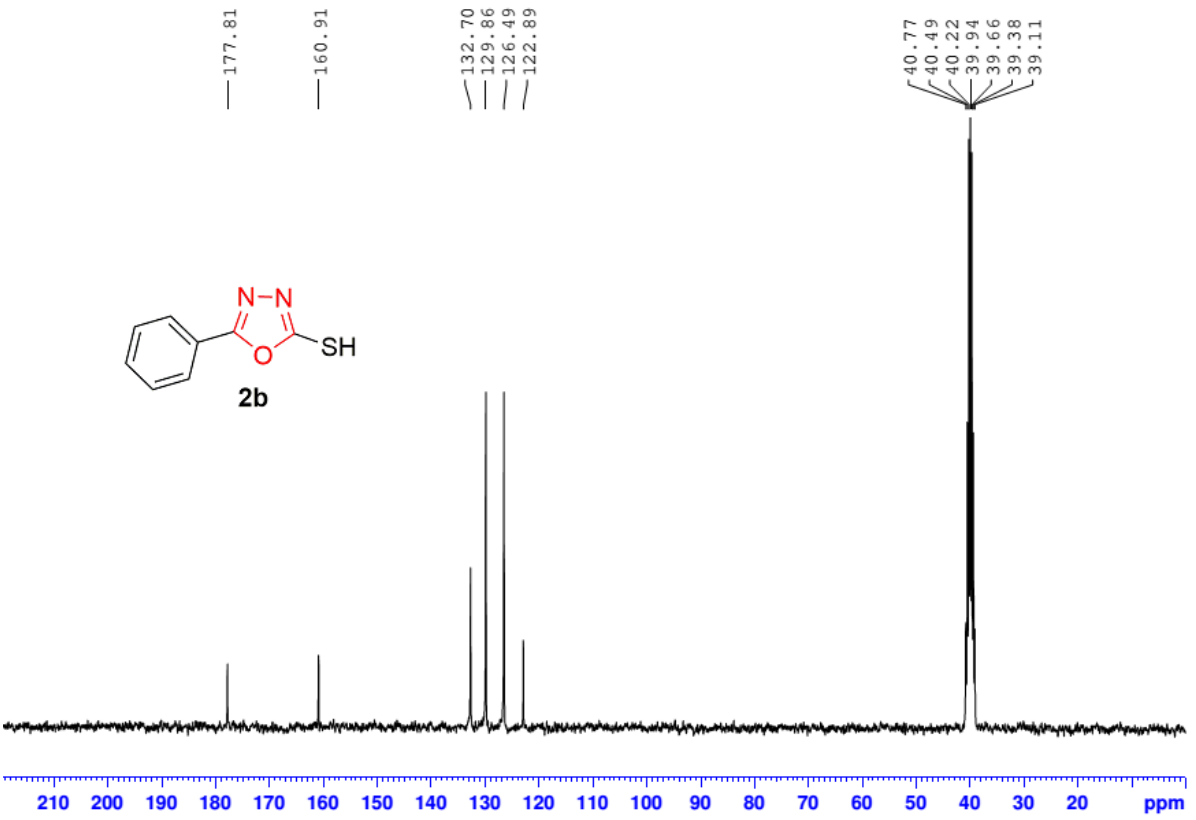


Figure S32. ^{13}C NMR spectrum of **2b**

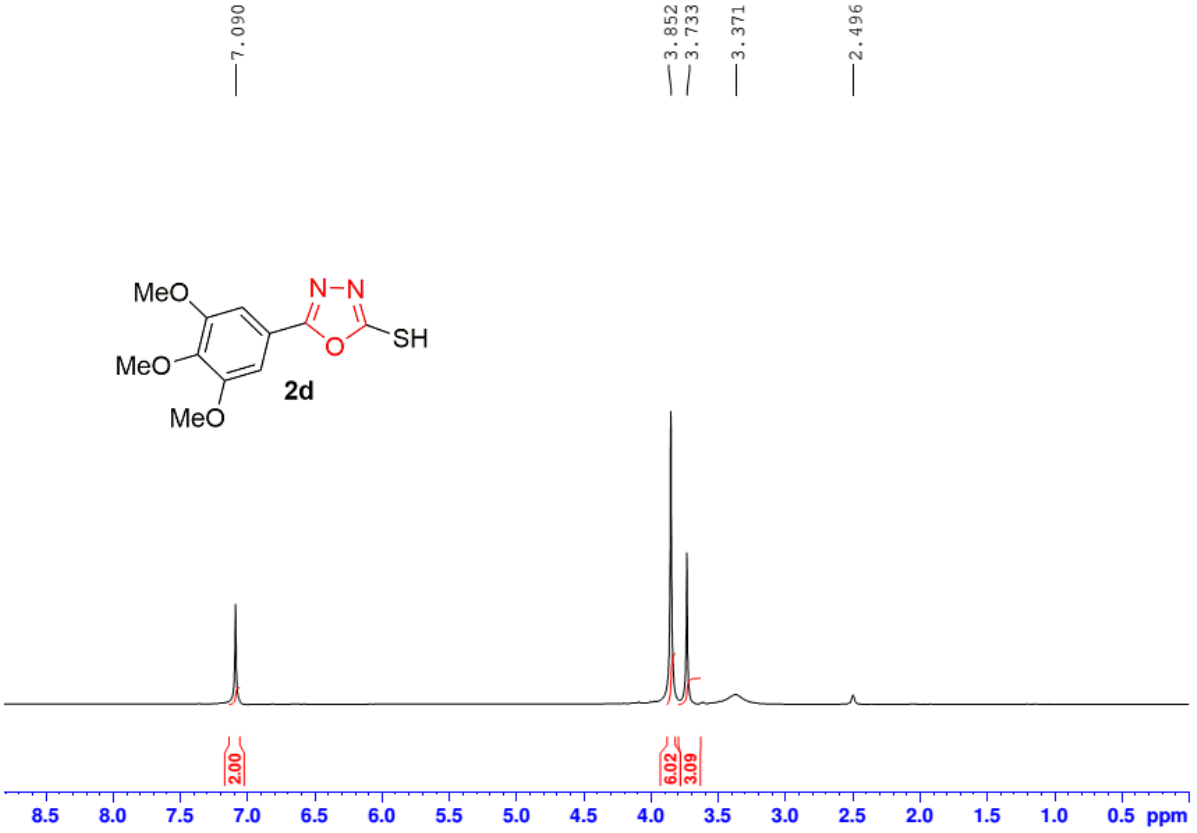


Figure S33. ^{1}H NMR spectrum of **2d**

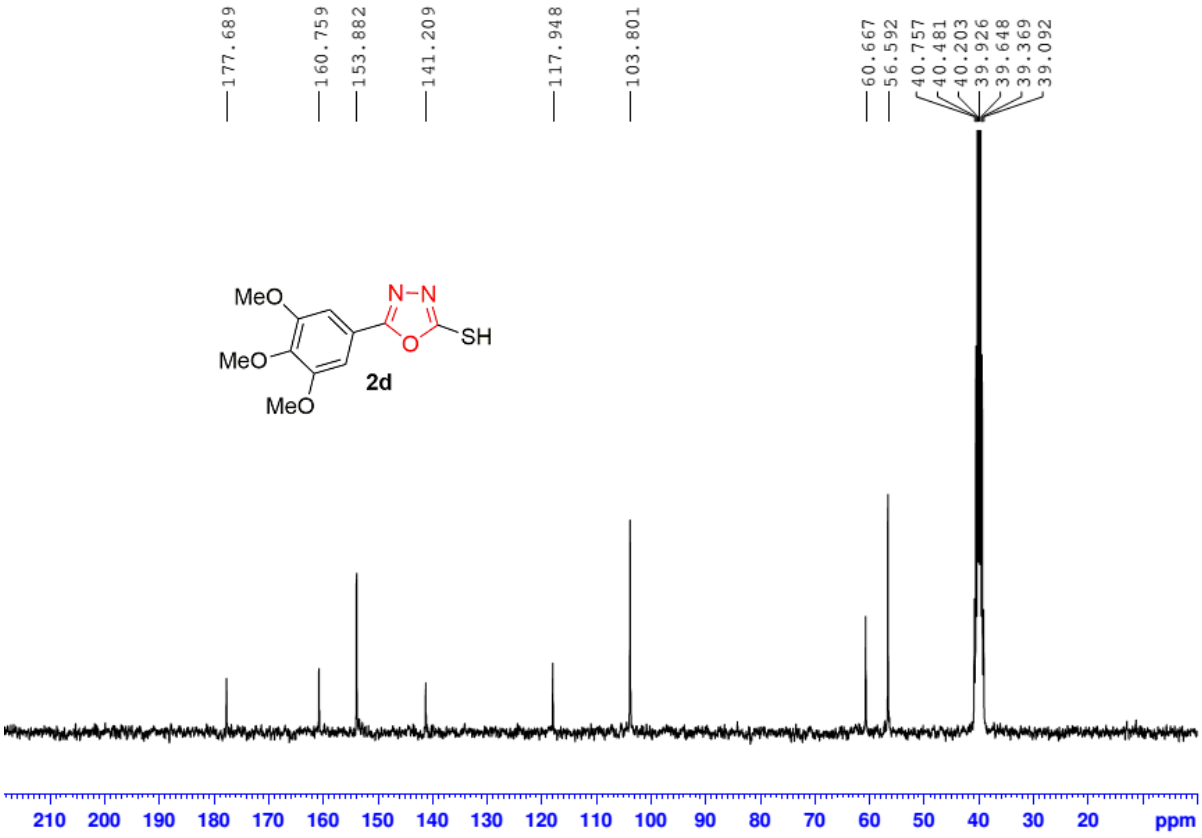


Figure S34. ^{13}C NMR spectrum of **2d**

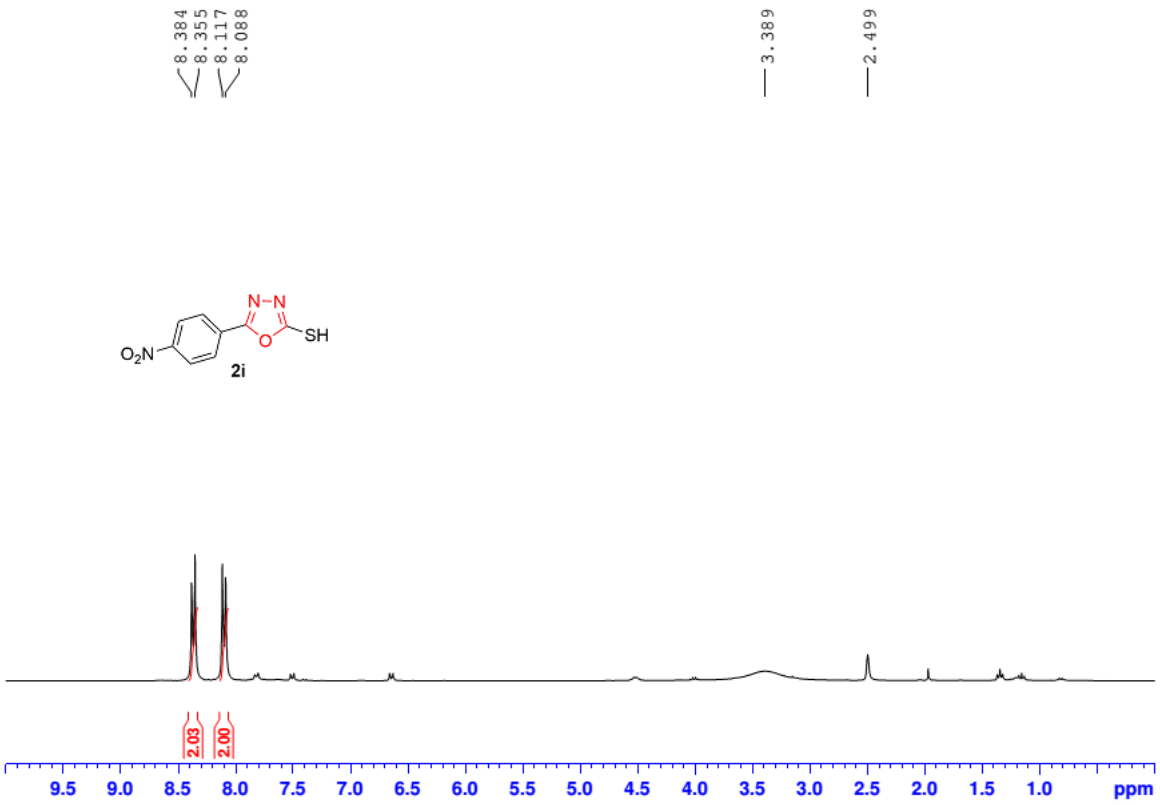


Figure S35. ^{1}H NMR spectrum of **2i**

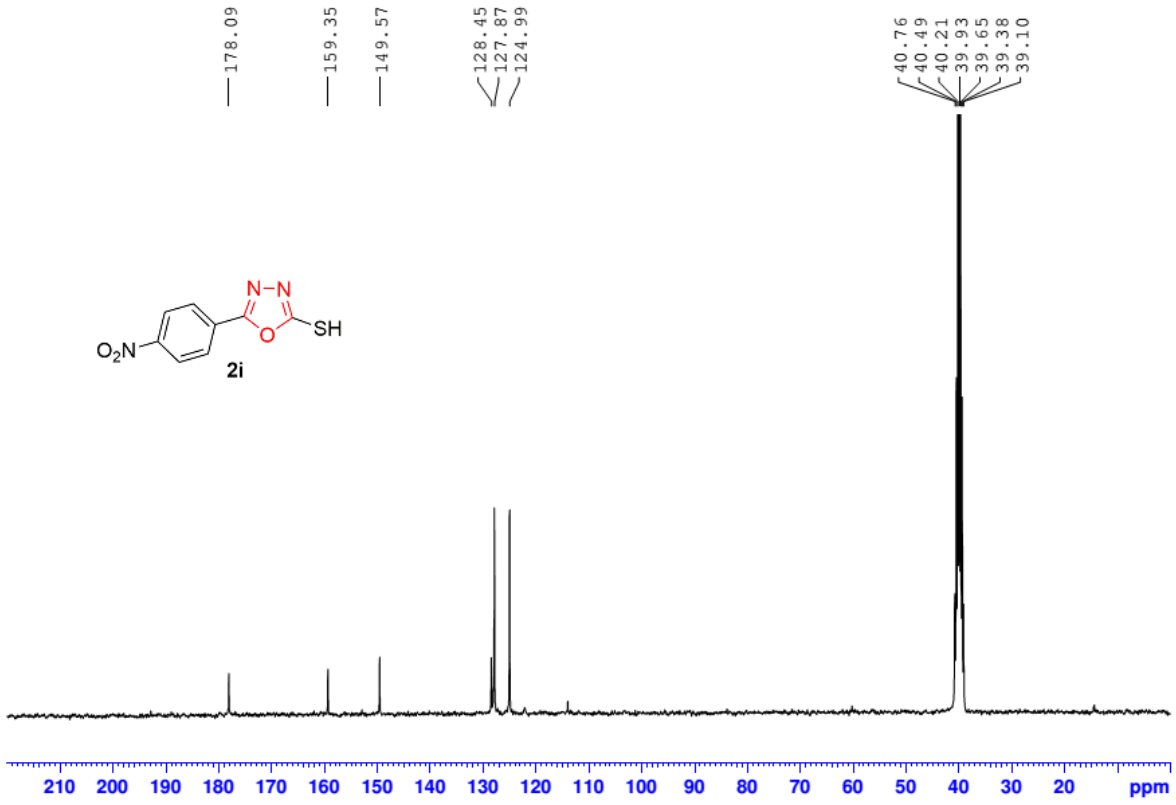


Figure S36. ^{13}C NMR spectrum of **2i**

5. References

1. Santaniello, B. S.; Price, M. J.; Murray, J. K. *J. Chem. Educ.* **2017**, *94*, 388-391. https://doi.org/10.1021/acs.jchemed.6b00286
2. Zhang, Y.; Chen, Z.; Wu, W.; Zhang, Y.; Su, W. *J. Org. Chem.* **2013**, *78*, 12494-12504. https://doi.org/10.1021/jo402134x
3. Okai, H.; Tanimoto, K.; Ohkado, R.; Lida, H. *Org. Lett.* **2020**, *20*, 8002-8006. https://doi.org/10.1021/acs.orglett.0c02929
4. Veer, B.; Singh, R. *Proc. R. Soc.* **475** A: 20190238. http://dx.doi.org/10.1098/rspa.2019.0238
5. Upadhyay, P. K.; Mishra, P. *Pak. J. Pharm. Sci*. **2019**, *32*, 1025-1032 https://scholar.google.co.in/scholar?cluster=7970997639781650167&hl=en&as_sdt=0,5&as_vis=1

