Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting Information

Thin film microfluidic synthesis of fluorescence highly substituted pyridines

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1. General Information:

Unless otherwise stated, all reagents and solvents were purchased from commercial suppliers and used without further purification. UV grade DMSO (Sigma-Aldrich) was used for all fluorescence experiments. ^{1}H NMR spectra were recorded on a Varian spectrometer at 400 MHz and ^{13}C NMR spectra at 100 MHz. Column chromatography was carried out on silica gel and thin layer chromatography was conducted with Silica gel 60 F_{254}. Fluorescence spectra were recorded on a Varian Cary Eclipse fluorescence spectrophotometer. Excitation ranges of 200-450 nm and emission wavelengths of 300-600 nm were used, respectively, with 5 mm slit openings and a scan rate of 600 nm/s. Plots were displayed as excitation on the y-axis and emission on the x-axis. Mass spectra were recorded with a Waters LCT Premier XE spectrometer, using the API method, with MeCN:H_2O (9:1) as a matrix.

The crystal data for **6d** are summarized in Table 1 with the structure depicted in the main text, where ellipsoids have been drawn at the 50% probability level. Crystallographic data for the structure were collected at 100(2) K on an Oxford Diffraction Xcalibur diffractometer fitted with Mo Kα radiation. Following multi-scan absorption corrections and solution by direct methods, the structure was refined against F^2 with full-matrix least-squares using the program SHELXL-97.[1] All Hydrogen atoms were added at calculated positions and refined by use of a riding model with isotropic displacement parameters based on those of the parent atom. Anisotropic displacement parameters were employed for the non-hydrogen atoms. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 972818. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

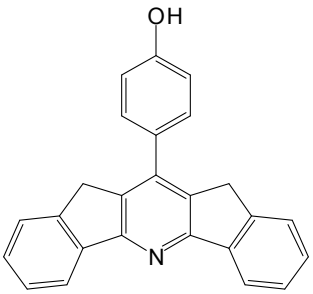
2. Typical procedure for preparation of polysubstituted pyridines (3a-e):

A mixture of 1-indanone **1** (1 mmol), aldehyde **2a-e** (0.5 mmol) and ammonium acetate (2 mmol) in 1 mL PEG300, was stirred for ≤ 1 minute at 80°C in a round bottom flask until all the reagents dissolved. The mixture was immediately placed in a glass tube and treated under confined mode in the VFD at 100°C, 7000 rpm and 45° tilt angle for 30 minutes. After cooling, the reaction mixture was diluted with water (25 mL) and the resulting precipitate was collected by filtration. The solid product was washed with water and EtOH and subsequently dried and then recrystallized from EtOH.

3. Typical procedure for preparation of 2,4,6-triarylpyridines (6a-e):

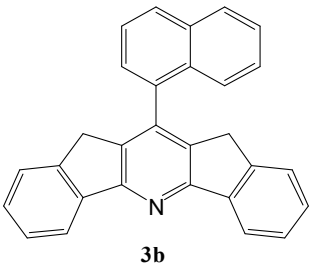
In a 25 mL round bottom flask, 4-(dimethylamino)benzaldehyde **4** (0.5 mmol), acetophenone **5a-e** (1 mmol), and ammonium acetate (2 mmol) was stirred in PEG300 (1.0 mL) at 80°C. When all the reactants dissolved, which takes ≤ 1 minute, the solution was immediately transferred to a glass tube and treated under confined mode in the VFD at 100°C, 7000 rpm and 45° tilt angle for 30 minutes. After this time the mixture was cooled to room temperature. The reaction was then quenched with H_2O (15 mL) and extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and then evaporated *in vacuo*. The residue was purified by column chromatography on silica gel to afford the corresponding pyridines **6a-e**.

4. NMR spectroscopic data for compounds



3a

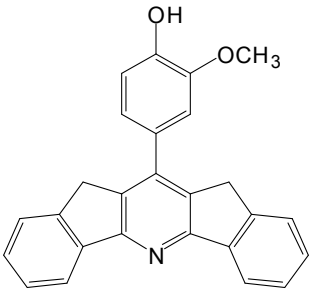
3a: ^{1}H NMR (DMSO-d_6) δ 9.77 (s, 1H), 8.09 (d, 2H, *J* = 7.4 Hz), 7.62 (d, 4H, *J* = 8.5 Hz), 7.52-7.40 (m, 4H), 6.96 (d, 2H, *J* = 8.5 Hz), 3.95 (s, 4H). ^{13}C NMR (DMSO-d_6) δ 159.7, 158.1 144.7, 143.4, 141.2, 133.8, 130.5, 128.7, 127.5, 127.4, 125.8, 120.7, 115.9, 34.3. HR-MS *m*/*z* 348.1399 $(M+H)^+$ requires 348.1388.



3b

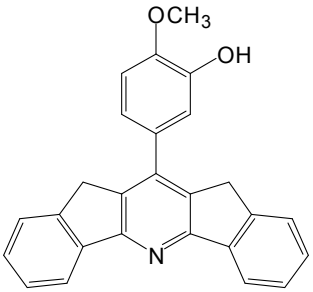
3b: ^{1}H NMR (DMSO-d_6) δ 8.39 (s, 1H), 8.14 (t, 3H, *J* = 7.8 Hz), 8.06 (q, 2H, *J* = 5.4 Hz), 7.93 (d, 1H, *J* = 8.5 Hz), 7.63 (t, 4H, *J* = 7.7 Hz), 7.52 (t, 2H, *J* = 7.4 Hz), 7.46 (t, 2H, *J* = 7.2 Hz), 4.03 (s, 4H). ^{13}C NMR (DMSO-d_6) δ 159.8, 144.7, 143.4, 141.0, 134.4, 134.0, 133.5,

133.1, 128.9, 128.8, 128.7, 128.3, 128.1, 127.6, 126.8, 125.9, 120.8, 34.2. HR-MS *m/z* 382.1586 $(M+H)^+$ requires 382.1596.



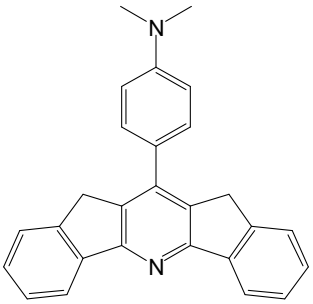
3c

3c: ^{1}H NMR and ^{13}C NMR spectroscopic data were consistent with the literature.[2]



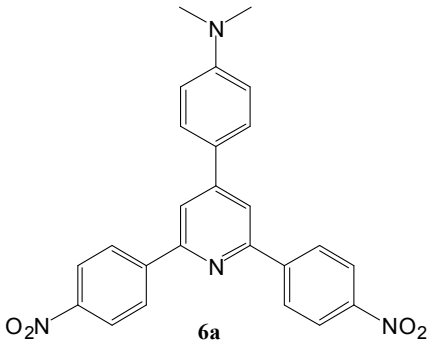
3d

3d: ^{1}H NMR (DMSO-d_6) δ 9.22 (s, 1H), 8.10 (d, 2H, *J* = 7.2 Hz), 7.63 (d, 2H, *J* = 7.2 Hz), 7.52-7.40 (m, 5H), 7.17 (s, 1H), 7.10 (d, 1H, *J* = 7.9 Hz), 3.94 (s, 4H), 3.88 (s, 3H). ^{13}C NMR (DMSO-d_6) δ 159.7, 148.3, 147.0, 144.6, 143.4, 141.2, 133.7, 129.4, 128.7, 127.5, 125.9, 120.7, 120.2, 116.2, 112.8, 56.1, 34.3. HR-MS *m/z* 378.1489 $(M+H)^+$ requires 378.1494.



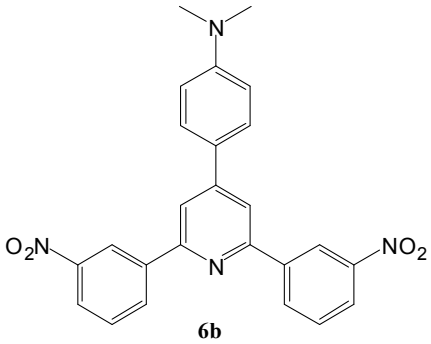
3e

3e: ^{1}H NMR (DMSO-d_6) δ 8.06 (d, 2H, *J* = 7.4 Hz), 7.61 (t, 4H, *J* = 8.9 Hz), 7.50-7.37 (m, 4H), 6.86 (d, 2H, *J* = 8.8 Hz), 3.96 (s, 4H), 2.98 (s, 6H). ^{13}C NMR (DMSO-d_6) δ 159.7, 151.2, 144.7, 143.6, 141.3, 133.6, 130.0, 128.6, 127.5, 125.8, 124.0, 120.7, 112.5, 34.5, 18.2. HR-MS *m/z* 413.1420 $(M+K)^+$ requires 413.1420.



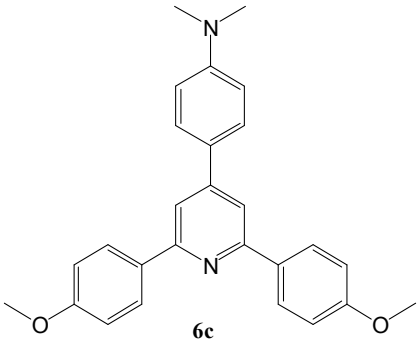
6a

6a: ^{1}H NMR and ^{13}C NMR spectroscopic data were consistent with the literature.[3]



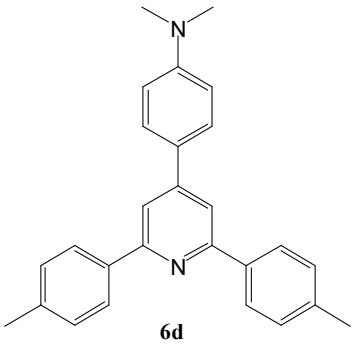
6b

6b: ^{1}H NMR (DMSO-d_6) δ 9.10 (s, 2H), 8.80 (d, 2H, *J* = 7.8 Hz), 8.39 (s, 2H), 8.34 (dd, 2H, *J* = 2.5, 8.2 Hz), 8.04 (d, 2H, *J* = 8.7 Hz), 7.86 (t, 2H, *J* = 7.9 Hz), 6.87 (d, 2H, *J* = 8.7 Hz), 3.02 (s, 6H). ^{13}C NMR (DMSO-d_6) δ 154.6, 148.9, 140.8, 133.7, 130.8, 128.7, 124.2, 123.8, 121.7, 116.9, 112.6, 112.5, 112.1, 70.1. HR-MS *m*/*z* 441.1541 $(M+H)^+$ requires 441.1563.



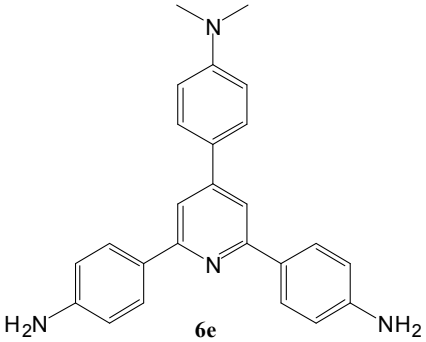
6c

6c: ^{1}H NMR (DMSO-d_6) δ 8.21 (d, 4H, *J* = 8.3 Hz), 7.93 (s, 2H), 7.86 (d, 2H, *J* = 8.3 Hz), 6.81 (d, 2H, *J* = 8.7 Hz), 3.81 (s, 6H, -OCH_3), 2.96 (s, 6H, -CH_3). ^{13}C NMR (DMSO-d_6) δ 160.5, 156.2, 132.1, 129.2, 128.6, 128.3, 125.0, 114.4, 114.3, 113.9, 112.7, 55.9, 55.7. HR-MS *m*/*z* 411.2067 $(M+H)^+$ requires 411.2073.



6d

6d: ^{1}H NMR (DMSO-d_6) δ 8.18 (d, 4H, J = 7.8 Hz), 8.02 (s, 2H), 7.89 (d, 2H, J = 8.8 Hz), 7.33 (d, 4H, J = 7.8 Hz), 6.84 (d, 2H, J = 8.8 Hz), 2.99 (s, 6H), 2.38 (s, 6H). ^{13}C NMR (DMSO-d_6) δ 156.6, 151.5, 149.6, 138.9, 136.8, 129.7, 128.3, 127.1, 124.9, 114.7, 112.7, 40.8, 21.3. HR-MS m/z 401.2000 $(M+Na)^+$ requires 401.1994.

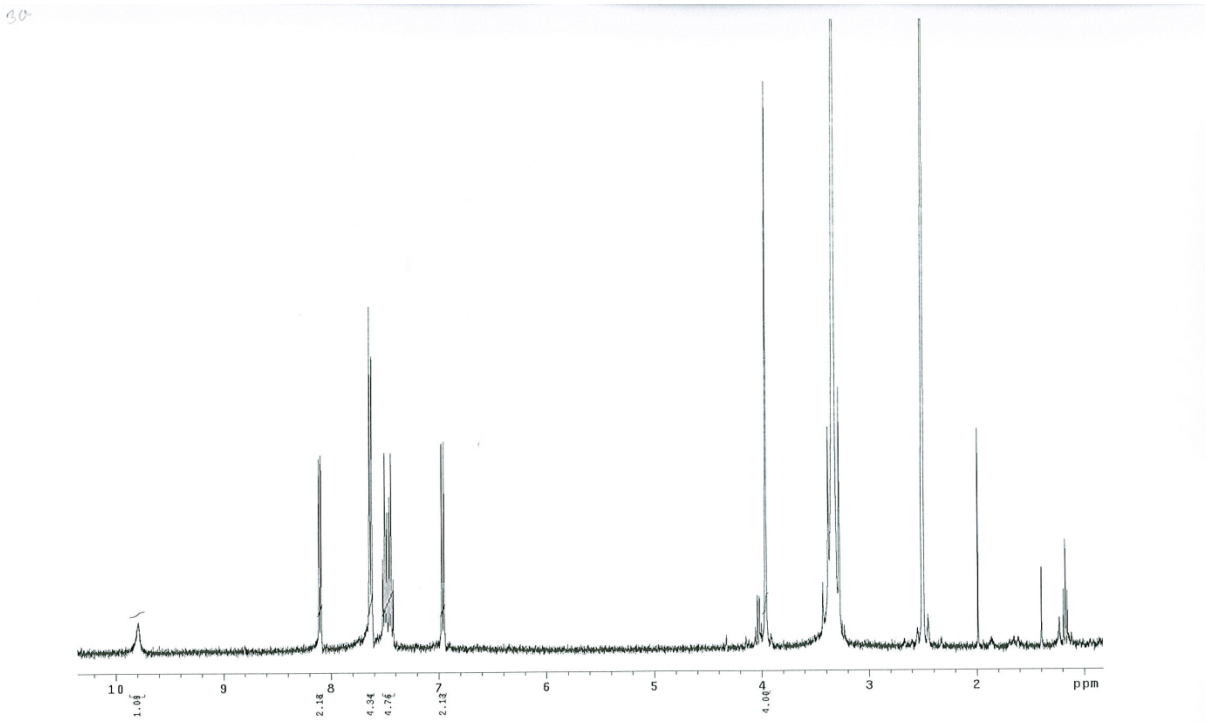


6e

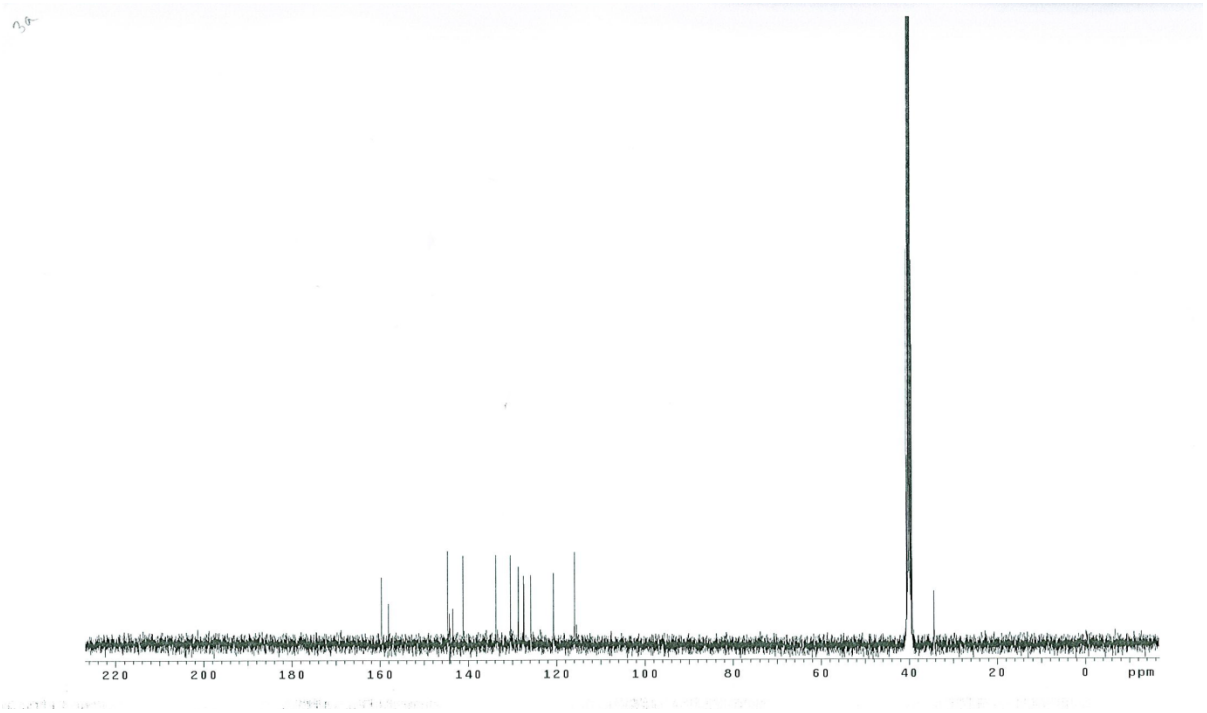
6e: ^{1}H NMR and ^{13}C NMR spectroscopic data were consistent with the literature.[4]

5. Copies of ^{1}H NMR and ^{13}C NMR spectra

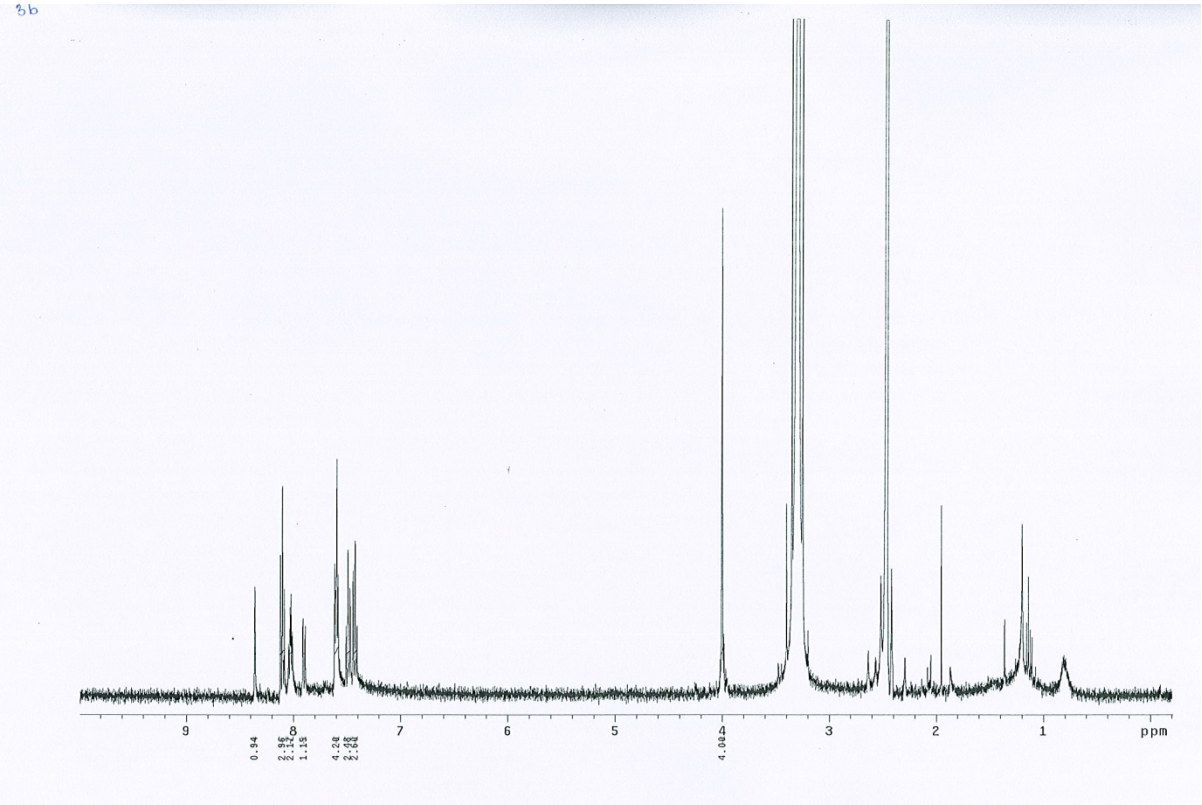
^{1}H NMR spectrum of **3a**



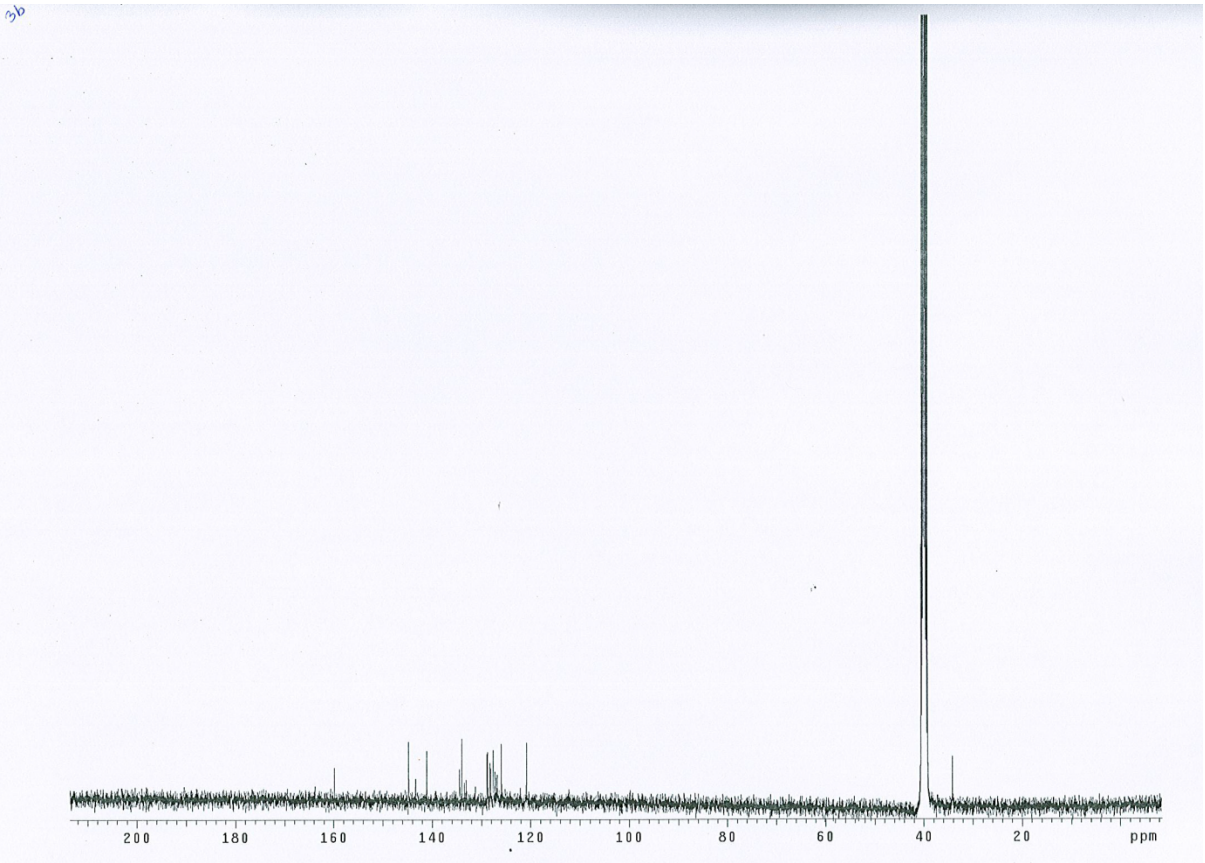
^{13}C NMR spectrum of **3a**



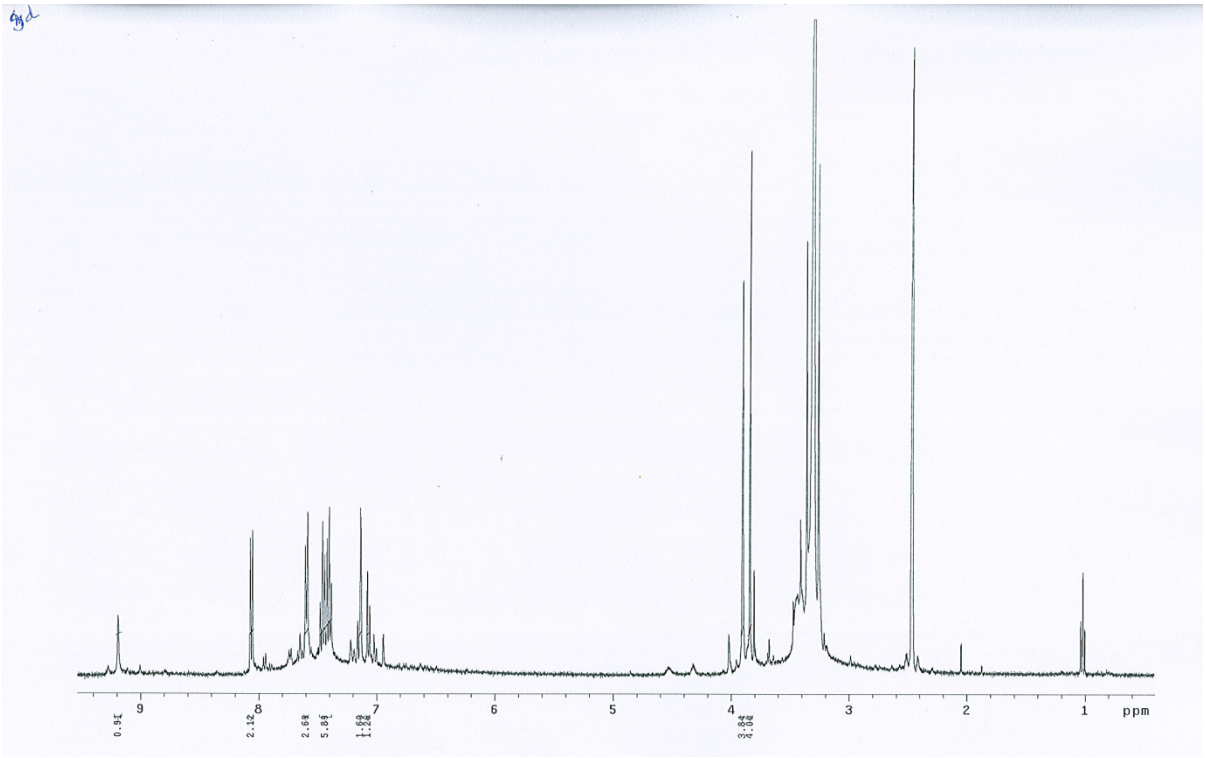
^{1}H NMR spectrum of **3b**



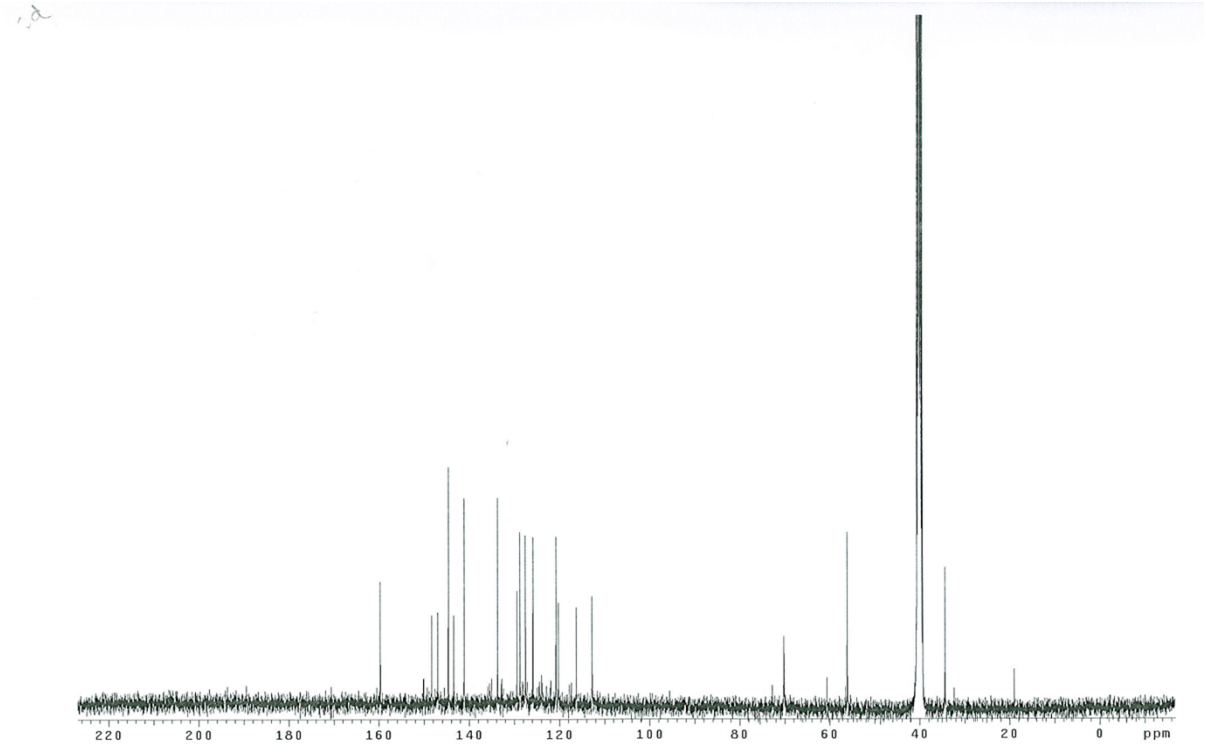
^{13}C NMR spectrum of **3b**



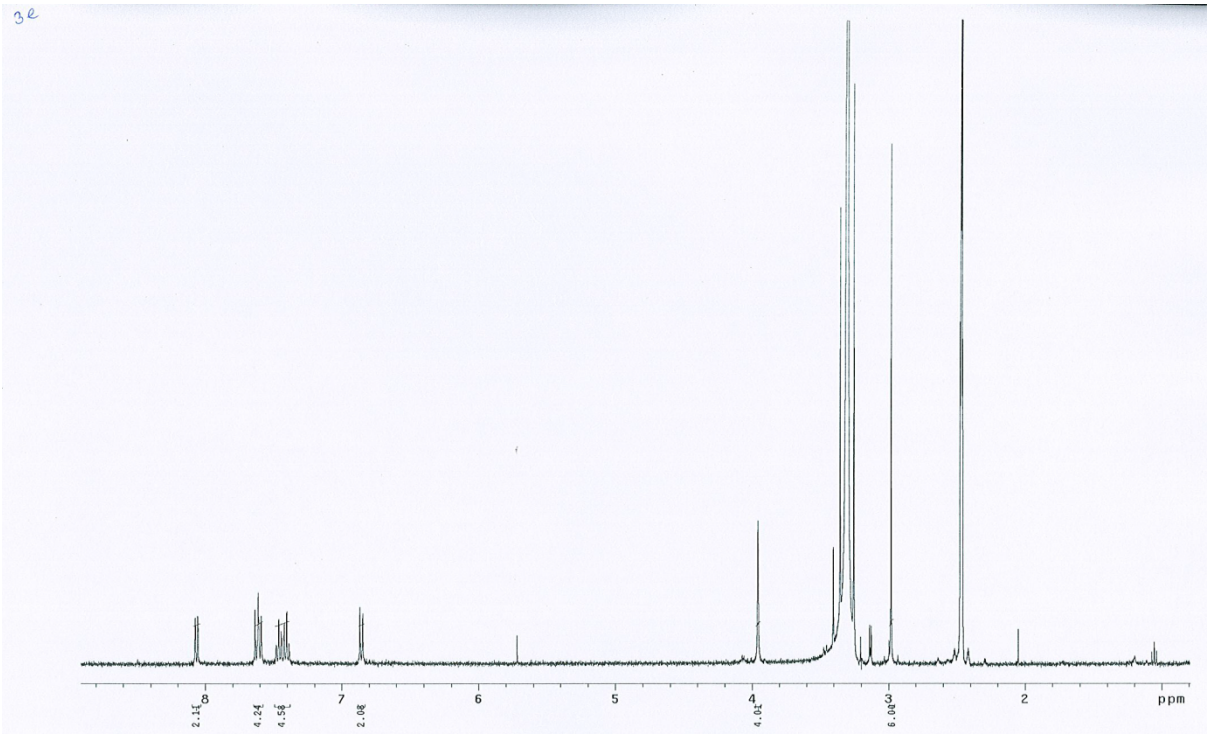
^{1}H NMR spectrum of **3d**



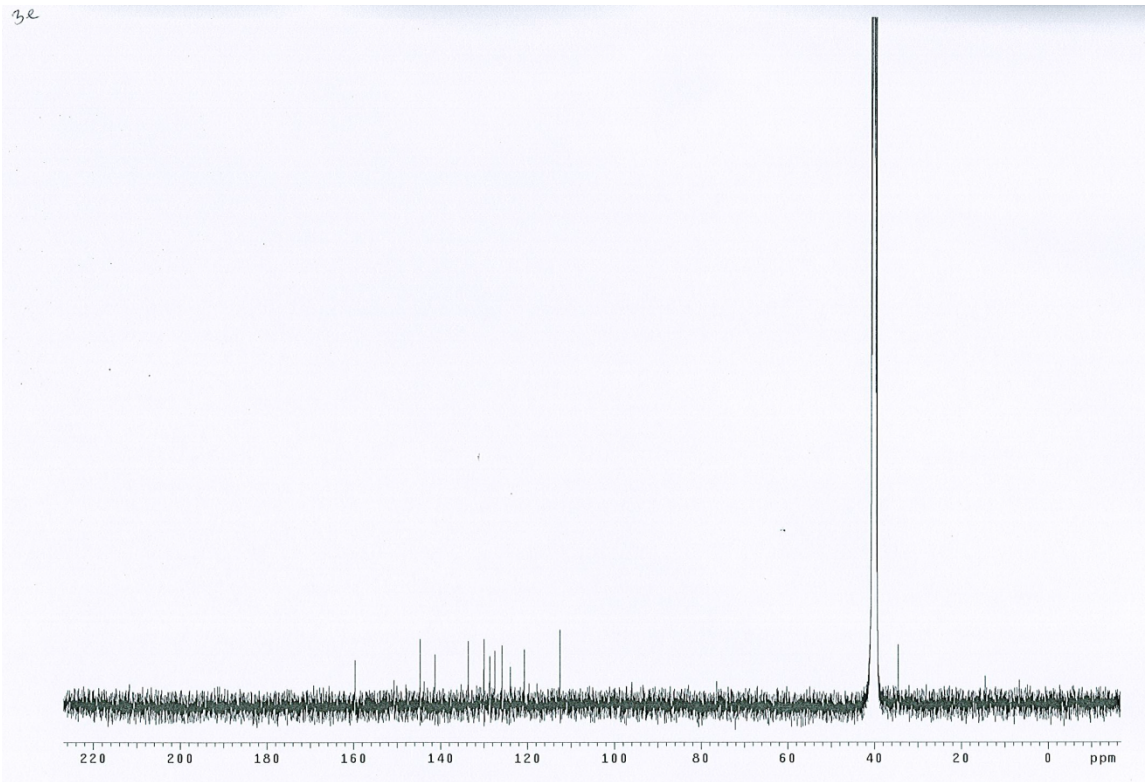
^{13}C NMR spectrum of **3d**



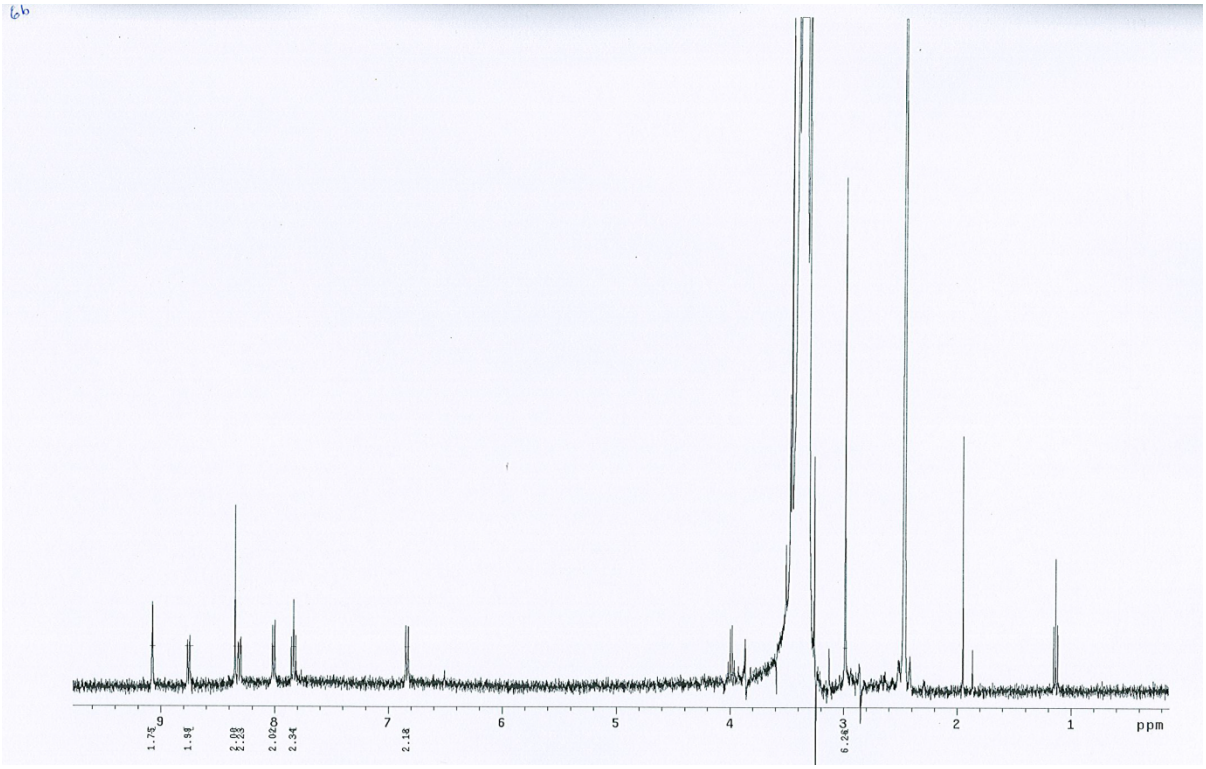
^{1}H NMR spectrum of **3e**



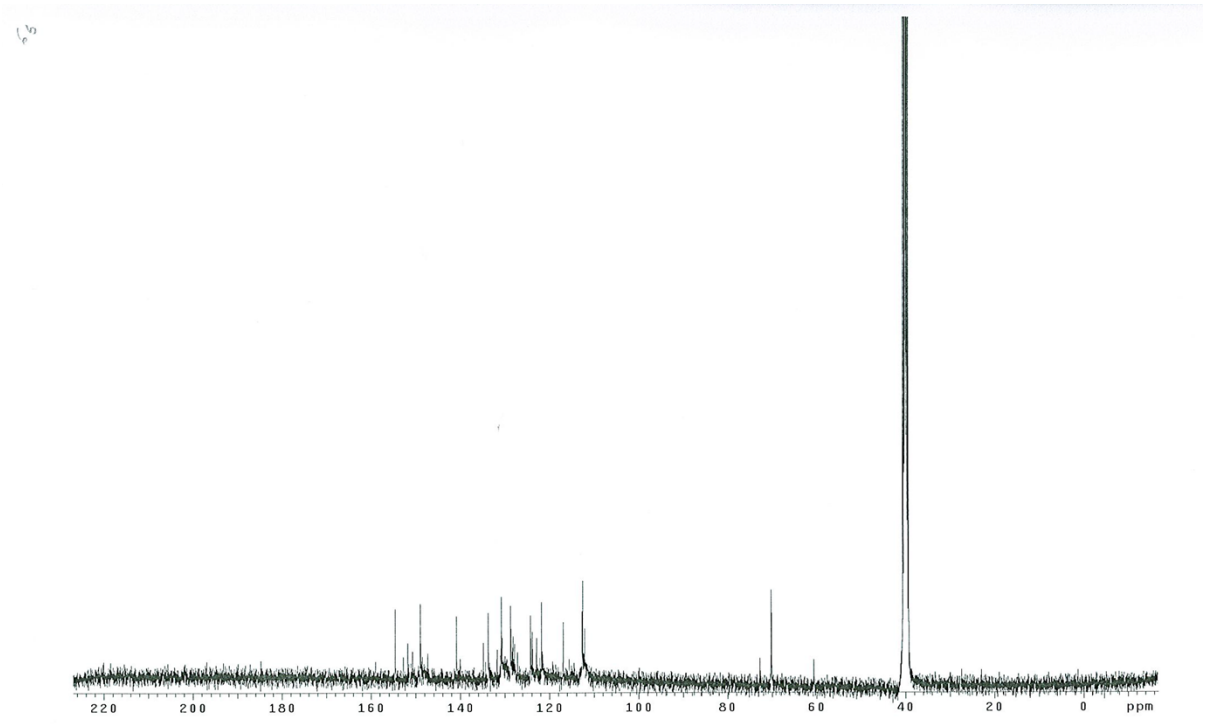
^{13}C NMR spectrum of **3e**



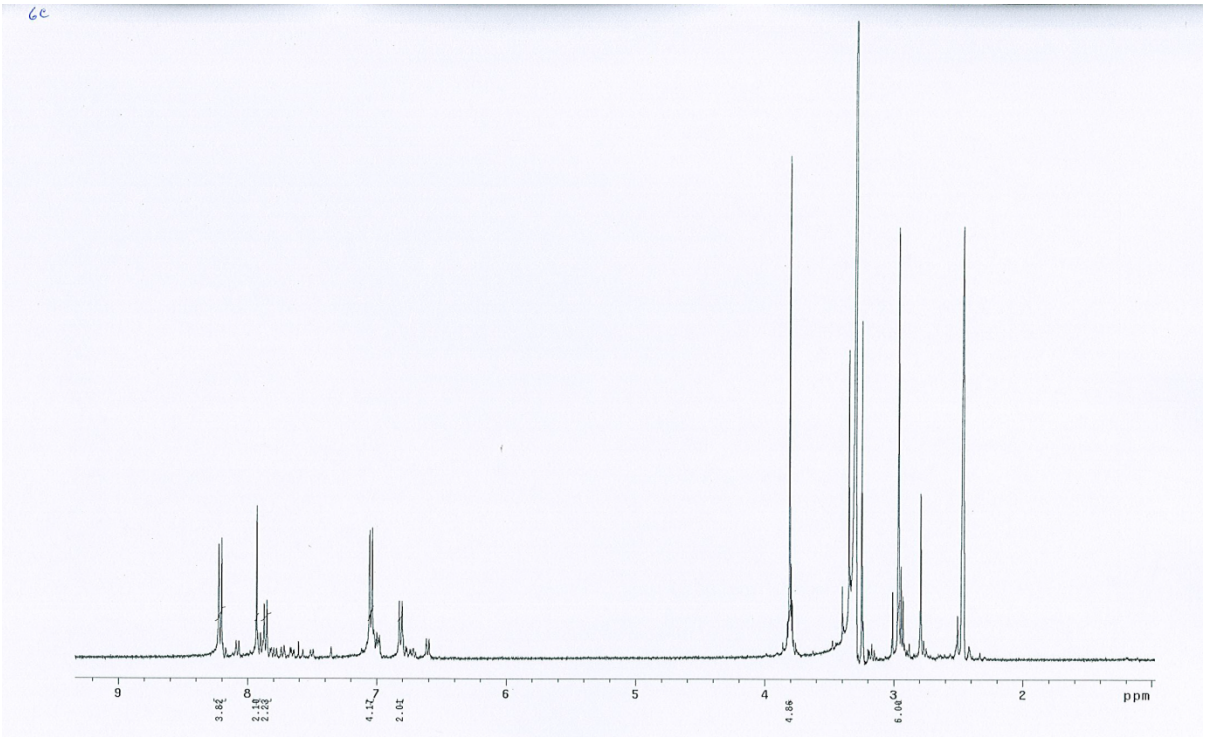
^{1}H NMR spectrum of **6b**



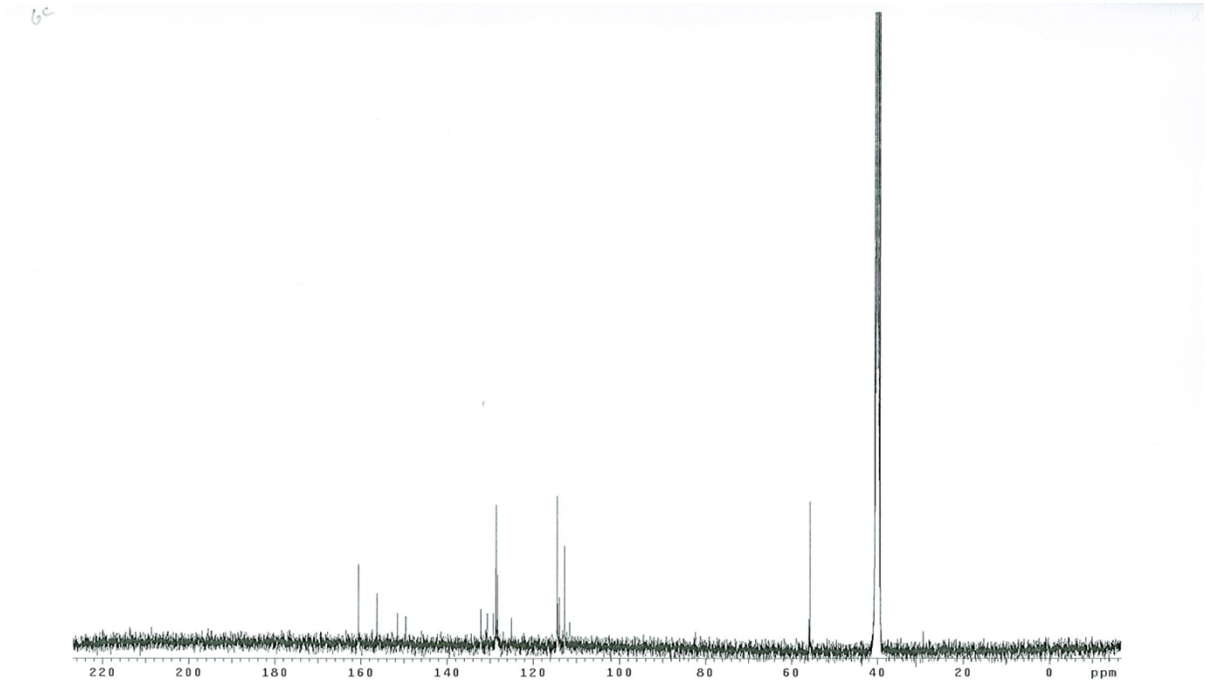
^{13}C NMR spectrum of **6b**



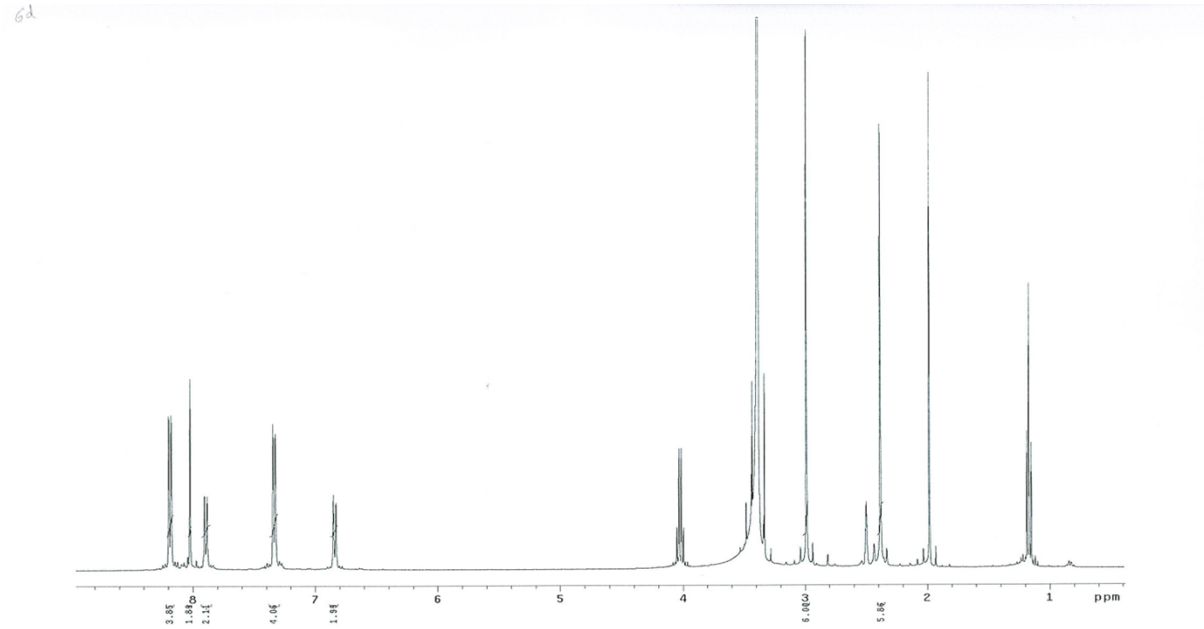
^{1}H NMR spectrum of **6c**



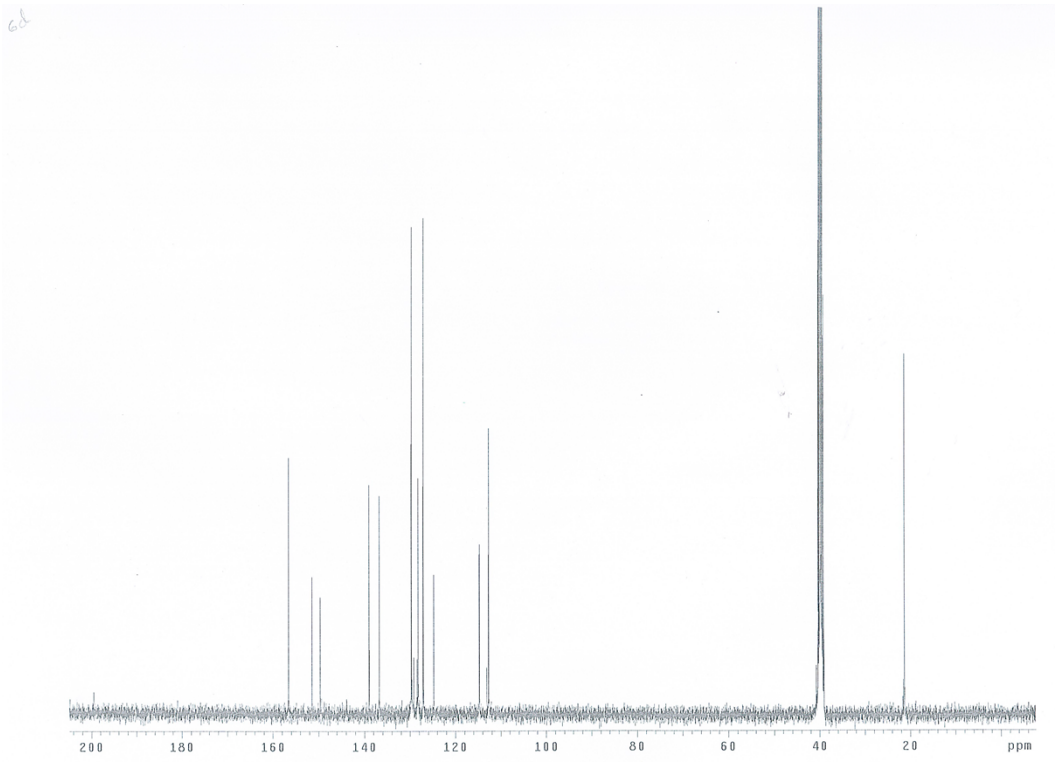
^{13}C NMR spectrum of **6c**



^{1}H NMR spectrum of **6d**



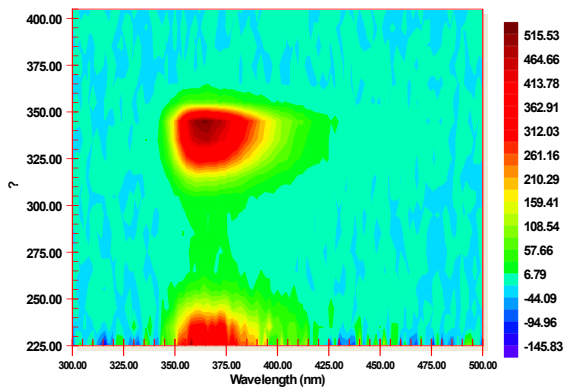
^{13}C NMR spectrum of **6d**



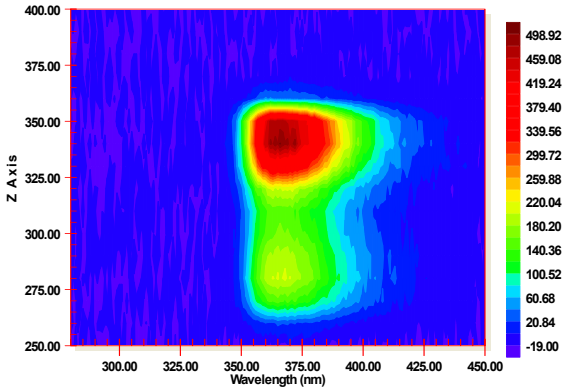
6. Crystal data and structure refinement for 6d.

Empirical formula	$C_{27}H_{26}N_2$
Formula weight	378.50
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 7.4217(3) Å
	b = 23.8402(8) Å
	c = 11.7942(4) Å
	β= 99.776(4)°
Volume	2056.50(13) $Å^3$
Z	4
Density (calculated)	1.222 Mg/m^3
μ	0.071 mm^{-1}
Crystal size	0.50 x 0.23 x 0.20 mm^3
θ range for data collection	2.78 to 26.00°
Index ranges	-9<=h<=9, -29<=k<=20, -14<=l<=13
Reflections collected	13457
Independent reflections	4047 [R(int) = 0.0428]
Completeness to θ = 26.00°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max./min. transmission	1.00/0.76
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4047 / 0 / 266
Goodness-of-fit on F^2	1.143
Final R indices [I>2σ(I)]	R1 = 0.0824, wR2 = 0.1897
R indices (all data)	R1 = 0.1015, wR2 = 0.2007
Largest diff. peak and hole	0.383 and -0.209 e.$Å^{-3}$

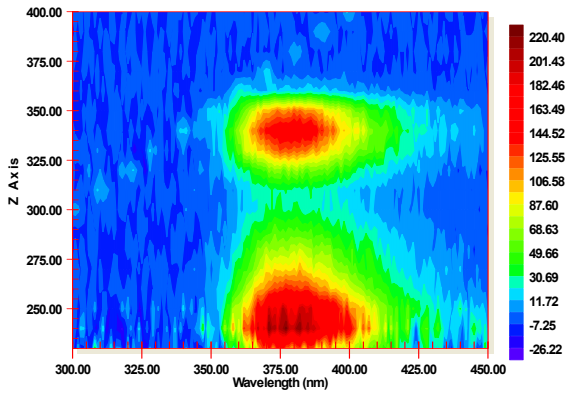
7. 2D Fluorescence spectra for compounds



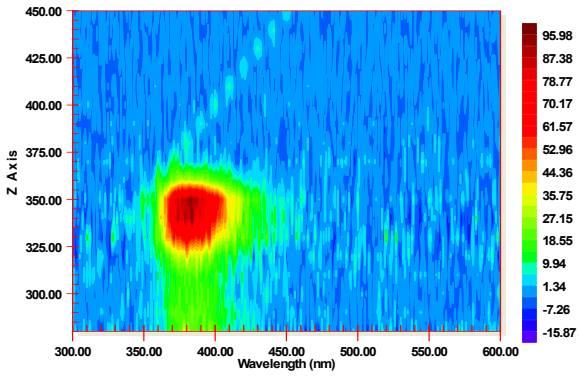
3a in Acetonitrile



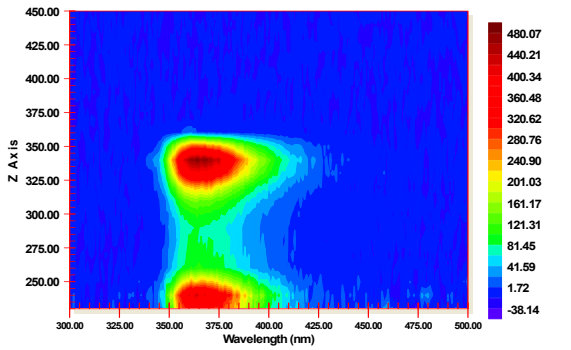
3a in DMSO



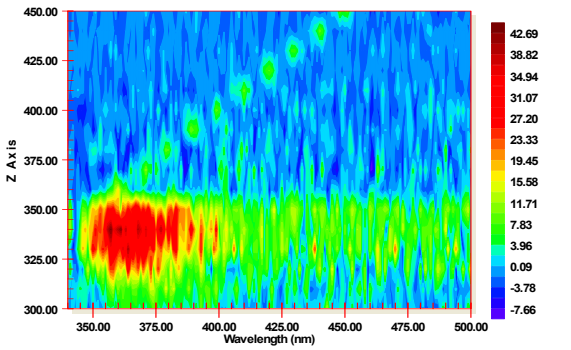
3b in Acetonitrile



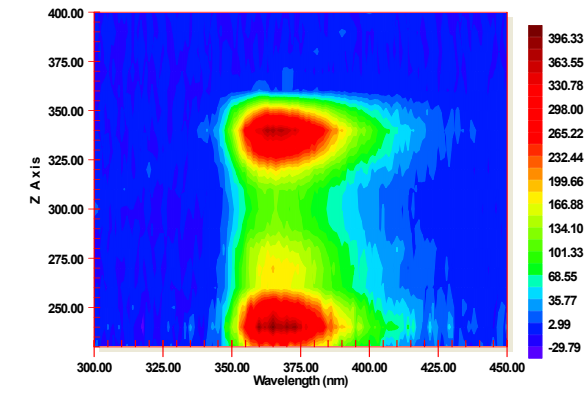
3b in DMSO



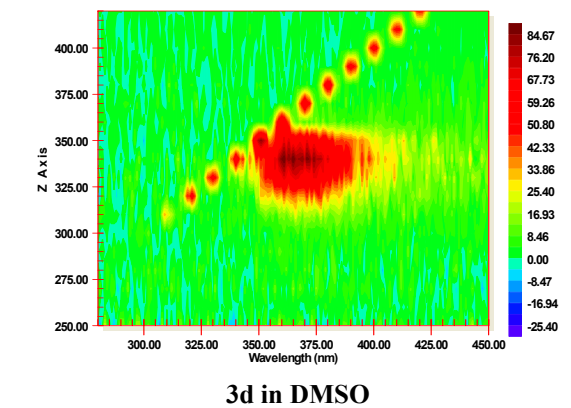
3c in Acetonitrile



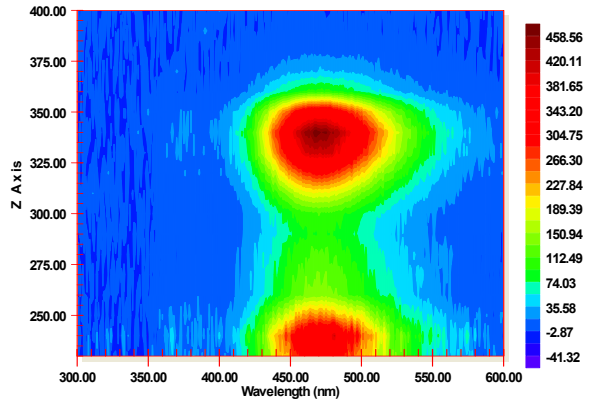
3c in DMSO



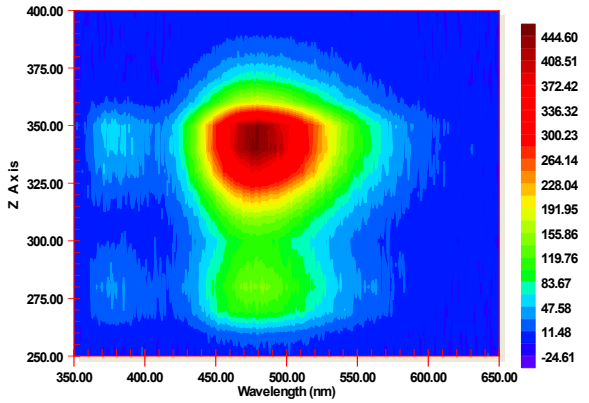
3d in Acetonitrile



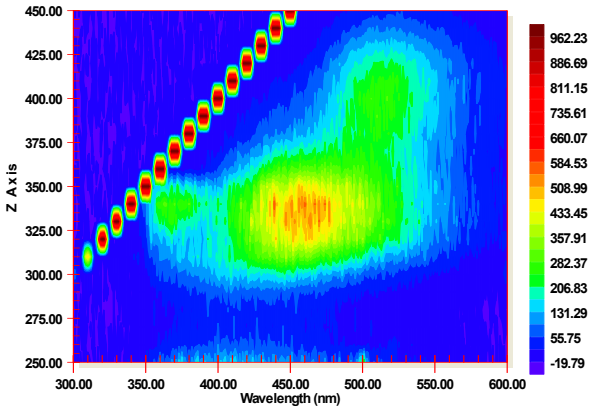
3d in DMSO



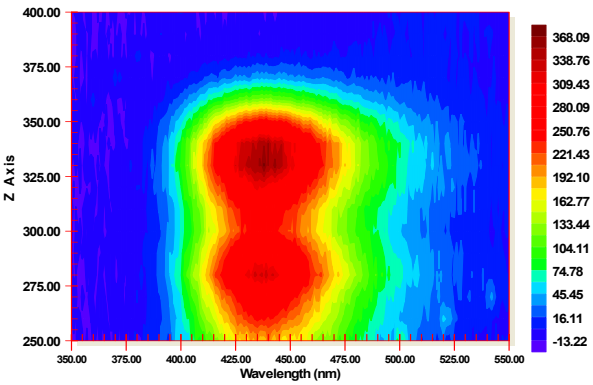
3e in Acetonitrile



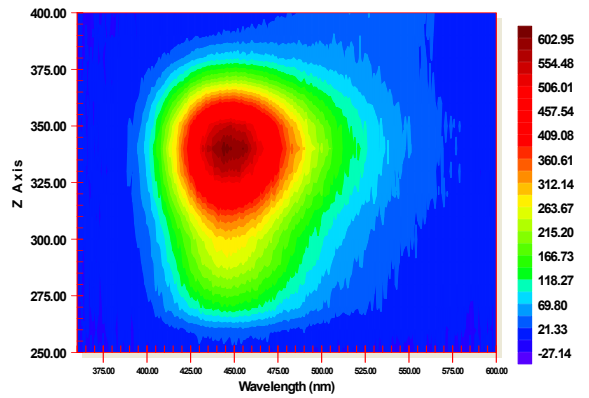
3e in DMSO



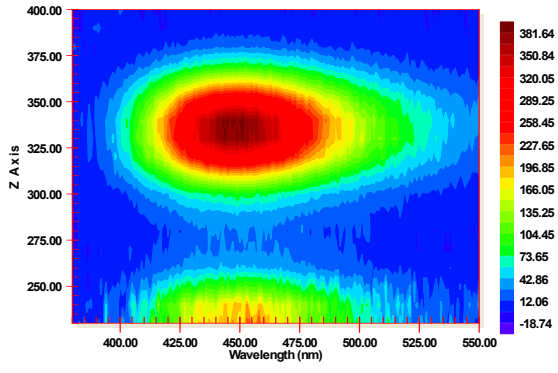
6a in Acetonitrile



6c in Acetonitrile



6c in DMSO



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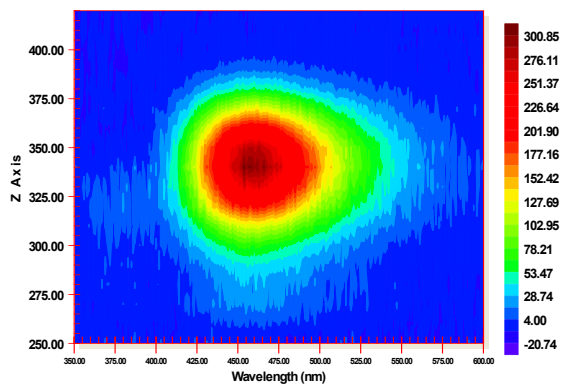
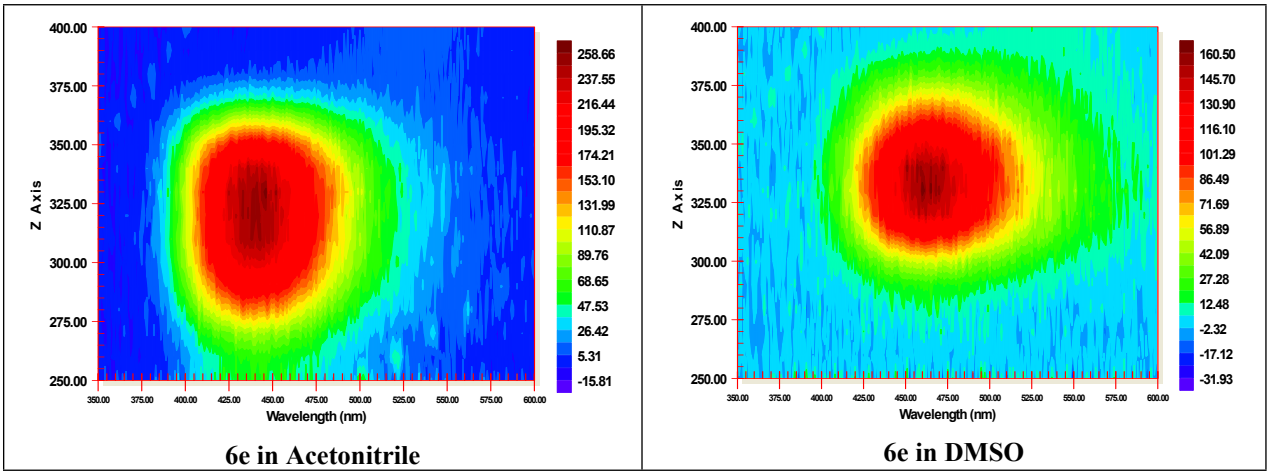


6d in DMSO



8. References

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