Electronic Supplementary Information

Mechanochemical synthesis of coumarins via Pechmann condensation under solvent-free conditions: An easy access to coumarins and annulated pyrano[2,3-*f*] and [3,2-*f*]indoles

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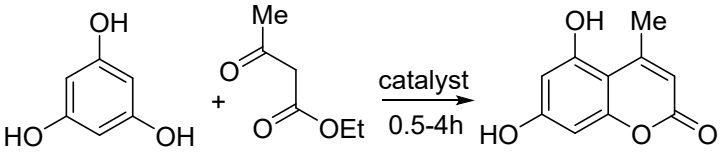
General Information

All commercially available chemicals were obtained from Aldrich, and used without further purifications. The ball mill was a Retsch PM 100 swing mill. 10 mL stainless steel ball mill vessels were applied for 5-25 mmol runs. Ten stainless steel balls with 5 mm diameter were used, and the milling frequency was at 8.33 Hz at the ambient temperatures. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were recorded on a Bruker DRX-400 Avance spectrometer with DMSO-d_6 as solvent at ambient temperature. All chemical shifts are given relative to residual signals of solvent. All yields refer to the isolated products.

Table 1. Optimization of the reaction conditions



1a **2a** **3aa**

Entry	catalyst	catalyst loading	scale	rotation	time	yield
1	no	-	5 mmol	500 rpm	1 h	0
2	TFA	10%	5 mmol	500 rpm	2 h	63
3	TsOH	5%	5 mmol	500 rpm	2 h	62
4	TsOH	10%	5 mmol	500 rpm	2 h	71
5	MsOH	5%	5 mmol	500 rpm	2 h	73%
6	MsOH	10%	5 mmol	500 rpm	2 h	87%
7	MsOH	10%	5 mmol	500 rpm	0.5 h	74%
8	MsOH	10%	5 mmol	500 rpm	4 h	80%
9	MsOH	15%	5 mmol	500 rpm	2 h	83%
10	MsOH	10%	25 mmol	500 rpm	2 h	91%
11	MsOH	10%	5 mmol	no	2 h	65%

General procedure for the mechanochemical preparation of crude coumarin derivatives 3a-ag and 4a-g

A mixture of phenol **1** (5.0 mmol, 1.0 equiv), β-ketoester **2** (5.5 mmol, 1.1 equiv), and MsOH (0.5 mmol, 0.1 equiv) were placed in a 10 mL stainless steel jar. Ten 5 mm diameter stainless steel balls were added, and the mixture was milled at 8.33 Hz for 2 h.

General procedure for the purification of coumarin derivatives 3a-ag

After completion of the mechanochemical synthesis, the resulting paste or solid was transferred from the jar to a 30 mL beaker using 10-15 mL of ethanol (for compounds **3a-e,g-v,x-ag**) or ethanol-water 1:1 mixture (for compounds **3f,w**) and the mixture was heated to reflux (complete dissolution may not occur, but it is sufficient to dissolve unreacted starting materials). Then the reaction mixture was cooled and the coumarin **3** was filtered off and dried to get the pure product.

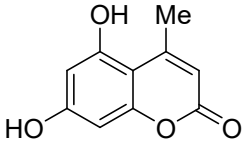
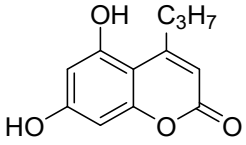
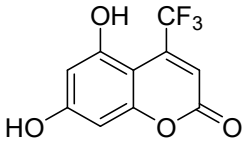
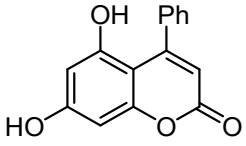
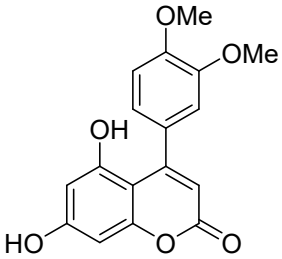
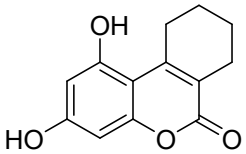
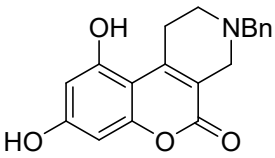
General procedure for the purification of coumarin derivatives 4a-g

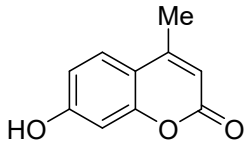
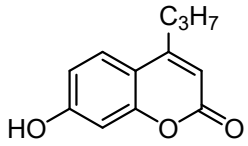
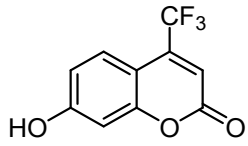
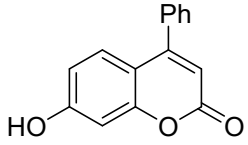
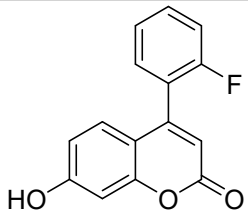
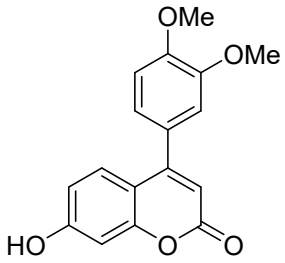
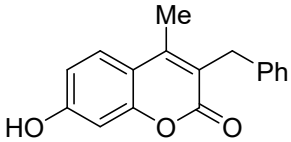
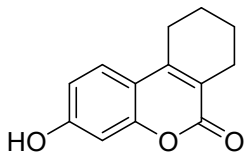
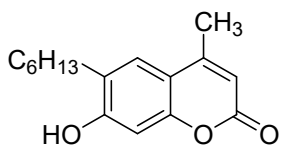
After completion of the mechanochemical synthesis, the resulting paste or solid was transferred from the jar to a 20 mL beaker using 5 mL of DMF (for compounds **4a-c,e-g**) or DMF or 1:1 DMF-ethanol mixture (for compound **4d**), the mixture was heated to reflux, and then cooled to RT. The precipitate of coumarin **4** was filtered off and dried at 100°C to get the pure product.

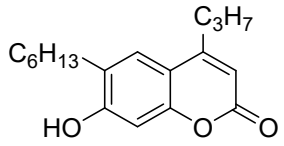
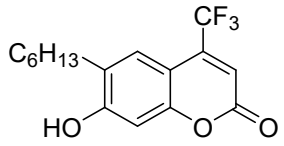
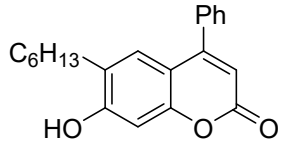
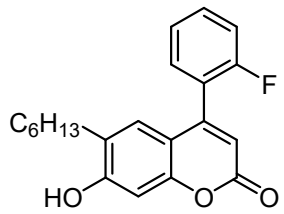
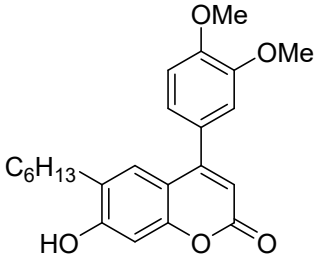
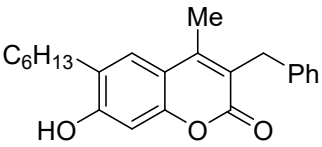
X-ray crystallographic data

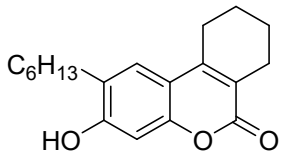
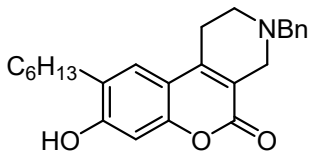
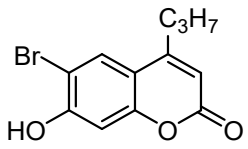
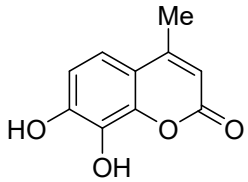
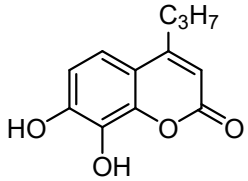
Single crystal was grown by the slow evaporation of the solution of compound **3v** in EtOAc. Single crystal X-ray data for the compound **3v** was collected using the Bruker D8 Quest diffractometer. The crystal was kept at 293.15 K during data collection. Using Olex2,[1] the structure was solved with the SHELXT[2] structure solution program using Intrinsic Phasing and refined with the SHELXL[3] refinement package using Least Squares minimization.

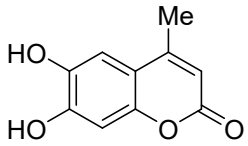
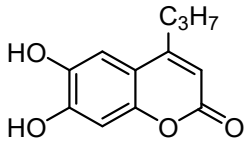
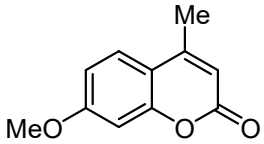
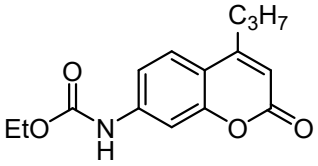
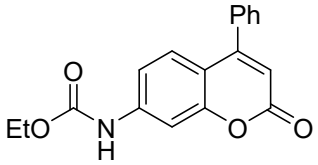
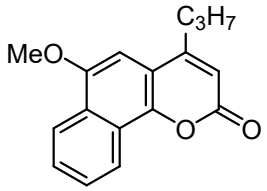
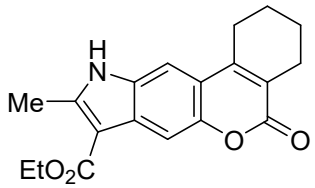
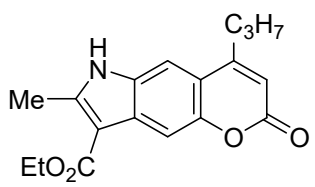
Table 2. NMR data for compounds **3a-3ag**

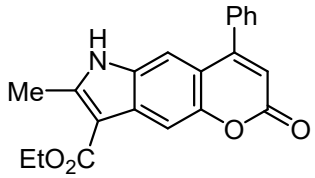
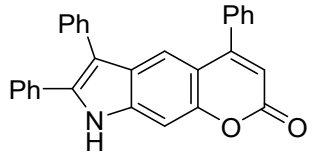
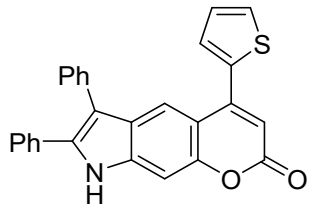
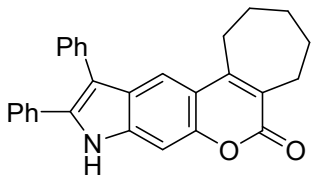
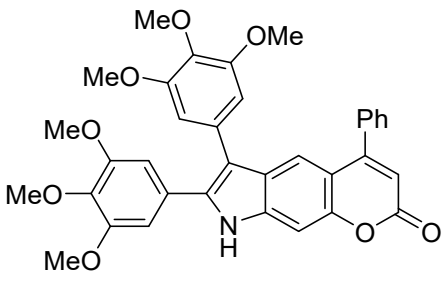
Structure	Analytical Data
	*5,7-Dihydroxy-4-methyl-2H-chromen-2-one*[4] ***(3a)***. Yield 835 mg, 87%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.24 (s, 1H), 10.01 (br s, 1H), 6.22 (br s, 1H), 6.12 (s, 1H), 5.73 (s, 1H), 2.52 (s, 3H).
	*5,7-Dihydroxy-4-propyl-2H-chromen-2-one*[5] ***(3b)***. Yield 902 mg, 82%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 9.96 (s, 1H), 6.21 (br s, 1H), 6.12 (br s, 1H), 5.70 (s, 1H), 2.84–2.88 (m, 2H), 1.62–1.66 (m, 2H), 0.98–1.01 (m, 3H).
	*5,7-Dihydroxy-4-triflouromethyl-2H-chromen-2-one*[6] ***(3c)***. Yield 923 mg, 75%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.90 (s, 1H), 10.65 (s, 1H), 6.53 (s, 1H), 6.32 (d, *J* = 2.2 Hz, 1H), 6.29 (d, *J* = 2.2 Hz, 1H).
	*5,7-Dihydroxy-4-phenyl-2H-chromen-2-one*[6] ***(3d)***. Yield 851 mg, 67%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.21 (s, 1H), 9.95 (s, 1H), 7.31–7.35 (m, 5H), 6.22 (d, *J* = 1.4 Hz, 1H), 6.13 (d, *J* = 1.4 Hz, 1H), 5.69 (s, 1H).
	*5,7-Dihydroxy-4-(3,4-dimethoxyphenyl)-2H-chromen-2-one*[7] ***(3e)***. Yield 1194 mg, 76%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.99 (s, 1H), 9.74 (s, 1H), 6.83–6.89 (m, 3H), 6.21 (d, *J* = 2.3 Hz, 1H), 6.13 (d, *J* = 2.3 Hz, 1H), 5.69 (s, 1H), 3.83 (s, 3H), 3.79 (s, 3H).
	*1,3-Dihydroxy-7,8,9,10-tetrahydro-6H-benzo[c]chromen-6-one*[5] ***(3f)***. Yield 904 mg, 78%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.00 (br s, 1H), 9.77 (br s, 1H), 6.18 (br s, 1H), 6.08 (br s, 1H), 3.07 (br s, 2H), 2.36 (br s, 2H), 1.69 (br s, 4H).
	*3-Benzyl-8,10-dihydroxy-1,2,3,4-tetrahydro-5H-chromeno[3,4-c]pyridin-5-one* ***(3g)***. Yield 1244 mg, 77%. Off-white solid, m.p. = 238–240°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.36 (br s, 1H), 7.34–7.35 (m, 4H), 7.24–7.28 (m, 1H), 6.24 (d, *J* = 1.5 Hz, 1H), 6.13 (d, *J* = 1.5 Hz, 1H), 3.63 (s, 2H), 3.18 (br s, 2H), 3.14 (br s, 2H), 2.60–2.62 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 160.3, 159.6, 157.8, 154.8, 148.5, 138.1, 128.7, 128.2, 127.0, 114.0, 101.5, 99.4, 94.1, 61.6, 50.7, 48.9, 29.9. Anal. Calcd for $C_{19}H_{17}NO_4$: C, 70.58; H, 5.30; N, 4.33. Found.: C, 70.39; H, 5.38; N, 4.18.

	*7-Hydroxy-4-methyl-2H-chromen-2-one*[6] ***(3h)***. Yield 832 mg, 80%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.27 (br s, 1H), 7.50 (d, *J* = 7.0 Hz, 1H), 6.74 (d, *J* = 7.0 Hz, 1H), 6.65 (s, 1H), 6.02 (s, 1H), 2.37 (s, 3H).
	*7-Hydroxy-4-propyl-2H-chromen-2-one*[8] ***(3i)***. Yield 755 mg, 74%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (br s, 1H), 7.52 (d, *J* = 8.7 Hz, 1H), 6.73 (dd, *J* = 8.7, 2.0 Hz, 1H), 6.66 (d, *J* = 2.0 Hz, 1H), 5.97 (s, 1H), 2.67–2.71 (m, 2H), 1.65–1.73 (m, 2H), 1.00–1.04 (m, 3H).
	*7-Hydroxy-4-trifluoromethyl-2H-chromen-2-one*[9] ***(3j)***. Yield 863 mg, 75%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.77 (s, 1H), 7.51 (d, *J* = 8.9 Hz, 1H), 6.86 (dd, *J* = 8.9, 2.0 Hz, 1H), 6.79 (d, *J* = 2.0 Hz, 1H), 6.60 (s, 1H).
	*7-Hydroxy-4-phenyl-2H-chromen-2-one*[8] ***(3k)***. Yield 869 mg, 73%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.40 (br s, 1H), 7.52 (br s, 3H), 7.45–7.47 (m, 2H), 7.25 (d, *J* = 8.7 Hz, 1H), 6.75 (br s, 1H), 6.71 (d, *J* = 8.7 Hz, 1H), 6.05 (s, 1H).
	*7-Hydroxy-4-(2-fluorophenyl)-2H-chromen-2-one*[10] ***(3l)***. Yield 829 mg, 61%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.45 (s, 1H), 7.55–7.60 (m, 1H), 7.42–7.45 (m, 1H), 7.31–7.38 (m, 2H), 7.01 (dd, $^3J_{H\text{-}H}$ = 8.7 Hz, $J_{H\text{-}F}$ = 1.5 Hz, 1H), 6.76 (d, *J* = 1.4 Hz, 1H), 6.70 (dd, $^3J_{H\text{-}H}$ = 8.7 Hz, $^4J_{H\text{-}H}$ = 1.4 Hz, 1H), 6.12 (s, 1H).
	*7-Hydroxy-4-(3,4-dimethoxyphenyl)-2H-chromen-2-one*[7] ***(3m)***. Yield 1013 mg, 68%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.37 (s, 1H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.02–7.06 (m, 3H), 6.71–6.74 (m, 2H), 6.06 (s, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 6.12 (s, 1H).
	*3-Benzyl-7-hydroxy-4-methyl-2H-chromen-2-one*[11] ***(3n)***. Yield 944 mg, 71%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.14 (br s, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.18–7.24 (m, 4H), 7.12–7.15 (m, 1H), 6.74 (d, *J* = 8.8 Hz, 1H), 6.66 (s, 1H), 3.92 (s, 2H), 2.38 (s, 3H).
	*3-Hydroxy-7,8,9,10-tetrahydro-6H-benzo[c]chromen-6-one*[4] ***(3o)***. Yield 702 mg, 65%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.03 (br s, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 6.70 (d, *J* = 8.5 Hz, 1H), 6.62 (s, 1H), 2.71 (br s, 2H), 2.39 (br s, 2H), 1.76–1.79 (m, 4H).
	*6-Hexyl-7-hydroxy-4-methyl-2H-chromen-2-one* ***(3p)***. Yield 1209 mg, 93%. Off-white solid, m.p. = 138–140°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.42 (s, 1H), 7.39 (s, 1H), 6.71 (s, 1H), 6.07 (s, 1H), 2.53–2.57 (m, 2H), 2.35 (s, 3H), 1.53 (br s, 2H), 1.27 (br s, 6H), 0.84 (br s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 160.4, 159.0, 153.5, 152.9, 126.3, 125.7, 111.6, 110.1, 101.6, 31.1, 29.3 (2C), 28.6, 22.1, 18.1, 13.9. Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.67; H, 7.83.

	*6-Hexyl-7-hydroxy-4-propyl-2H-chromen-2-one (**3q**)*. Yield 1282 mg, 89%. Off-white solid, m.p. = 183–185°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.42 (s, 1H), 7.43 (s, 1H), 6.72 (s, 1H), 6.02 (s, 1H), 2.67–2.71 (m, 2H), 2.54–2.57 (m, 2H), 1.59–1.65 (m, 2H), 1.52 (br s, 2H), 1.26 (br s, 6H), 0.94–0.98 (m, 3H), 0.84 (br s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 160.5, 158.9, 156.8, 153.2, 126.3, 125.5, 110.8, 109.1, 101.8, 32.8, 31.1, 29.2 (2C), 28.5, 22.1, 21.3, 13.9, 13.6. Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 75.03; H, 8.28.
	*6-Hexyl-7-hydroxy-4-trifluoromethyl-2H-chromen-2-one (**3r**)*. Yield 1271 mg, 81%. Light purple solid, m.p. = 142–145°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.91 (s, 1H), 7.31 (s, 1H), 6.83 (s, 1H), 6.69 (s, 1H), 2.55–2.59 (m, 2H), 1.47–1.53 (m, 2H), 1.26 (br s, 6H), 0.84 (br s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 160.2, 158.9, 154.1, 140.2, 139.7 (q, *J* = 31.8 Hz), 127.5, 121.8 (q, *J* = 275.4 Hz) 111.6 (q, *J* = 5.5 Hz), 104.8, 102.5, 31.0, 29.1, 28.9, 28.3, 22.0, 13.8. ^{19}F NMR (376 MHz, DMSO-d_6): δ −63.51 (s, 3F). Anal. Calcd for $C_{16}H_{17}F_3O_3$: C, 61.14; H, 5.45. Found: C, 61.23; H, 5.51.
	*6-Hexyl-7-hydroxy-4-phenyl-2H-chromen-2-one*[12] *(**3s**)*. Yield 1208 mg, 75%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 7.53–7.55 (m, 3H), 7.47–7.49 (m, 2H), 7.08 (s, 1H), 6.83 (s, 1H), 6.09 (s, 1H), 2.44–2.47 (m, 2H), 1.39–1.44 (m, 2H), 1.19 (br s, 6H), 0.78–0.81 (m, 3H).
	*6-Hexyl-7-hydroxy-4-(2-fluorophenyl)-2H-chromen-2-one (**3t**)*. Yield 1139 mg, 67%. Off-white solid, m.p. = 175–177°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.70 (s, 1H), 7.63–7.68 (m, 1H), 7.52–7.55 (m, 1H), 7.41–7.48 (m, 2H), 6.88 (br s, 2H), 6.25 (s, 1H), 2.55 (br s, 2H), 1.46 (br s, 2H), 1.24 (br s, 6H), 0.85 (br s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 160.0, 159.5, 158.5 (d, *J* = 246.2 Hz), 153.3, 150.2, 131.8 (d, *J* = 8.1 Hz), 130.7, (d, *J* = 2.4 Hz), 126.8, 126.6, 125.1 (d, *J* = 3.0 Hz), 122.8 (d, *J* = 15.4 Hz), 116.0 (d, *J* = 21.3 Hz), 111.9, 110.2, 101.9, 31.0, 28.9 (2C), 28.2, 22.0, 13.9. ^{19}F NMR (376 MHz, DMSO-d_6): δ −113.05 (s, 1F). Anal. Calcd for $C_{21}H_{21}FO_3$: C, 74.10; H, 6.22. Found: C, 74.02; H, 6.31.
	*6-Hexyl-7-hydroxy-4-(3,4-dimethoxyphenyl)-2H-chromen-2-one (**3u**)*. Yield 1225 mg, 64%. Pale purple solid, m.p. = 173–175°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.45 (s, 1H), 7.27 (s, 1H), 7.06–7.15 (m, 3H), 6.84 (s, 1H), 6.12 (s, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 2.52–2.55 (m, 2H), 1.46–1.51 (m, 2H), 1.22–1.30 (m, 6H), 0.83–0.86 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 160.1, 159.0, 155.0, 153.6, 149.9, 148.7, 127.6, 127.1, 126.2, 120.9, 112.2, 111.9, 110.3, 109.6, 102.0, 55.5 (2C), 30.8, 28.9, 28.8, 28.1, 21.7, 13.6. Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.03; H, 6.90.
	*3-Benzyl-6-hexyl-7-hydroxy-4-methyl-2H-chromen-2-one (**3v**)*. Yield 1400 mg, 80%. Peach solid, m.p. = 162–164°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.35 (s, 1H), 7.44 (s, 1H), 7.15–7.26 (m, 5H), 6.73 (s, 1H), 3.90 (s, 2H), 2.54–2.58 (m, 2H), 2.37 (s, 3H), 1.50–1.55 (m, 2H), 1.27 (br s, 6H), 0.82–0.84 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 161.4,

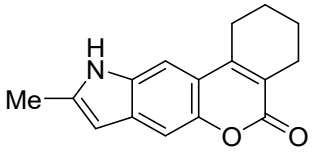
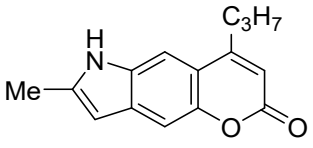
	158.3, 151.5, 148.5 (2C), 139.5, 128.3, 128.0, 126.4, 125.9, 119.9, 112.1, 101.4, 32.1, 31.1, 29.4 (2C), 28.6, 22.1, 15.1, 13.9. Anal. Calcd for $C_{23}H_{26}O_3$: C, 78.83; H, 7.48. Found: C, 78.98; H, 7.56. Crystal Data: monoclinic, space group $P_2$1/n (no. 14), a = 11.353(8) Å, b = 13.367(8) Å, c = 12.835(7) Å, β = 100.25(2)°, V = 1917(2) Å^3, Z = 4, T = 293.15 K, μ(MoKα) = 0.079 mm-1, Dcalc = 1.214 g/cm3, 46605 reflections measured (6.098° ≤ 2Θ ≤ 57°), 4847 unique (Rint = 0.0388, Rsigma = 0.0200) which were used in all calculations. The final R1 was 0.0705 (I > 2σ(I)) and wR2 was 0.2405 (all data).
	*2-Hexyl-3-hydroxy-7,8,9,10-tetrahydro-6H-benzo[c]chromen-6-one (**3w**)*. Yield 1050 mg, 70%. Off-white solid, m.p. = 171–173°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.21 (s, 1H), 7.31 (s, 1H), 6.69 (s, 1H), 2.71 (br s, 2H), 2.52–2.56 (m, 2H), 2.35 (br s, 2H), 1.69–1.73 (m, 4H), 1.52 (br s, 2H), 1.27 (br s, 6H), 0.85 (br s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 161.1, 157.7, 151.1, 147.6, 126.1, 124.2, 118.2, 111.6, 101.4, 31.1, 29.3 (2C), 28.6, 24.6, 23.5, 22.1, 21.3, 20.9, 13.9. Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.83; H, 7.99.
	*3-Benzyl-9-hexyl-8-hydroxy-1,2,3,4-tetrahydro-5H-chromeno[3,4-c]pyridin-5-one (**3x**)*. Yield 1271 mg, 65%. White solid, m.p. = 162–164°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.34–7.41 (m, 6H), 6.75 (s, 1H), 3.93 (s, 2H), 3.43–3.47 (m, 1H), 2.96 (s, 4H), 2.55–2.58 (m, 2H), 1.50–1.57 (m, 2H), 1.28 (br s, 6H), 1.04–1.07 (m, 1H), 0.84–0.87 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 161.7, 159.3, 158.3, 151.3, 146.1, 135.6, 129.2, 128.2, 127.6, 126.5, 124.3, 114.6, 110.6, 101.5, 60.4, 49.0, 47.6, 30.9, 29.1, 29.0, 28.3, 24.2, 21.8, 13.6. Anal. Calcd for $C_{25}H_{29}NO_3$: C, 76.70; H, 7.47; N, 3.58. Found: C, 76.74; 7.36.
	*6-Bromo-7-hydroxy-4-propyl-2H-chromen-2-one (**3y**)*. Yield 877 mg, 62%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.19 (s, 1H), 7.80 (s, 1H), 6.86 (s, 1H), 6.05 (s, 1H), 2.69–2.72 (m, 2H), 1.64–1.70 (m, 2H), 1.02–1.04 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 159.9, 157.1, 156.0, 153.9, 128.7, 112.7, 110.2, 106.0, 103.2, 32.5, 21.1, 13.6. Anal. Calcd for $C_{12}H_{11}BrO_3$: C, 50.91; H, 3.92. Found: C, 50.77; H, 3.74.
	*7,8-Dihydroxy-4-methyl-2H-chromen-2-one*[6] *(**3z**)*. Yield 595 mg, 62%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.69 (br s, 1H), 9.13 (br s, 1H), 7.00 (d, *J* = 8.6 Hz, 1H), 6.75 (d, *J* = 8.6 Hz, 1H), 6.02 (s, 1H), 2.36 (s, 3H).
	*7,8-Dihydroxy-4-propyl-2H-chromen-2-one*[6] *(**3aa**)*. Yield 781 mg, 71%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.68 (br s, 1H), 9.14 (br s, 1H), 7.03 (d, *J* = 8.6 Hz, 1H), 6.75 (d, *J* = 8.6 Hz, 1H), 5.98 (s, 1H), 2.67–2.70 (m, 2H), 1.64–1.70 (m, 2H), 1.01–1.04 (m, 3H).

	*6,7-Dihydroxy-4-methyl-2H-chromen-2-one*[13] ***(3ab)***. Yield 586 mg, 61%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.92 (br s 1H), 9.01 (br s, 1H), 6.95 (s, 1H), 6.68 (s, 1H), 5.99 (d, *J* = 1.0 Hz, 1H), 2.32 (d, *J* = 1.0 Hz, 3H).
	*6,7-Dihydroxy-4-propyl-2H-chromen-2-one*[14] ***(3ac)***. Yield 715 mg, 65%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.93 (br s, 1H), 8.97 (br s, 1H), 6.98 (s, 1H), 6.68 (s, 1H), 5.94 (s, 1H), 2.62–2.65 (m, 2H), 1.66–1.71 (m, 2H), 1.01–1.05 (m, 3H).
	*7-Methoxy-4-methyl-2H-chromen-2-one*[15] ***(3ad)***. Yield 608 mg, 64%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (d, *J* = 9.3 Hz, 1H), 6.88-6.90 (m, 2H), 6.11 (s, 1H), 3.87 (s, 3H), 2.41 (s, 3H).
	*Ethyl (2-oxo-4-propyl-2H-chromen-7-yl)carbamate*[16] ***(3ae)***. Yield 702 mg, 51%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 7.72 (d, *J* = 8.7 Hz, 1H), 7.54 (d, *J* = 1.0 Hz, 1H), 7.39 (dd, *J* = 8.7, 1.0 Hz, 1H), 6.16 (s, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.69–2.73 (m, 2H), 1.58–1.68 (m, 2H), 1.24–1.28 (m, 3H), 0.97 (t, *J* = 7.1 Hz, 3H).
	*Ethyl (2-oxo-4-phenyl-2H-chromen-7-yl)carbamate*[16] ***(3af)***. Yield 773 mg, 50%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.18 (s, 1H), 7.53–7.64 (m, 6H), 7.36 (br s, 2H), 6.24 (s, 1H), 4.17 (q, *J* = 6.6 Hz, 2H), 1.26 (t, *J* = 6.6 Hz, 3H).
	*6-Methoxy-4-propyl-2H-benzo[h]chromen-2-one* ***(3ag)***. Yield 804 mg, 60%. Off-white solid, m.p. = 170–172 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.28–8.29 (m, 1H), 8.15–8.16 (m, 1H), 7.67–7.72 (m, 2H), 6.94 (s, 1H), 6.35 (m, 1H), 4.01 (s, 3H), 2.79–2.82 (m, 2H), 1.66–1.72 (m, 2H), 1.00–1.02 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 160.3, 157.7, 151.5, 144.8, 128.7, 128.3, 126.8, 123.6, 122.3, 122.1, 114.8, 113.4, 98.1, 56.4, 33.5, 21.2, 14.1. Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 75.93; H, 5.94.
	*Ethyl 9-methyl-5-oxo-1,2,3,4,5,10-hexahydroisochromeno[3,4-f]indole-8-carboxylate* ***(4a)***. Yield 1398 mg, 86%. Off-white solid, m.p. > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.00 (s, 1H), 7.62 (s, 1H), 7.43 (s, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.75 (s, 2H); 2.66 (s, 3H), 2.38 (s, 2H), 1.68-1.78 (m, 2H), 1.37 (t, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.6, 161.0, 148.6, 147.3, 146.9, 131.8, 128.5, 120.2, 114.8, 105.8, 104.9, 102.7, 59.0, 24.6, 23.7, 21.2, 20.9, 14.4, 13.9. Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 70.02; H, 5,95; N, 4.27.
	*Ethyl 2-methyl-6-oxo-8-propyl-1,6-dihydropyrano[2,3-f]indole-3-carboxylate* ***(4b)***. Light brown solid, m.p. > 300 °C. Yield 751 mg, 48%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.98 (br s, 1H), 7.76 (br s, 1H), 7.67 (br s, 1H), 6.40 (s, 1H), 4.32 (q, *J* = 6.8 Hz, 2H), 2.74–2.89 (m, 2H), 2.70 (s, 3H), 1.70–1.75 (m, 2H), 1.38 (t, *J* = 6.8 Hz, 3H), 1.00–1.04 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 164.3, 160.3, 156.4, 149.1, 148.5, 131.8, 129.5, 113.8, 111.1, 106.2 (2C), 102.9, 58.8, 32.9, 20.9, 14.2, 13.7, 13.5. Anal. Calcd for $C_{18}H_{19}NO_4$: C, 69.00;

	H, 6.11; N, 4.47. Found: C, 68.86; H, 6.23; N, 4.39.
	*Ethyl 2-methyl-6-oxo-8-phenyl-1,6-dihydropyrano[2,3-f]indole-3-carboxylate (**4c**)*. Light brown solid, m.p. > 300 °C. Yield 781 mg, 45%.^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 7.86 (s, 1H), 7.60 (br s, 5H), 7.37 (s, 1H), 6.30 (s, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.67 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 164.4, 160.3, 155.7, 149.5, 148.9, 135.4, 131.8, 129.8, 129.5, 128.8, 128.5, 113.6, 112.4, 108.6, 106.5, 103.0, 59.1, 14.4, 14.0. Anal. Calcd for $C_{21}H_{17}NO_4$: C, 72.61; H, 4.93; N, 4.03. Found: C, 72.79; H, 4.98; N, 3.90.
	*4,6,7-Triphenylpyrano[3,2-f]indol-2(8H)-one (**4d**)*. Off-white solid, m.p. > 300 °C. Yield 1282 mg, 62%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.01 (s, 1H), 7.26-7.59 (m, 17H), 6.23 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 160.3, 156.3, 150.3, 137.9, 136.3, 135.6, 134.1, 131.5, 129.6 (2C), 128.7 (4C), 128.6 (2C), 128.5 (2C), 128.1 (2C), 126.7, 125.8, 117.1, 113.8, 112.6, 111.2, 98.1. Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 70.02; H, 5,95; N, 4.27.
	*6,7-Diphenyl-4-(thiophen-2-yl)pyrano[3,2-f]indol-2(8H)-one (**4e**)*. Off-white solid, m.p. > 300 °C. Yield 1111 mg, 53%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (br s, 1H), 8.07 (br s, 1H), 7.87 (br s, 1H), 7.64 (br s, 1H), 7.29-7.47 (m, 13H), 6.35 (br s, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 160.05, 150.21, 148.49, 137.9, 136.5, 136.0, 134.1, 131.5, 129.9, 129.6 (2C), 129.5, 128.8 (2C), 128.6 (2C), 128.3, 128.1 (3C), 126.7, 125.9, 116.8, 113.9, 111.7, 111.0, 98.3. Anal. Calcd for $C_{27}H_{17}NO_2S$: C, 77.31; H, 4.08; N, 3.34; S, 7.64. Found: C, 77.16; H, 4.20; N, 3.27; S, 7.73.
	*10,11-Diphenyl-1,2,3,4,5,9-hexahydro-6H-cyclohepta[4,5] pyrano[3,2-f]indol-6-one (**4f**)*. Off-white solid, m.p. > 300 °C. Yield 1520 mg, 75%. ^{1}H NMR (600 MHz, DMF-d_7) δ 11.93 (s, 1H), 7.98 (s, 1H), 7.36-7.58 (m, 11H), 3.05-3.07 (m, 2H), 2.88-2.90 (m, 2H), 1.87-1.89 (m, 2H), 1.65-1.67 (m, 2H), 1.55-1.57 (2H). ^{13}C{^{1}H} NMR (151 MHz, DMF-d_7) δ 156.0, 150.8, 139.0, 137.5, 136.1, 133.4, 131.3, 130.0, 129.7, 129.4, 129.0, 127.8, 127.4, 125.5, 115.5, 115.4, 115.1, 98.9, 32.8, 28.9, 27.5, 26.9, 26.3. Anal. Calcd for $C_{28}H_{23}NO_2$: C, 82.94; H, 5.72; N, 3.45. Found: C, 82.85; H, 5.80; N, 3.31.
	*4-Phenyl-6,7-bis(3,4,5-trimethoxyphenyl)pyrano[3,2-f]indol-2(8H)-one (**4g**)*. Off-white solid, m.p. 210–212 °C. Yield 2018 mg, 68%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 7.61-7.63 (m, 3H), 7.53-7.54 (m, 3H), 7.48 (s, 1H), 6.84 (s, 2H), 6.62 (s, 2H), 6.23 (s, 1H), 3.68 (s, 3H), 3.66 (s, 6H), 3.64 (s, 3H), 3.60 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 160.4, 156.4, 153.0 (2C), 152.7 (2C), 150.3, 137.6, 137.5, 136.3, 136.1, 135.8, 129.5, 128.7 (2C), 128.5 (2C), 126.6, 125.6, 117.3, 113.6, 112.6, 111.2, 107.0 (2C), 105.8 (2C), 97.9, 60.14 (3C), 60.07 (3C), 55.8 (6C), 55.7 (6C). Anal. Calcd for $C_{35}H_{31}NO_8$: C, 70.82; H, 5.26; N, 2.36. Found: C, 70.72; H, 5.16; N, 2.51.

Decarboxylation of ethyl indole-3-carboxylates

Compound **4a** or **4b** (0.32 mmol) was added to a solution of 0.07 mL H_2SO_4 in 0.5 mL AcOH. The reaction mixture was stirred under heating for 36 hours, then poured into water and the precipitate was filtered off. The resulting precipitate was purified by flash chromatography (chloroform/silica gel) to give decarboxylated indole **6a** and **6b**, respectively.

Structure	Analytical Data
	*9-Methyl-2,3,4,10-tetrahydroisochromeno[3,4-f]indol-5(1H)-one (**6a**).* Light yellow solid with m.p. = 279–281 °C. Yield 38 mg, 47%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.19 (s, 1H), 7.51 (s, 1H), 7.33 (s, 1H), 6.21 (s, 1H), 2.84-2.87 (m, 2H), 2.43 (m, 5H), 1.72-1.84 (m, 4H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 161.4, 147.9, 145.7, 140.8, 133.4, 130.5, 119.2, 113.6, 104.1, 104.0, 99.3, 24.8, 23.8, 21.4, 21.1, 13.6. Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: 75.79; H, 6.08; N, 5.35.
	*2-Methyl-6-oxo-8-propyl-1,6-dihydropyrano[2,3-f]indole (6b).* Light yellow solid with m.p. = 147–149 °C. Yield 32 mg, 41%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (br s, 1H), 7.51 (s, 1H), 7.42 (s, 1H), 6.28 (s, 1H), 6.19 (s, 1H), 2.75–2.79 (m, 2H), 1.73–1.80 (m, 2H), 1.04–1.08 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 156.7, 148.4, 140.6, 133.4, 132.2, 114.0, 111.4, 106.1, 104.6, 100.9, 34.1, 29.7, 21.6, 14.1, 14.0. Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81. Found: C, 74.57; H, 6.38; N, 5.64.

Calculation of Green Chemistry Metrics (EcoScale and E-factor)

(a) Calculation of EcoScale indexes under ball milling (This work)

The penalty points for synthesis of coumarin derivatives under ball milling (This work)

Parameter	**Penalty**
1. Yields 50-93	25-3.5
2. Price of reaction components β-ketoester Phenol MsOH	 0 0 0
3. Safety non-dangerous for environment, non-toxic, non-flammable	 0
4. Technical setup Unconventional activation technique	 2
5. Temperature/time Room temperature < 24 h	 1
6. Workup and purification Crystallization and filtration	 1
Penalty points total:	29-7.5

EcoScale Score = 100 - Total penalty points = 71-92.5

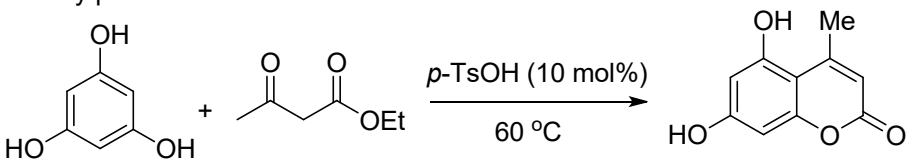
EcoScale Score for the synthesis of 5,7-dihydroxy-4-methyl-2H-chromen-2-one (3a) under the ball-milling conditions:

Parameter	Penalty
1. Yields 87%	6.5
2. Price of reaction components Ethyl acetoacetate 3,5-Dihydroxy phenol MsOH	 0 0 0
3. Safety non-dangerous for environment, non-toxic, non-flammable	 0
4. Technical setup Unconventional activation technique	 2
5. Temperature/time Room temperature < 24 h	 1
6. Workup and purification Crystallization and filtration	 1
Penalty points total:	10.5

EcoScale Score = 100 - Total penalty points
= 89.5

(b) Calculation of EcoScale index for the synthesis of 5,7-dihydroxy-4-methyl-2H-chromen-2-one (3a) under the conventional stirring under solvent-free heating conditions (*Chem. Lett*., 2001, 30, 110)[17]

Penalty points calculations:

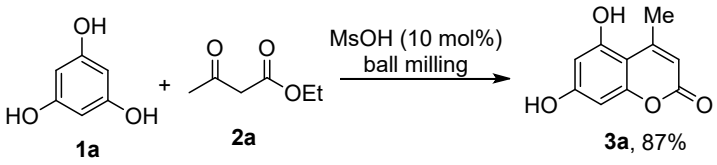


1a **2a** **3a**, 81%

Parameter	Penalty
1. Yields 81%	9.5
2. Price of reaction components Ethyl acetoacetate 3,5-Dihydroxy phenol l *p*-TsOH	 0 0 0
3. Safety non-dangerous for environment, non-toxic, non-flammable	 0
4. Technical setup Unconventional activation technique	 2
5. Temperature/time Room temperature < 1 h	 0
6. Workup and purification Crystallization and filtration	 1
Penalty points total:	12.5

EcoScale Score = 100 - Total penalty points = 87.5

(c) Calculation of E-factor for the synthesis of 5,7-dihydroxy-4-methyl-2H-chromen-2-one (3a) under the ball-milling conditions (this work):



E-factor calculation for the synthesis of 3a under ball-milling conditions:

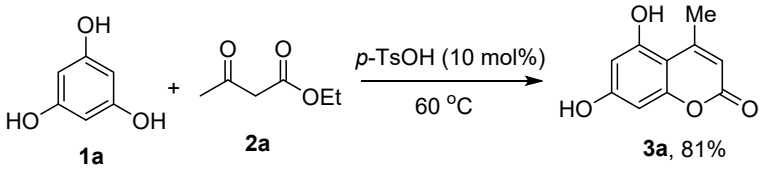
Reactant 1 (**1a**):	3,5-Dihydroxy phenol	0.126 g	1 mmol	FW 126.11
Reactant 2 (**2a**):	Ethyl acetoacetate	0.143 g	1.1 mmol	FW 130.14
Reagent:	MsOH	0.010 g	0.1 mmol	FW 96.11
Solvent:	------	------	------	------
Auxiliary (grinding):	------	------	------	------
Product (**3a**):	5,7-dihydroxy-4-methyl-2*H*-chromen-2-one	0.167 g	0.87 mmol	FW 192.17

Product yield = 87%

$$\text{E-factor} = \frac{0.126 + 0.143 + 0.010 - (0.167)}{0.167} = \textbf{0.67 Kg waste/1 Kg product}$$

Note: (i) Calculations were done on 1 mmol scale. (ii) When the authors have not reported the amount of solvent used in the work-up procedure, we have not accounted for solvent and considered that solvent can be recovered.

(d) Calculation of E-factor for the synthesis of 5,7-dihydroxy-4-methyl-2H-chromen-2-one (3a) under the conventional stirring under solvent-free heating conditions (*Chem. Lett.*, 2001, 30, 110)[17]



E-factor calculation for the synthesis of 3a under the conventional stirring under solvent-free heating conditions:

Reactant 1 (**1a**):	3,5-Dihydroxy phenol	0.126 g	1 mmol	FW 126.11
Reactant 2 (**2a**):	Ethyl acetoacetate	0.130 g	1 mmol	FW 130.14
Reagent:	*p*-TsOH	0.017 g	0.1 mmol	FW 172.20
Solvent:	------	------	------	------
Auxiliary (grinding):	------	------	------	------
Product (**3a**):	5,7-dihydroxy-4-methyl-2*H*-chromen-2-one	0.155 g	0.81 mmol	FW 192.17

Product yield = 81%

$$\text{E-factor} = \frac{0.126 + 0.130 + 0.017 - (0.155)}{0.155} = \textbf{0.76 Kg waste/1 Kg product}$$

Note: (i) Calculations were done on 1 mmol scale. (ii) When the authors have not reported the amount of solvent used in the work-up procedure, we have not accounted for solvent and considered that solvent can be recovered.

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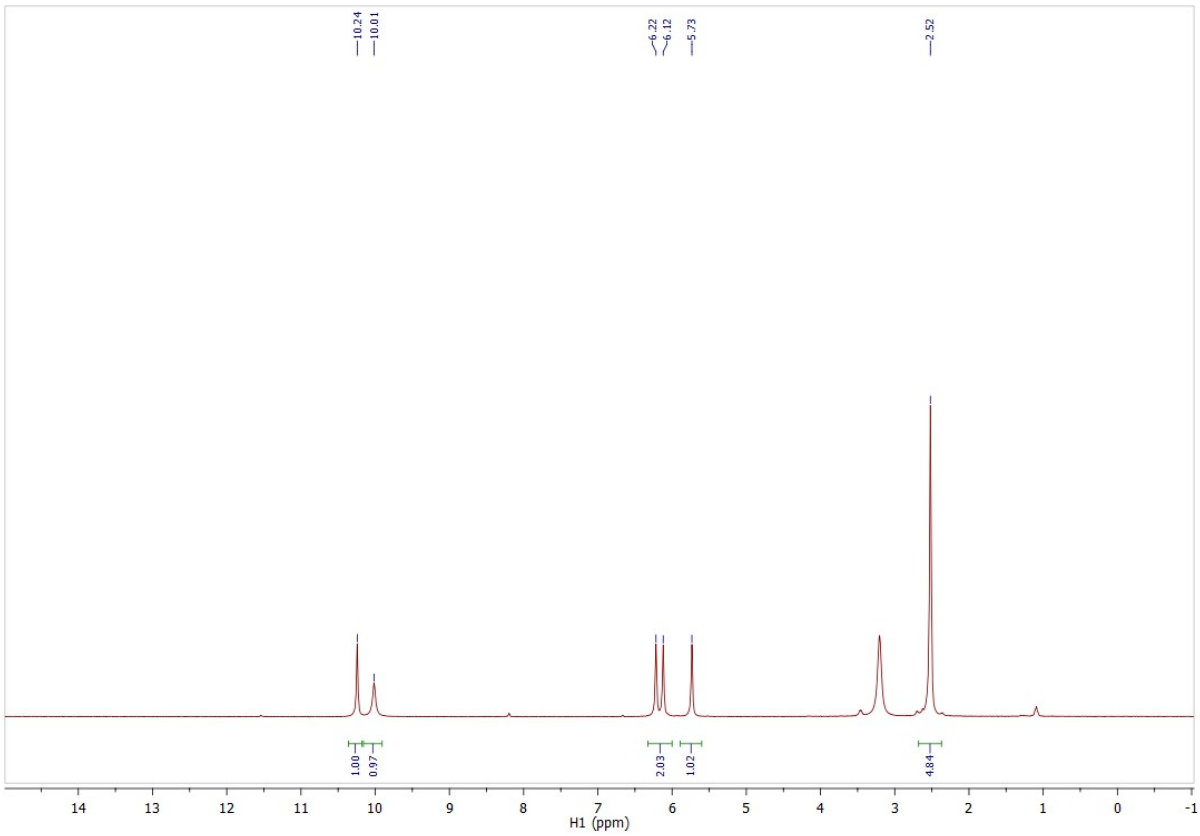

Figure S1. ^{1}H NMR spectrum of 3a

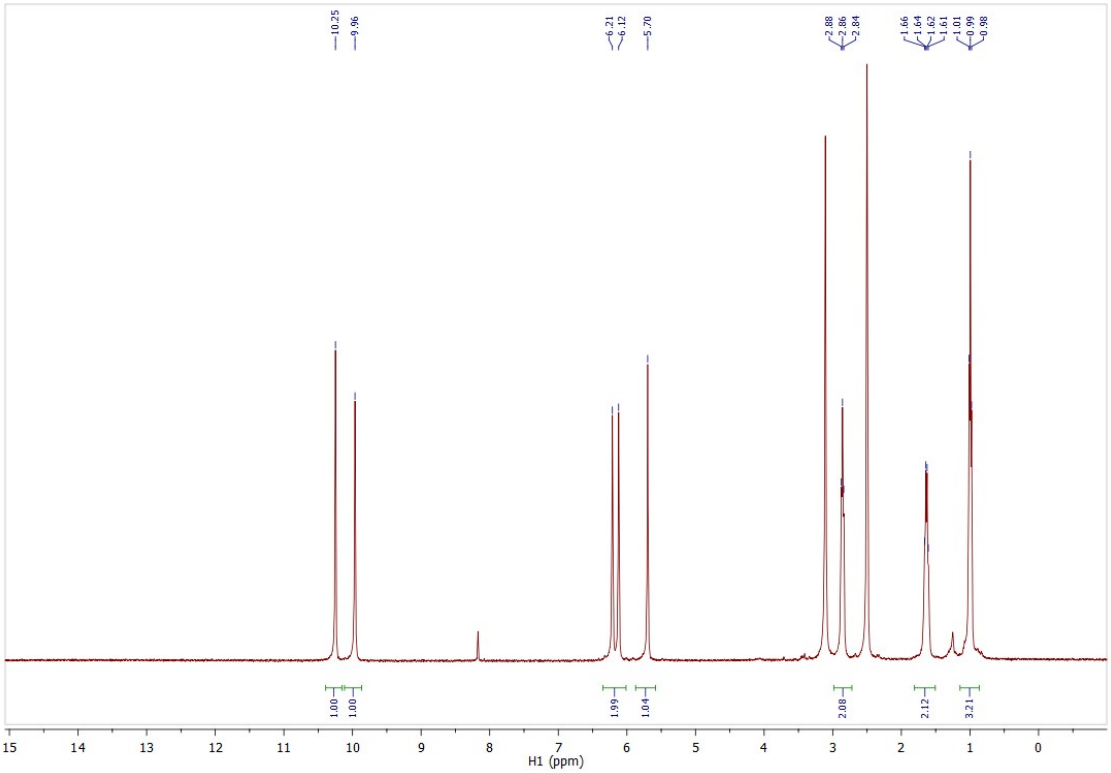

Figure S2. ^{1}H NMR spectrum of 3b

A B

Figure S3. View of the reactor with the reaction mass containing compound 3a after completion of the reaction; 25 mmol scaling.

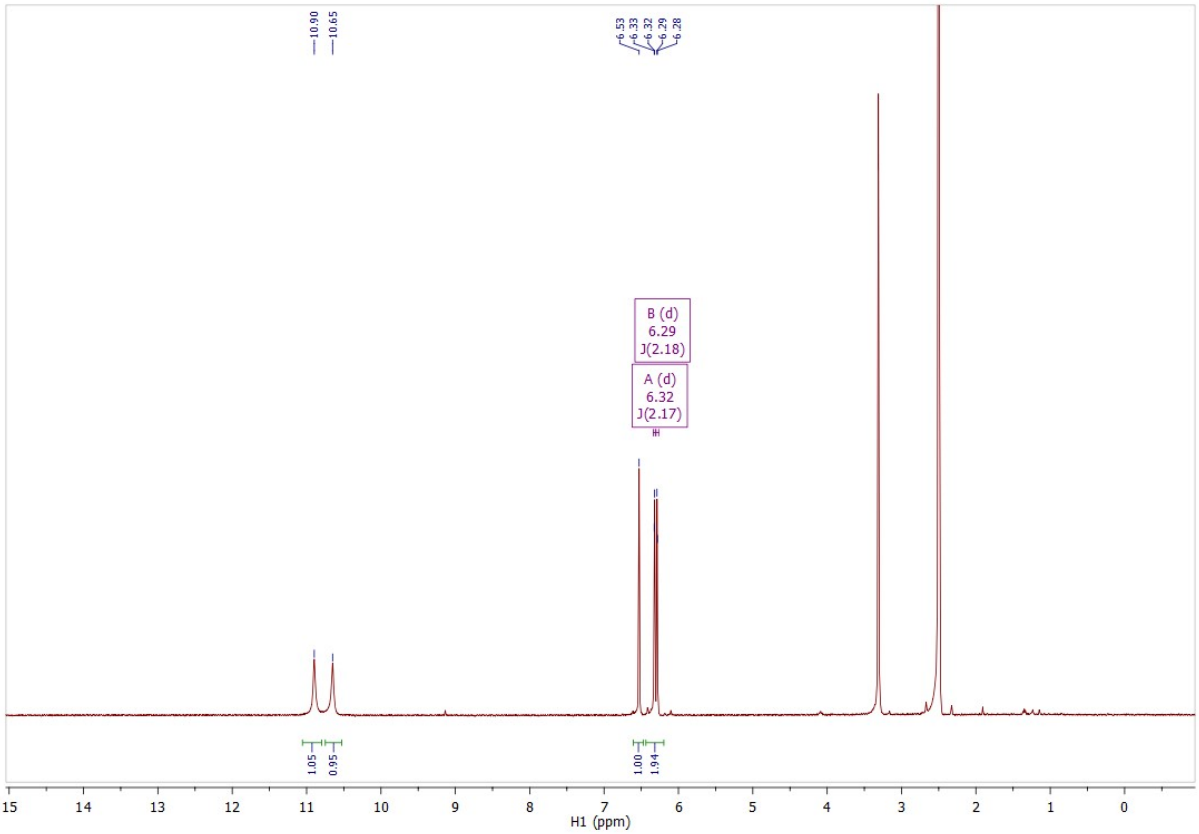

Figure S4. ^{1}H NMR spectrum of 3c

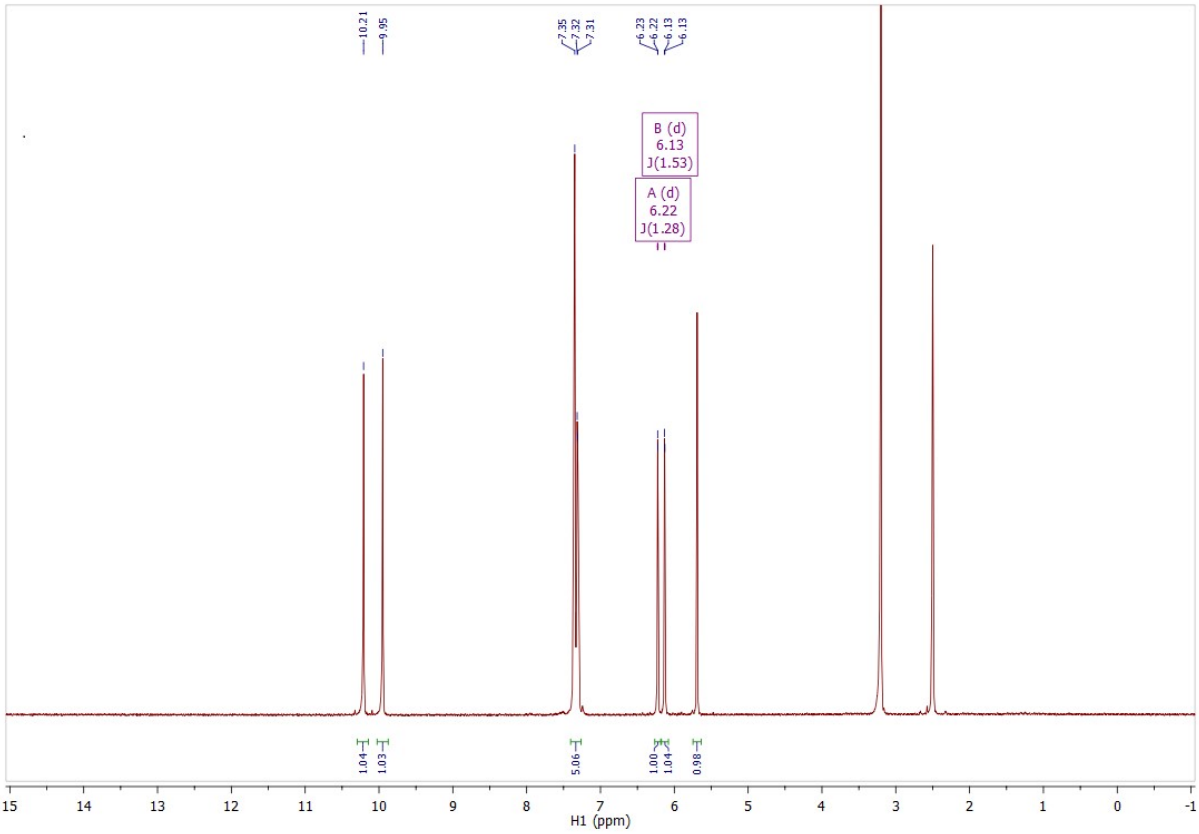

Figure S5. ^{1}H NMR spectrum of 3d

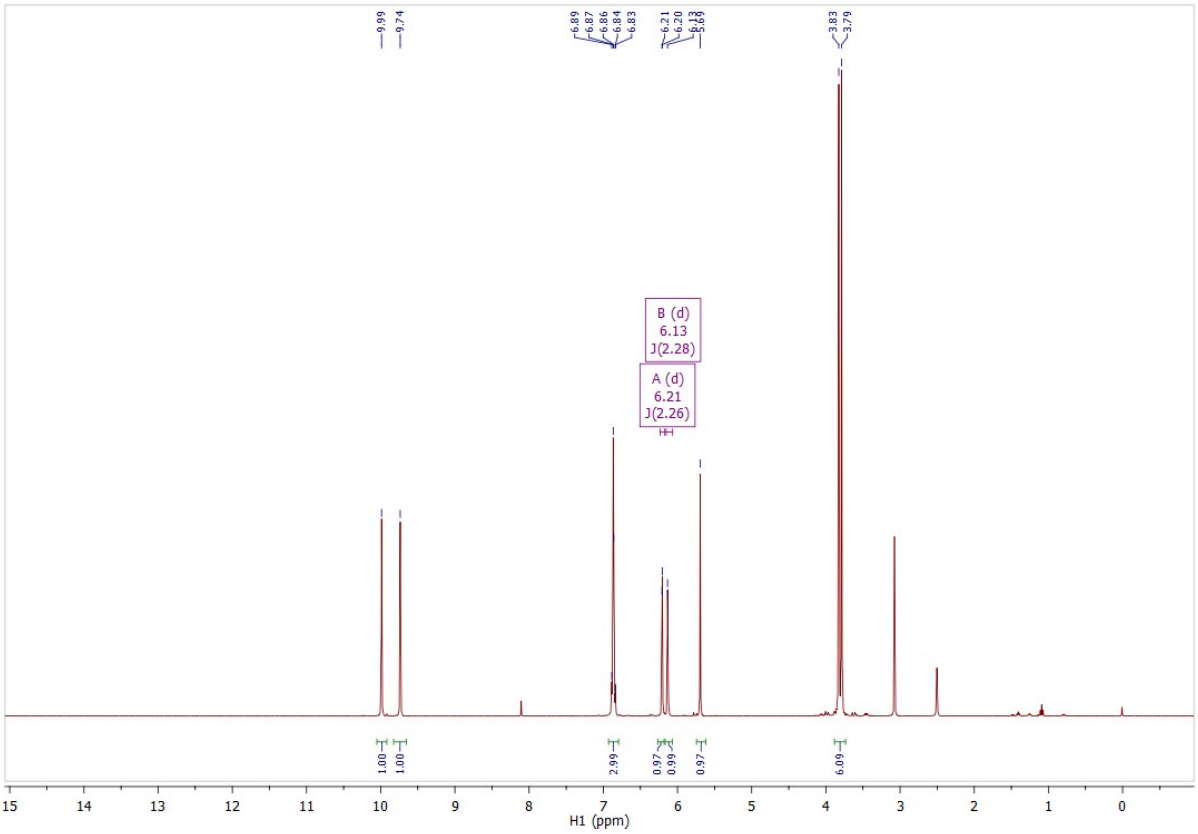

Figure S6. ^{1}H NMR spectrum of 3e

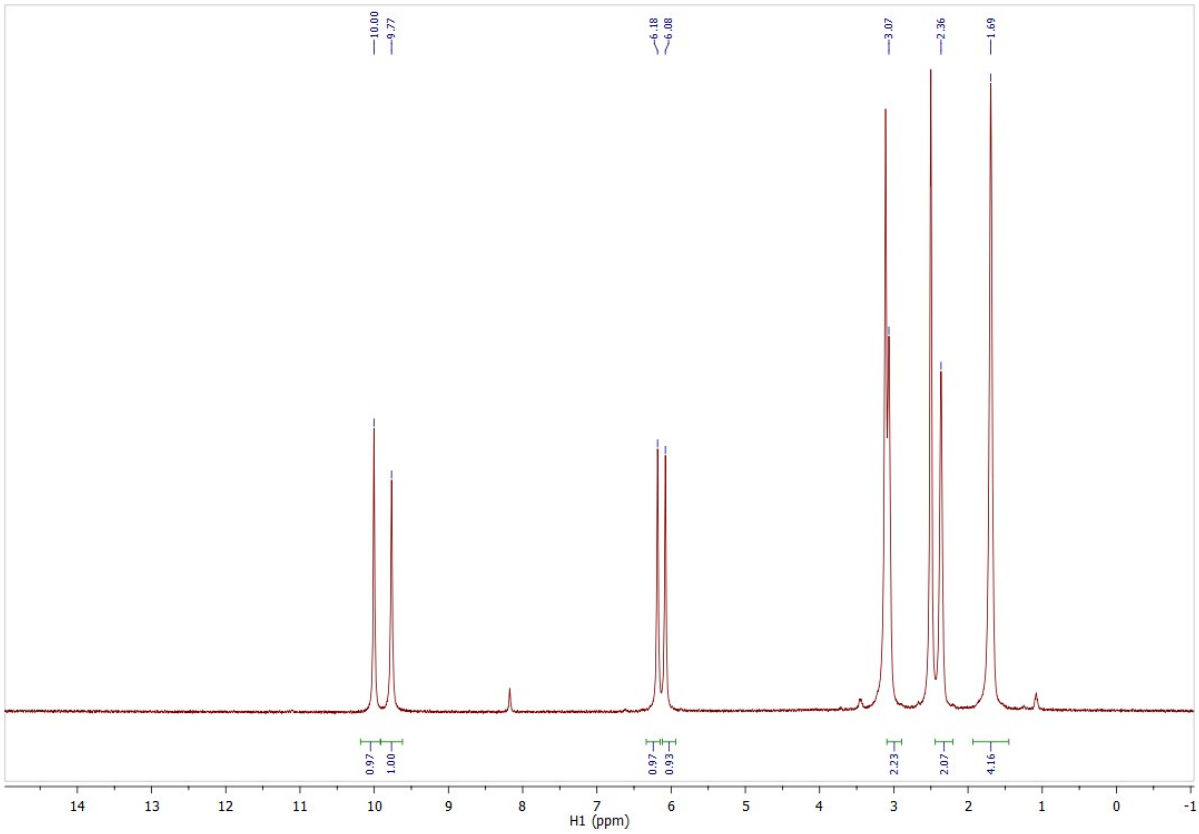

Figure S7. ^{1}H NMR spectrum of 3f

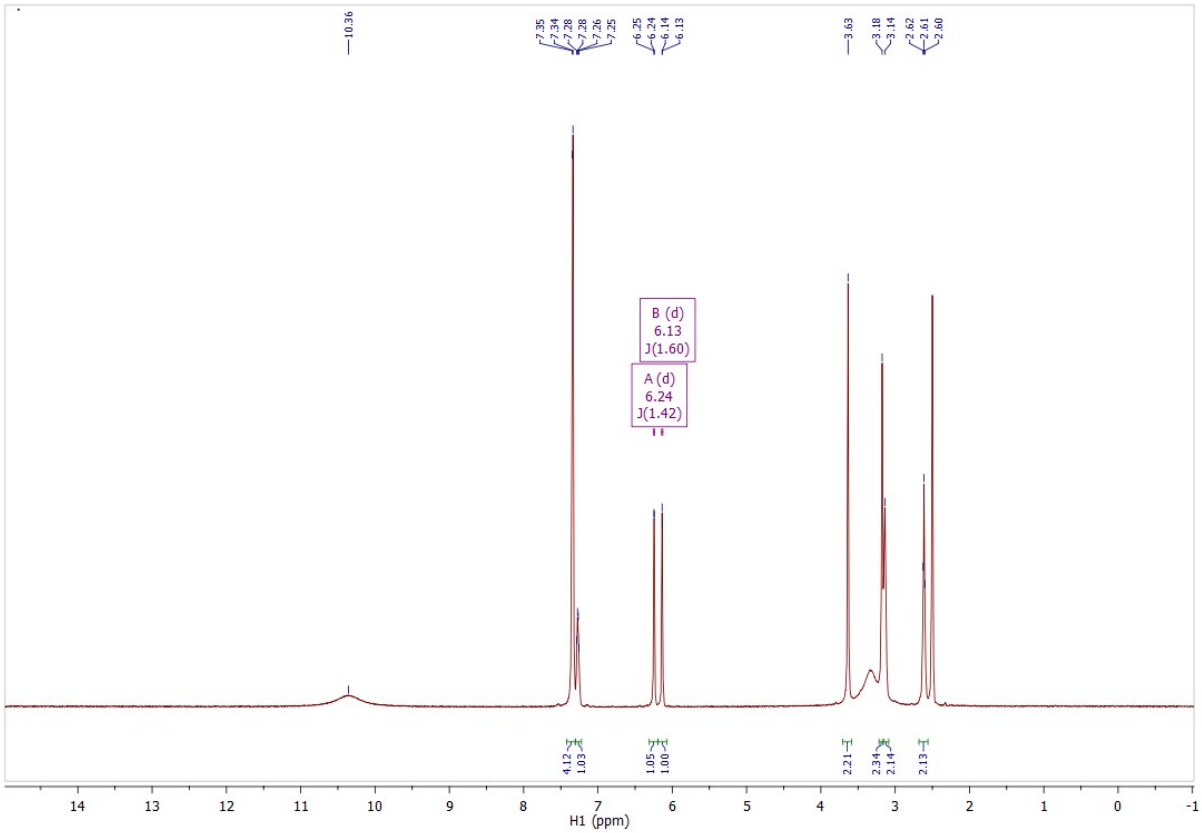

Figure S8. ^{1}H NMR spectrum of 3g

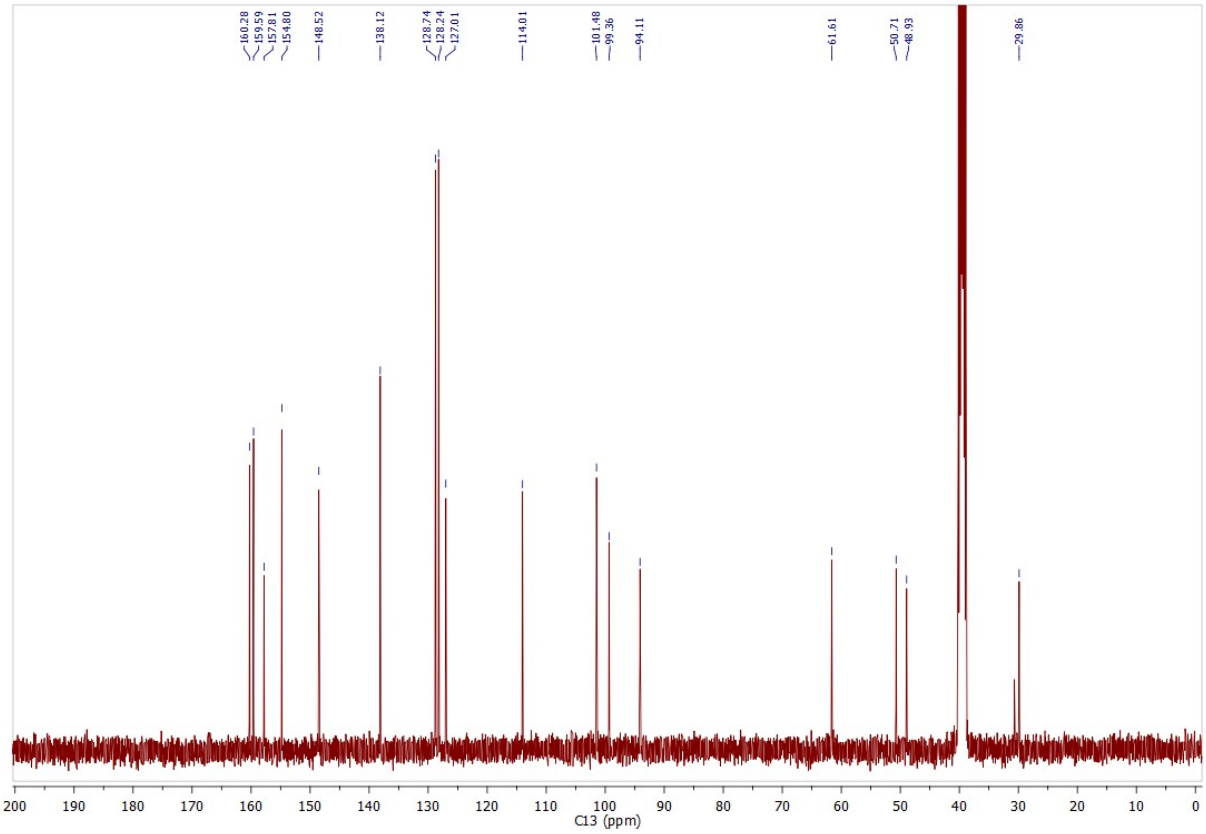

Figure S9. ^{13}C NMR spectrum of 3g

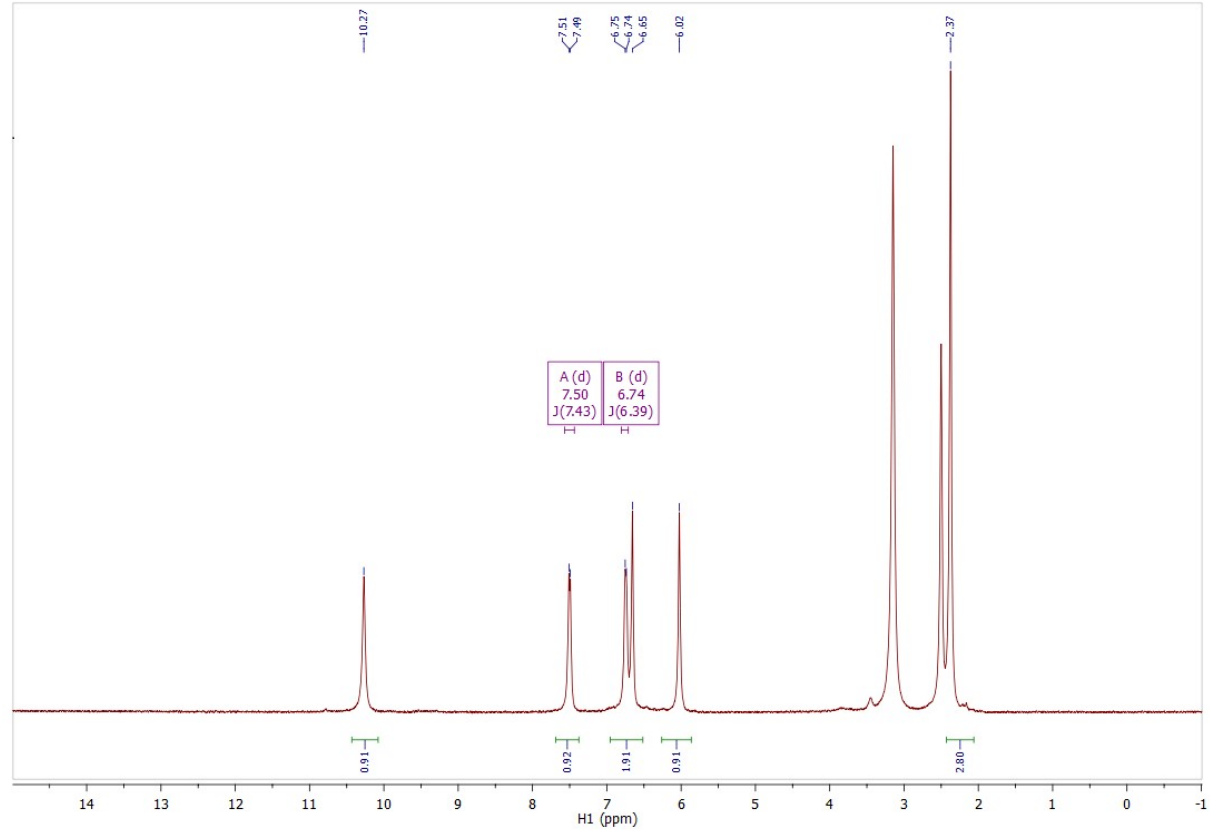

Figure S10. ^{1}H NMR spectrum of 3h

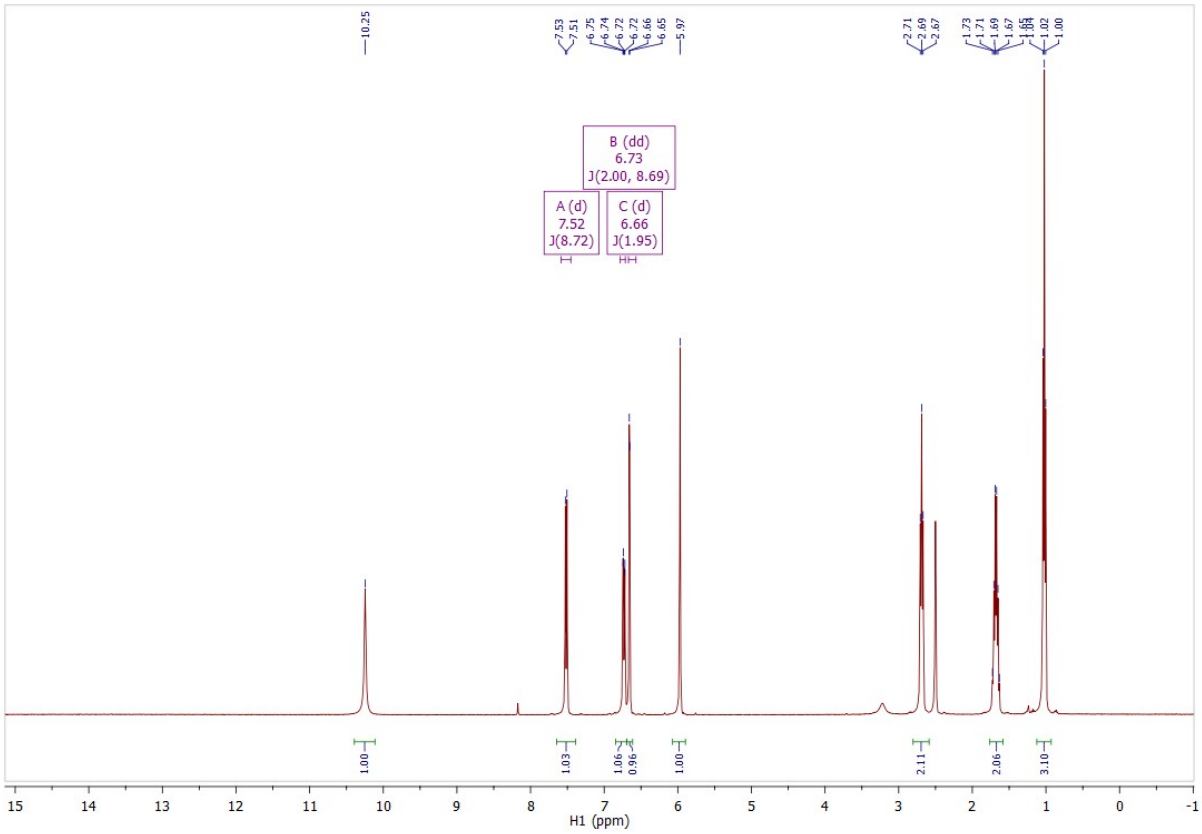

Figure S11. ^{1}H NMR spectrum of 3i

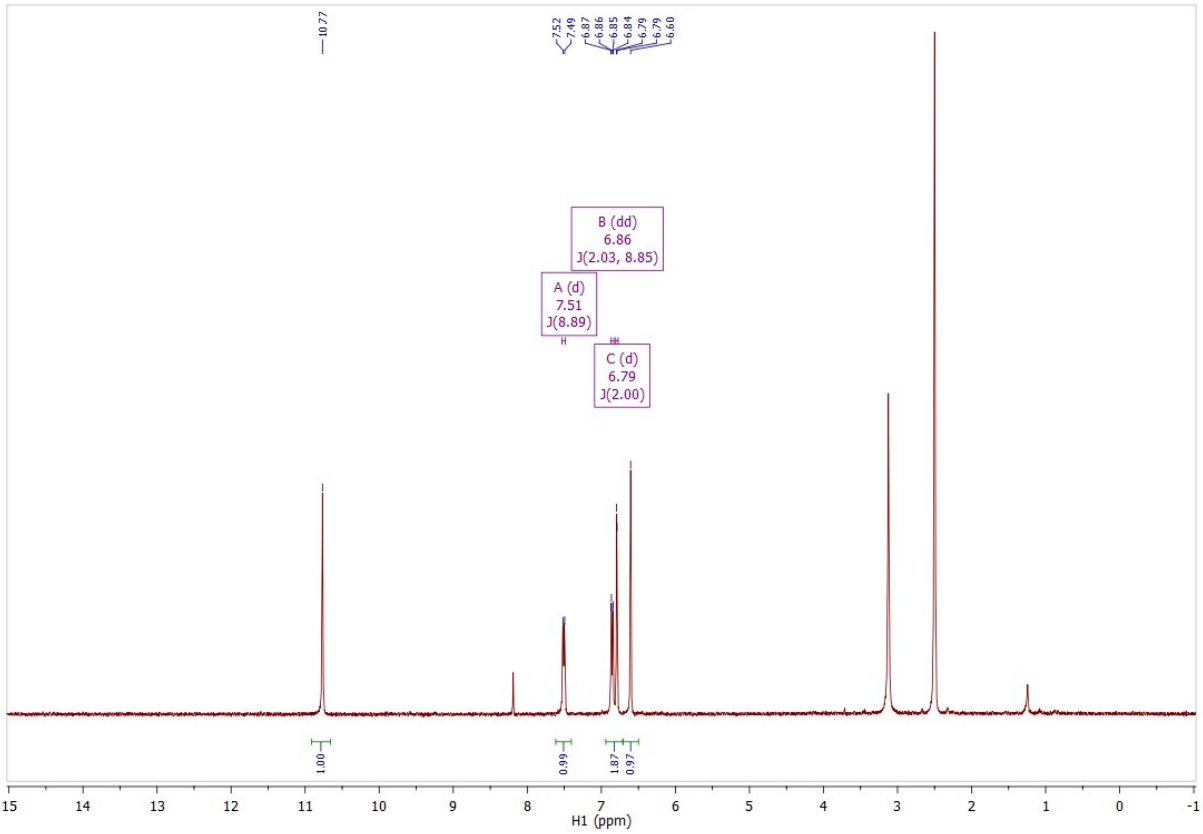

Figure S12. ^{1}H NMR spectrum of 3j

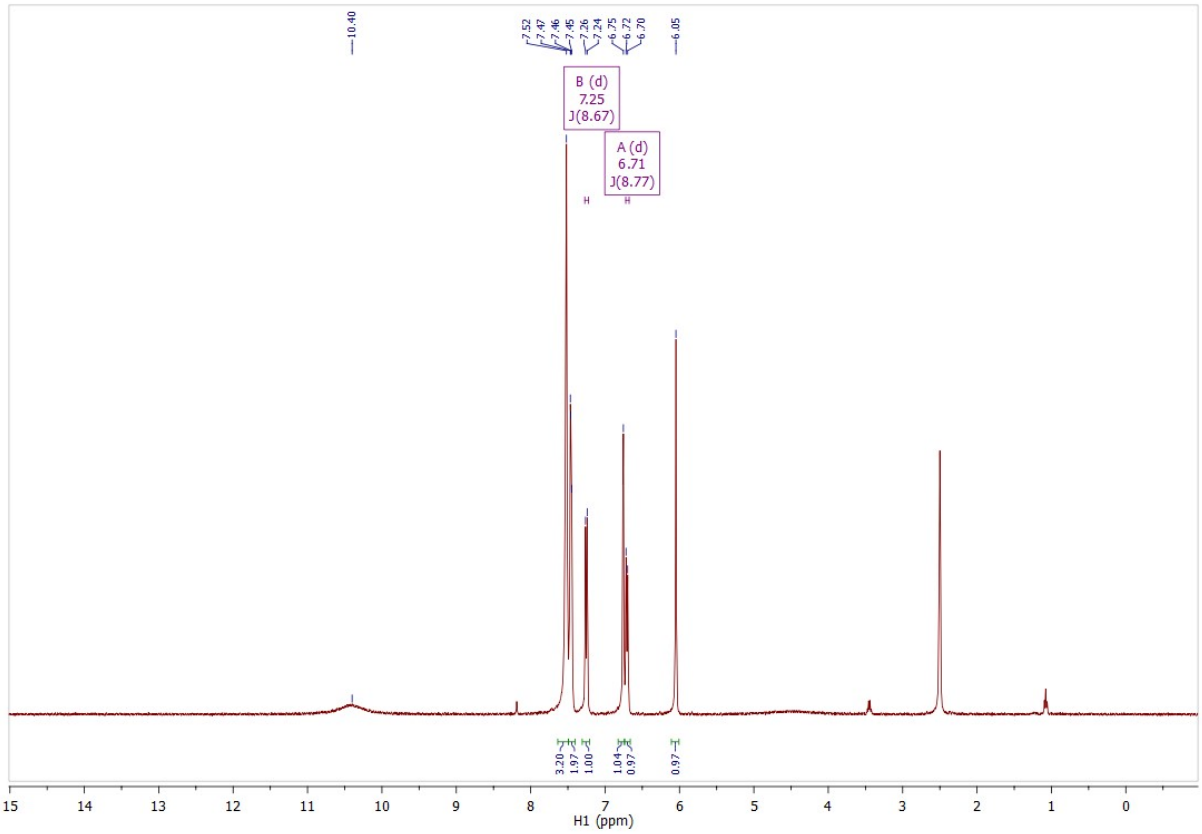

Figure S13. ^{1}H NMR spectrum of 3k

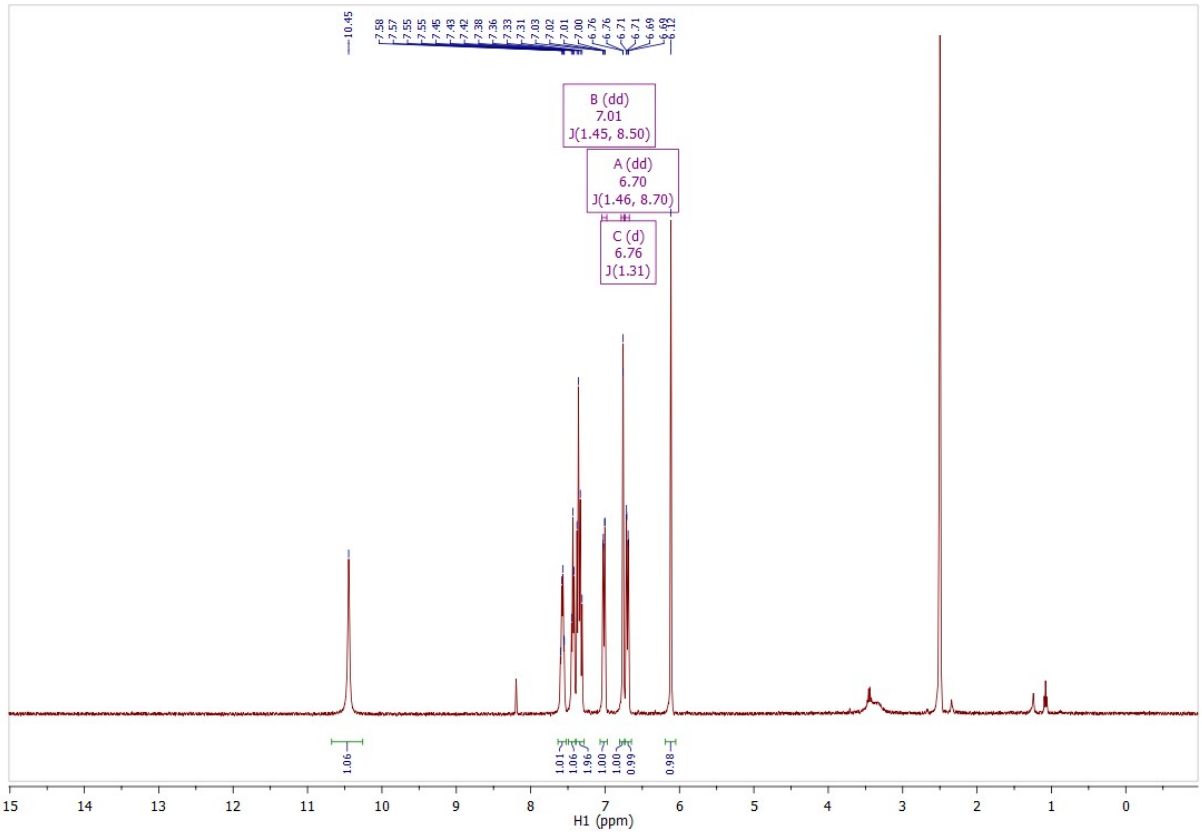

Figure S14. ^{1}H NMR spectrum of 3l

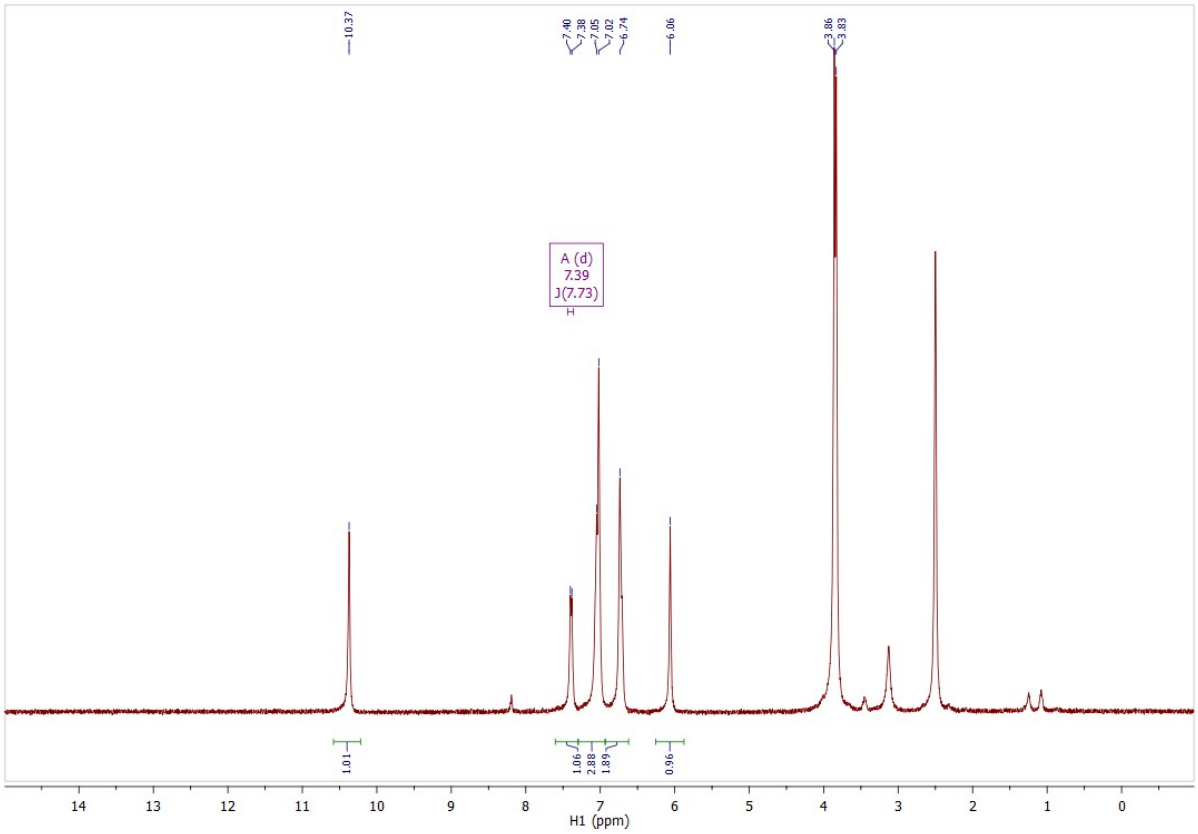

Figure S15. ^{1}H NMR spectrum of 3m

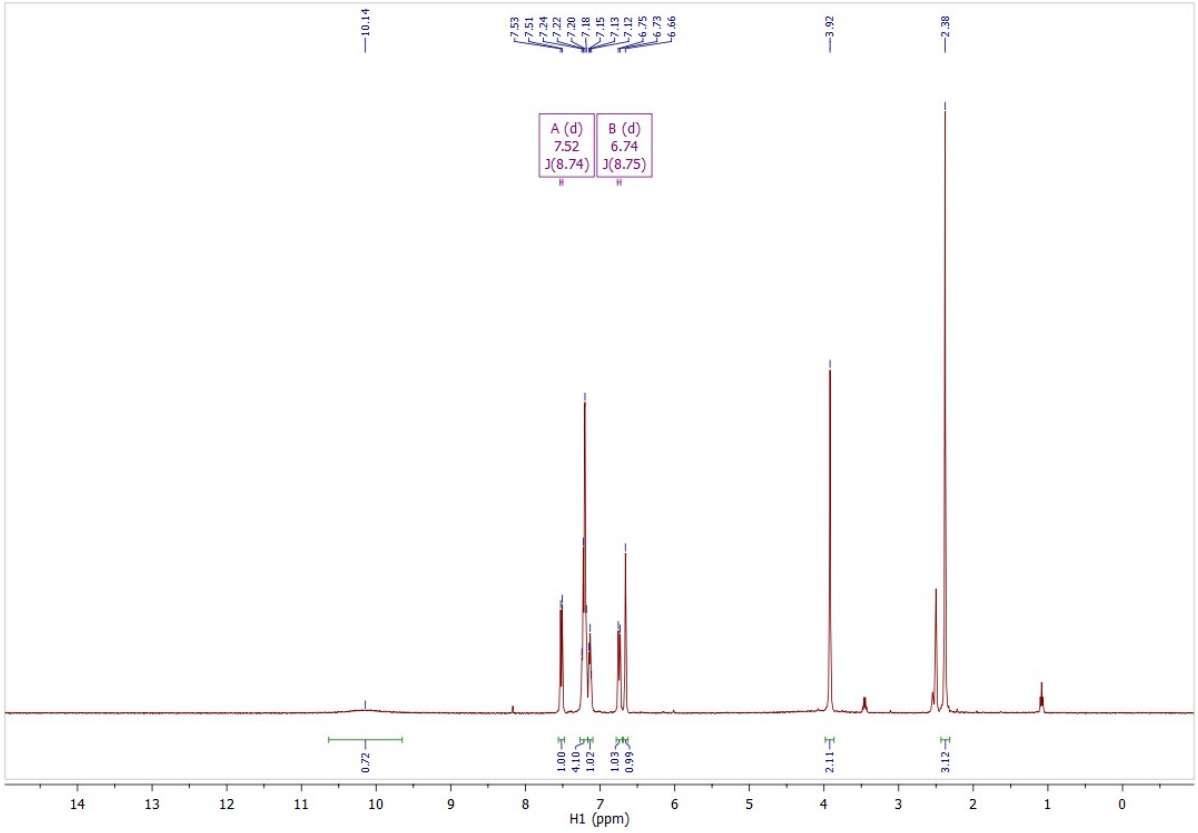

Figure S16. ^{1}H NMR spectrum of 3n

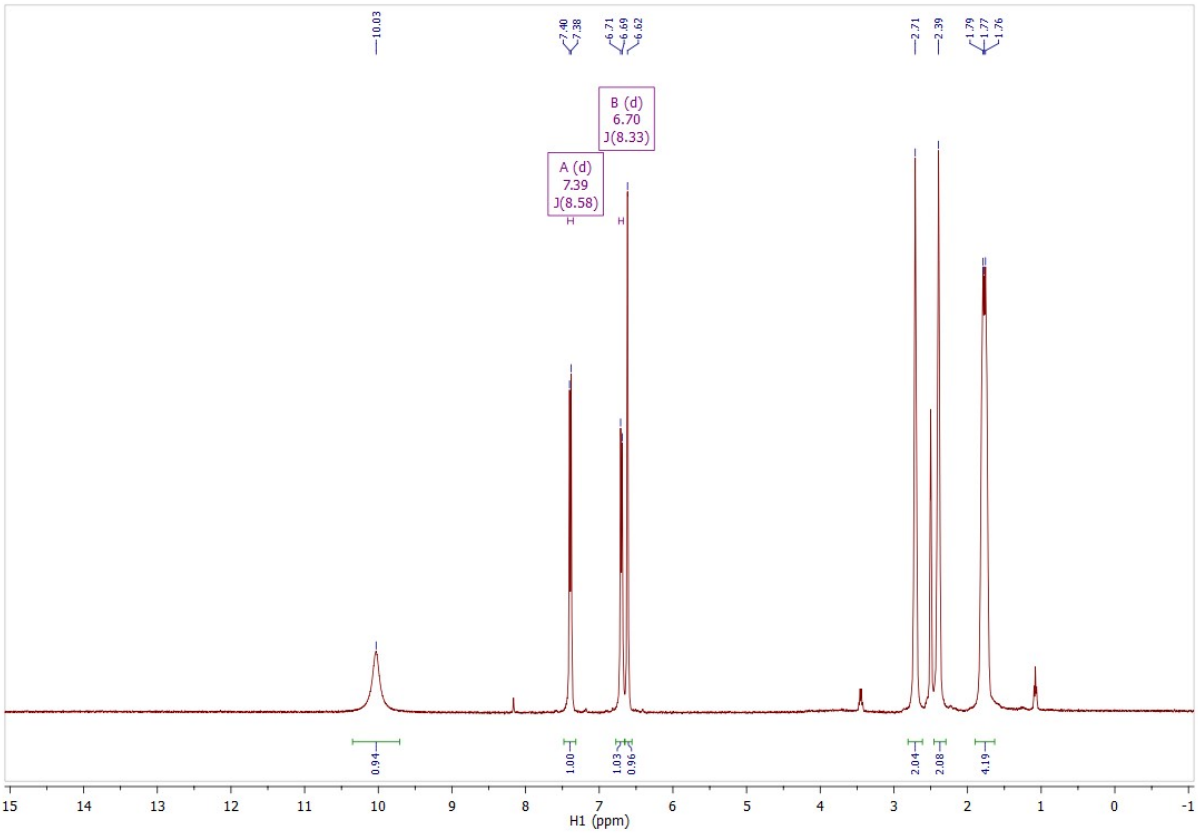

Figure S17. ^{1}H NMR spectrum of 3o

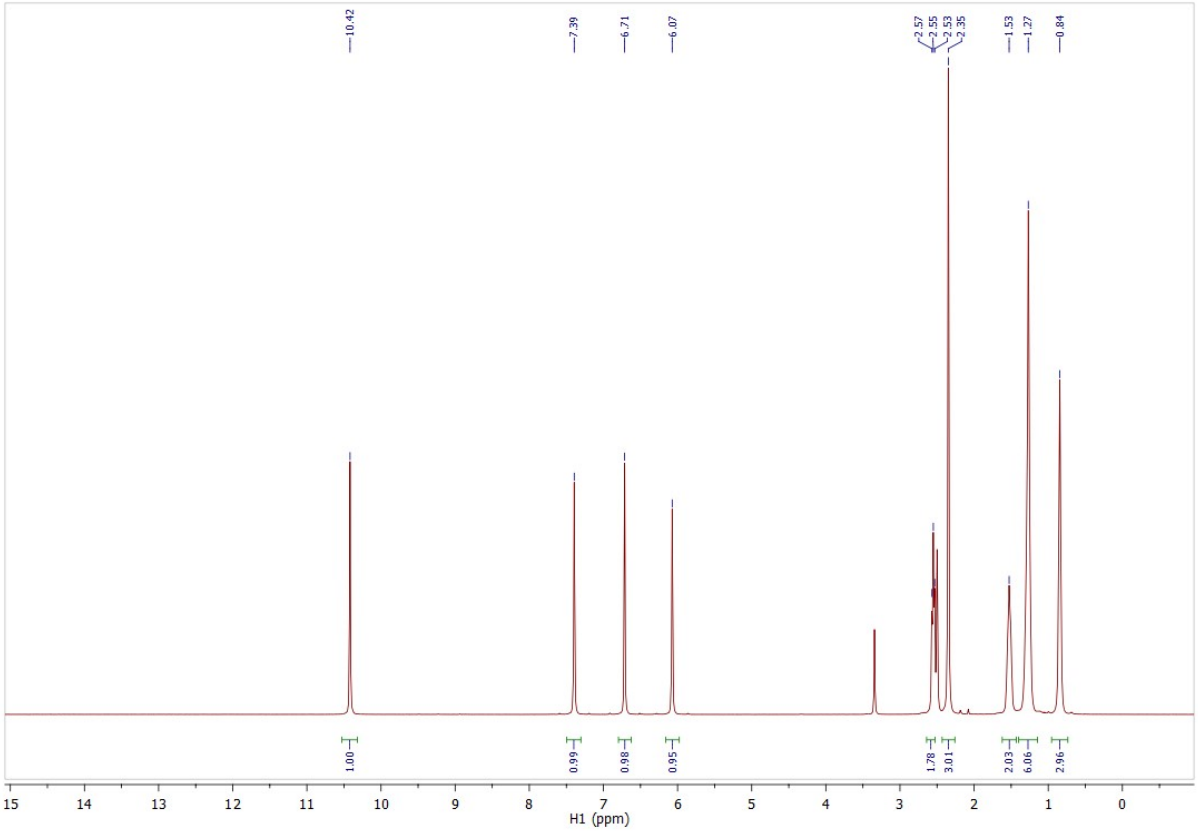

Figure S18. ^{1}H NMR spectrum of 3p

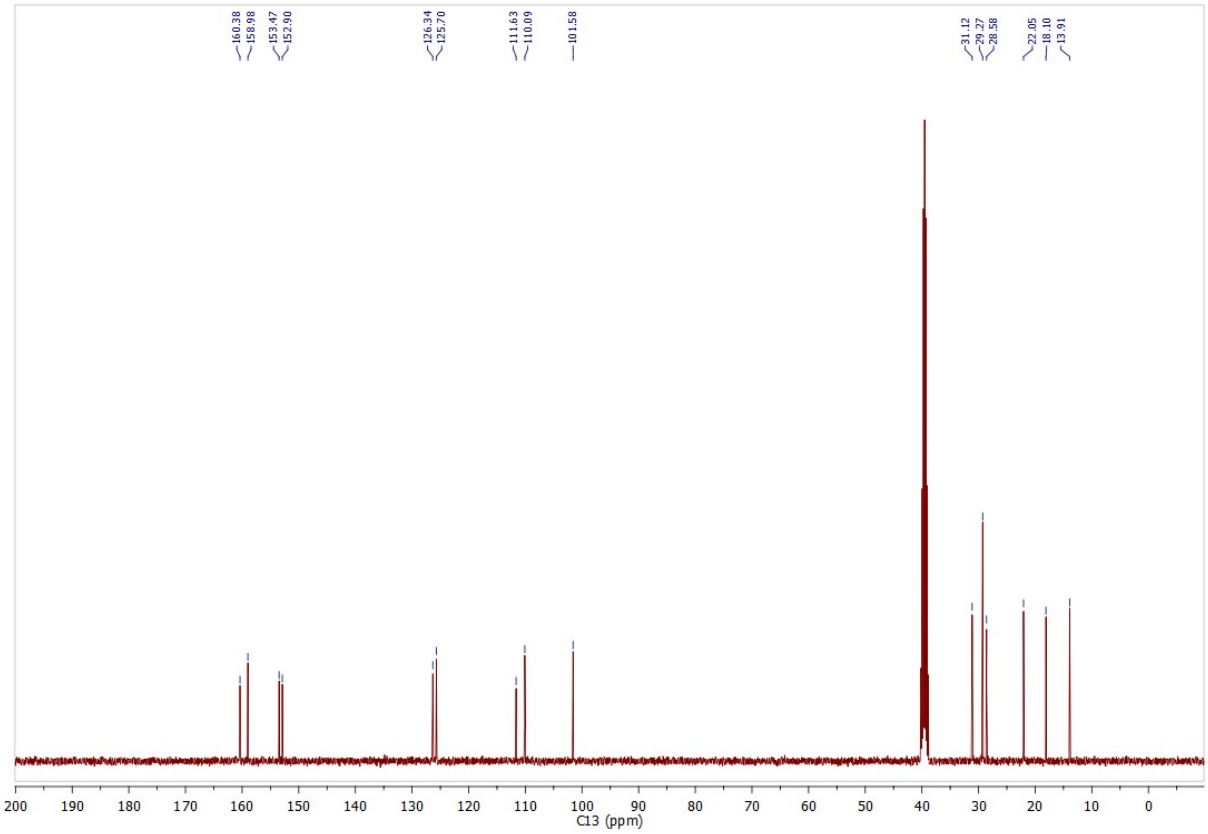

Figure S19. ^{13}C NMR spectrum of 3p

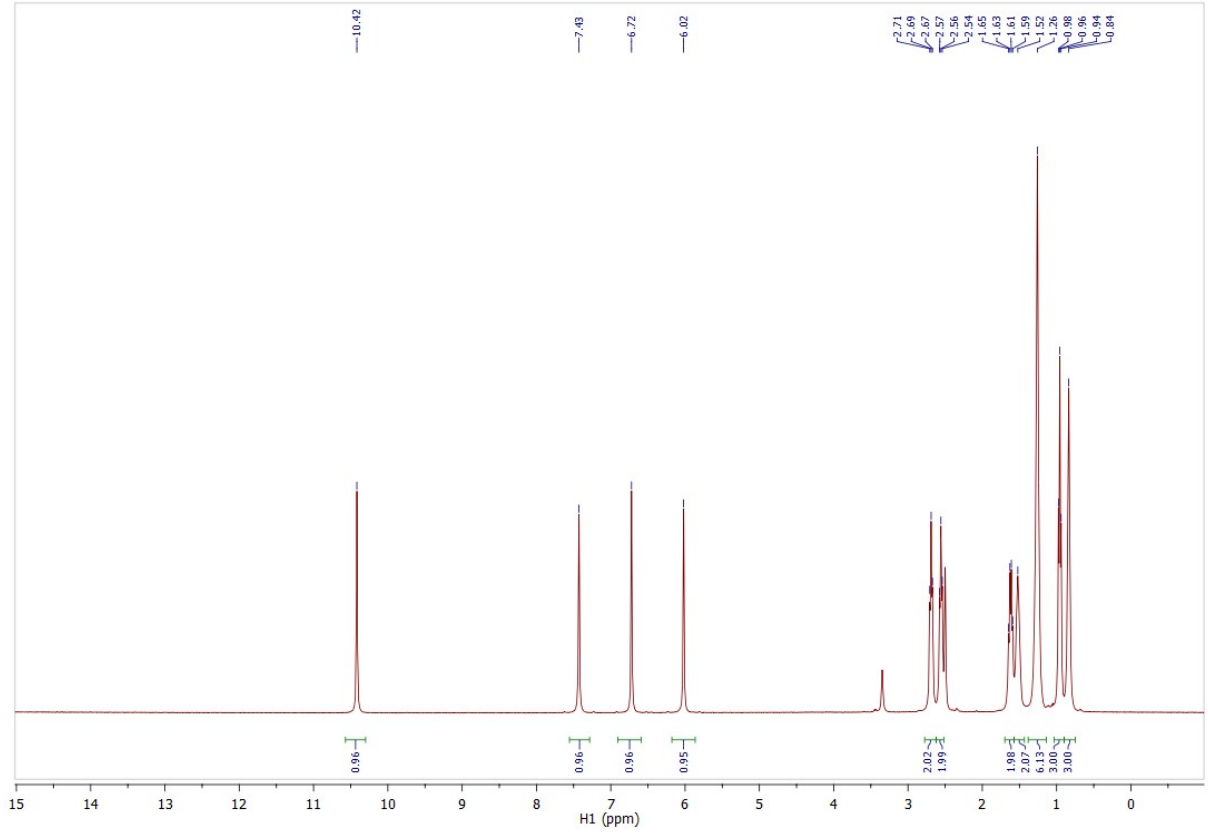

Figure S20. ^{1}H NMR spectrum of 3q

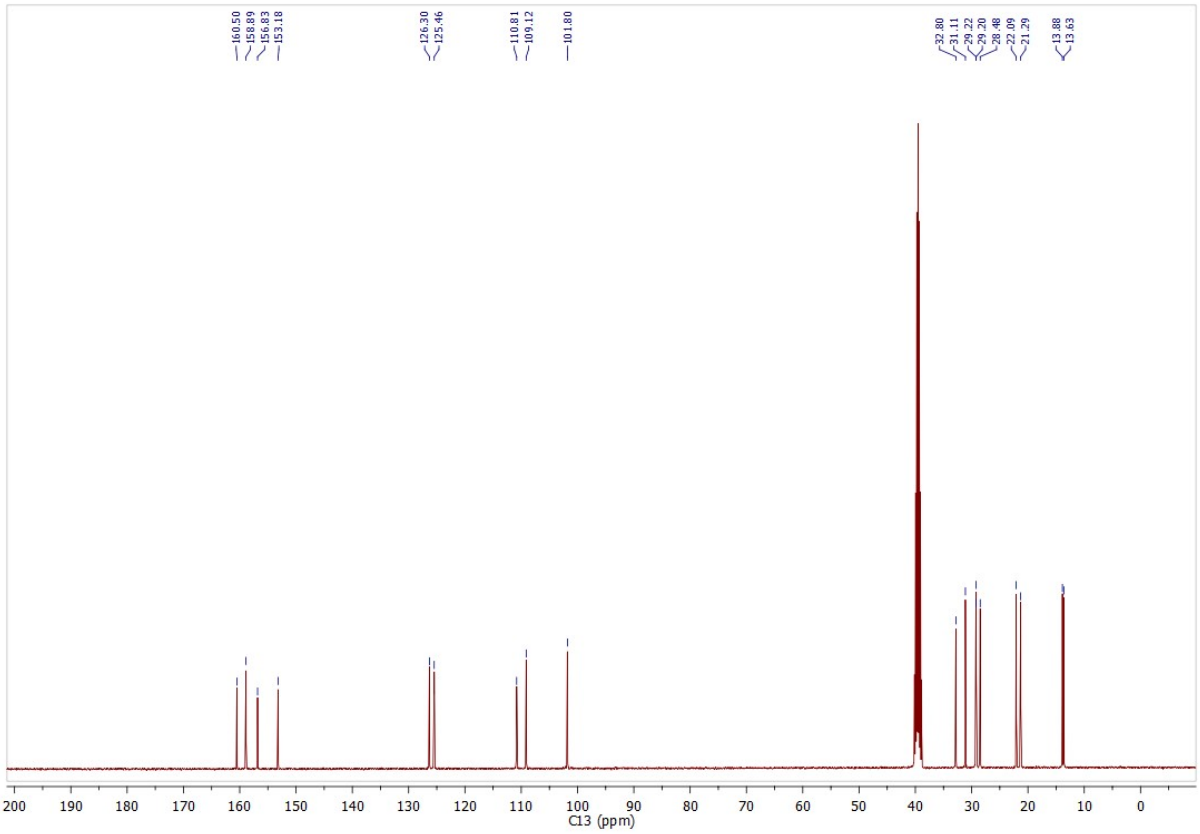

Figure S21. ^{13}C NMR spectrum of 3q

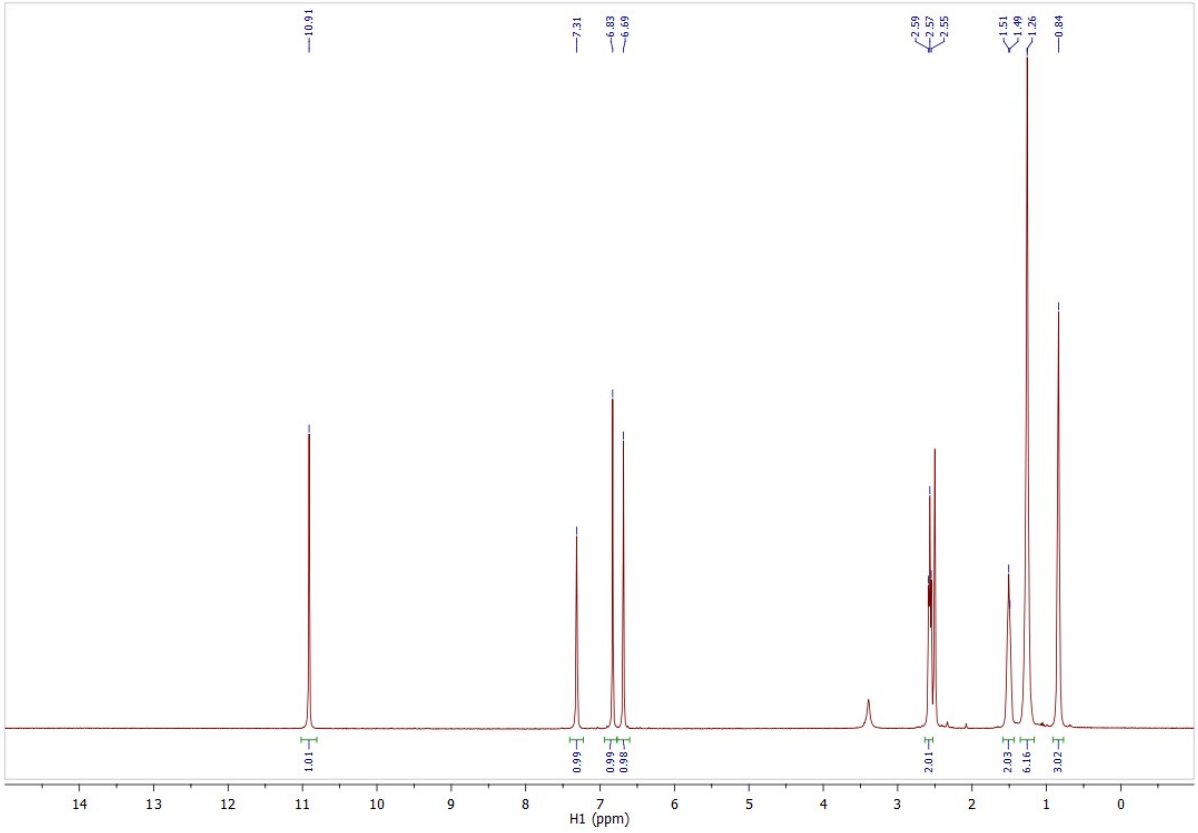

Figure S22. ^{1}H NMR spectrum of 3r

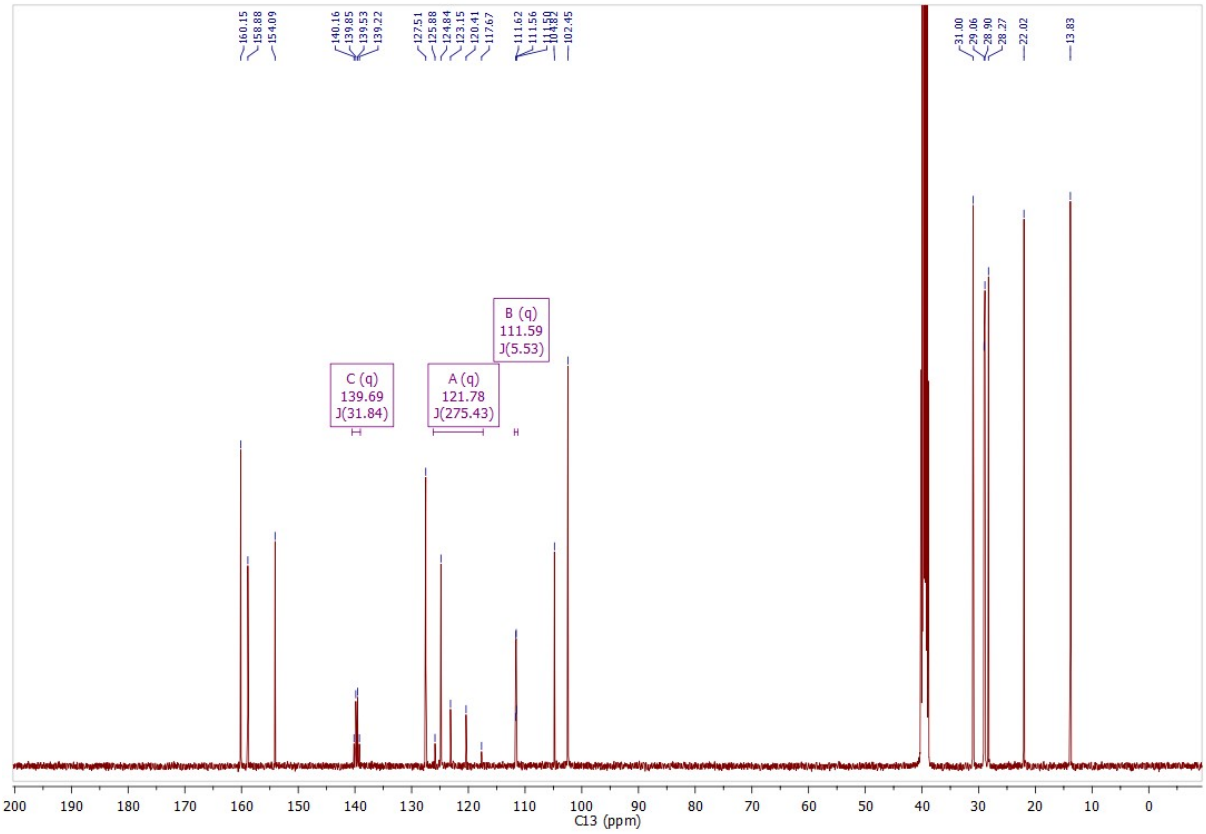

Figure S23. ^{13}C NMR spectrum of 3r

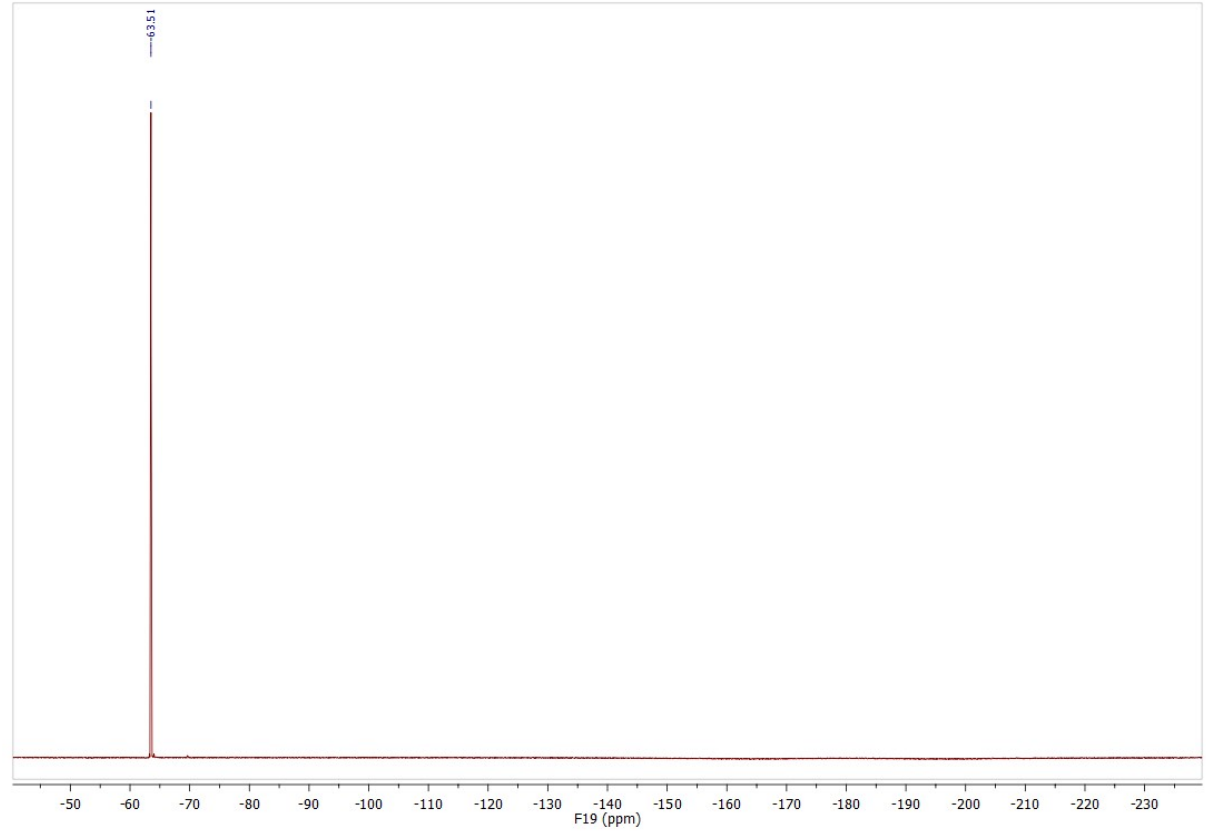

Figure S24. ^{19}F NMR spectrum of 3r

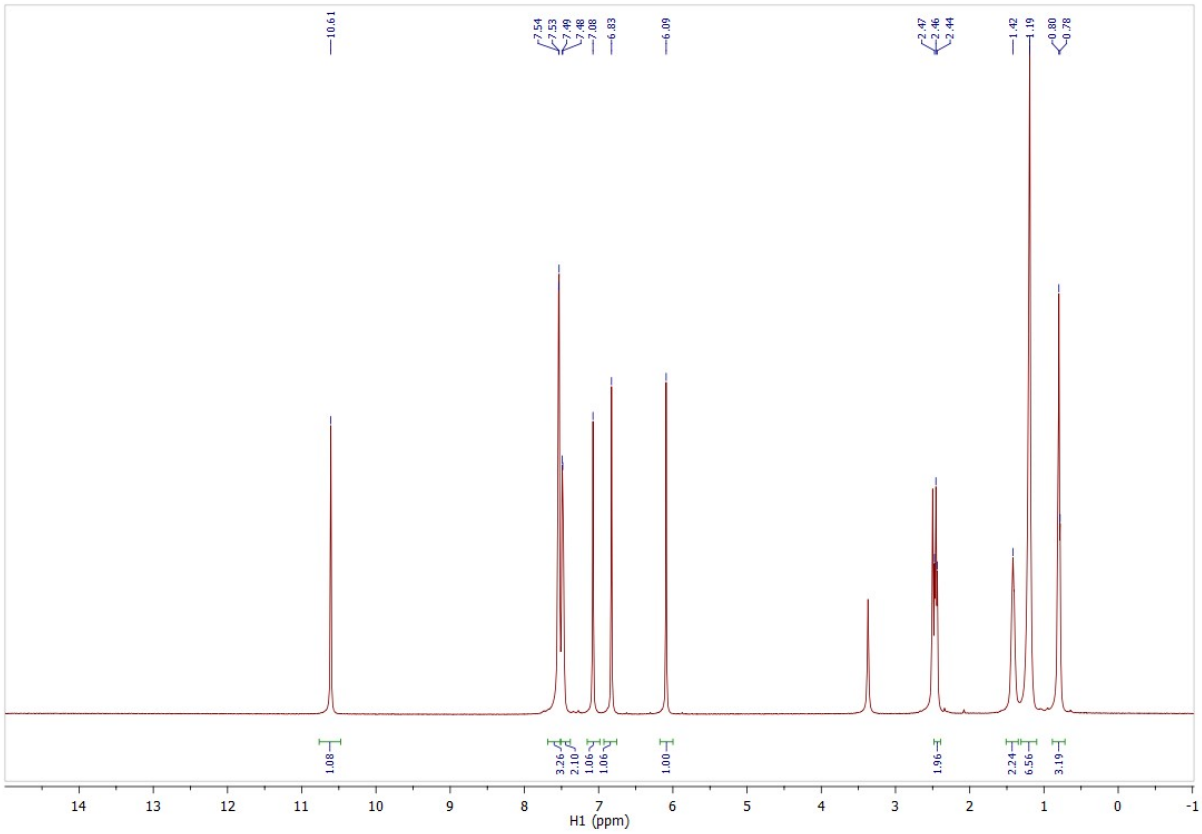

Figure S25. ^{1}H NMR spectrum of 3s

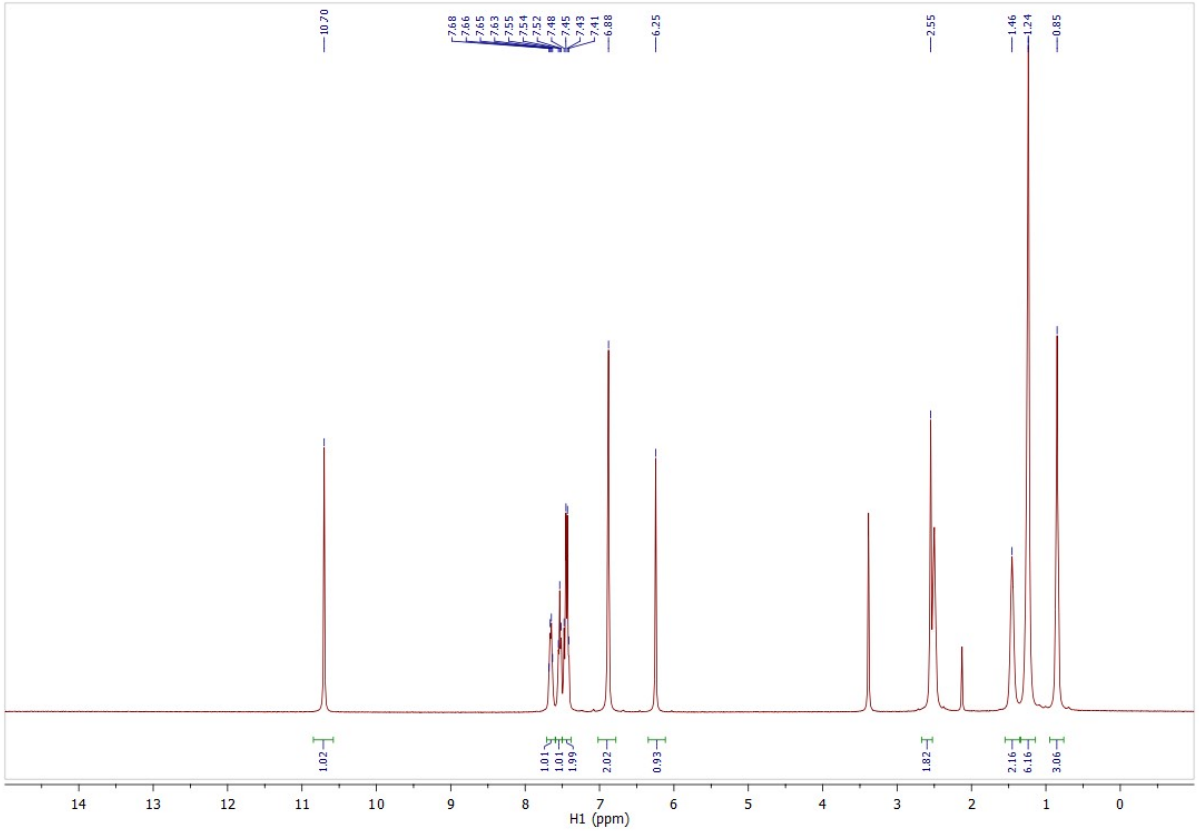

Figure S26. ^{1}H NMR spectrum of 3t

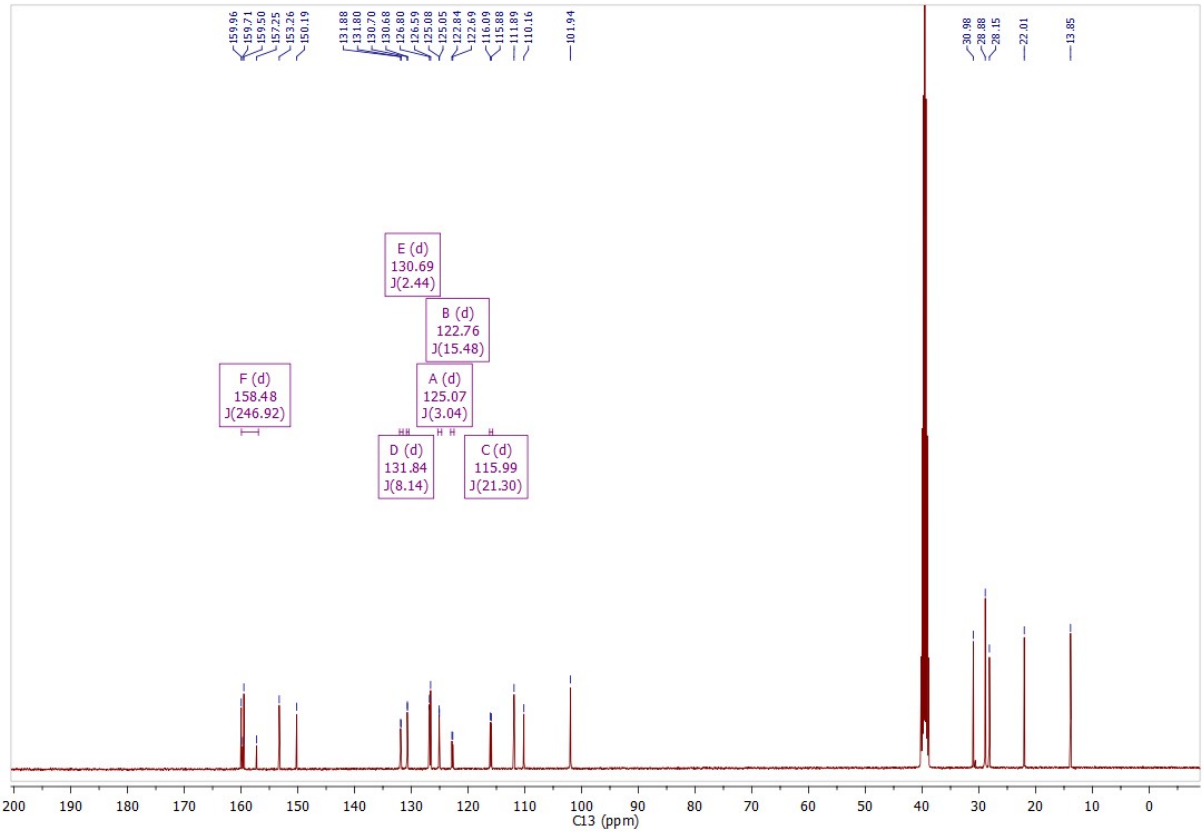

Figure S27. ^{13}C NMR spectrum of 3t

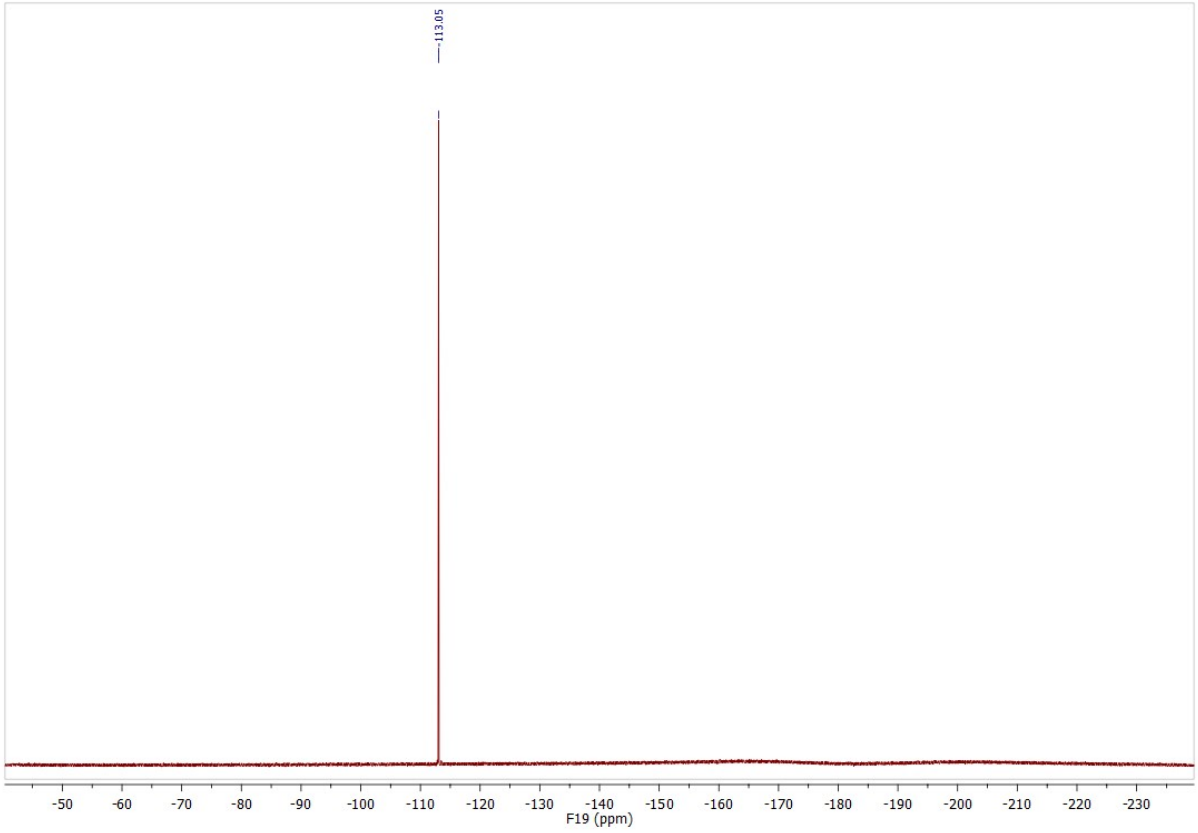

Figure S28. ^{19}F NMR spectrum of 3t

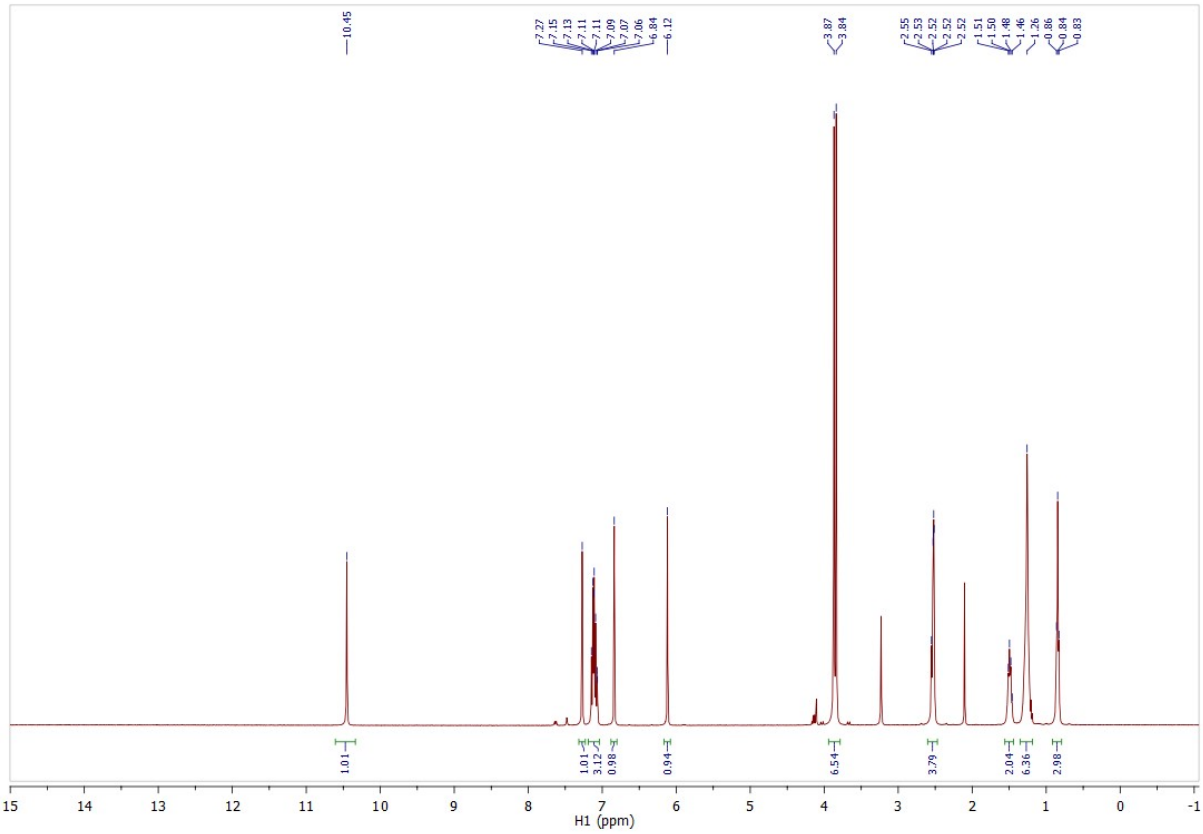

Figure S29. ^{1}H NMR spectrum of 3u

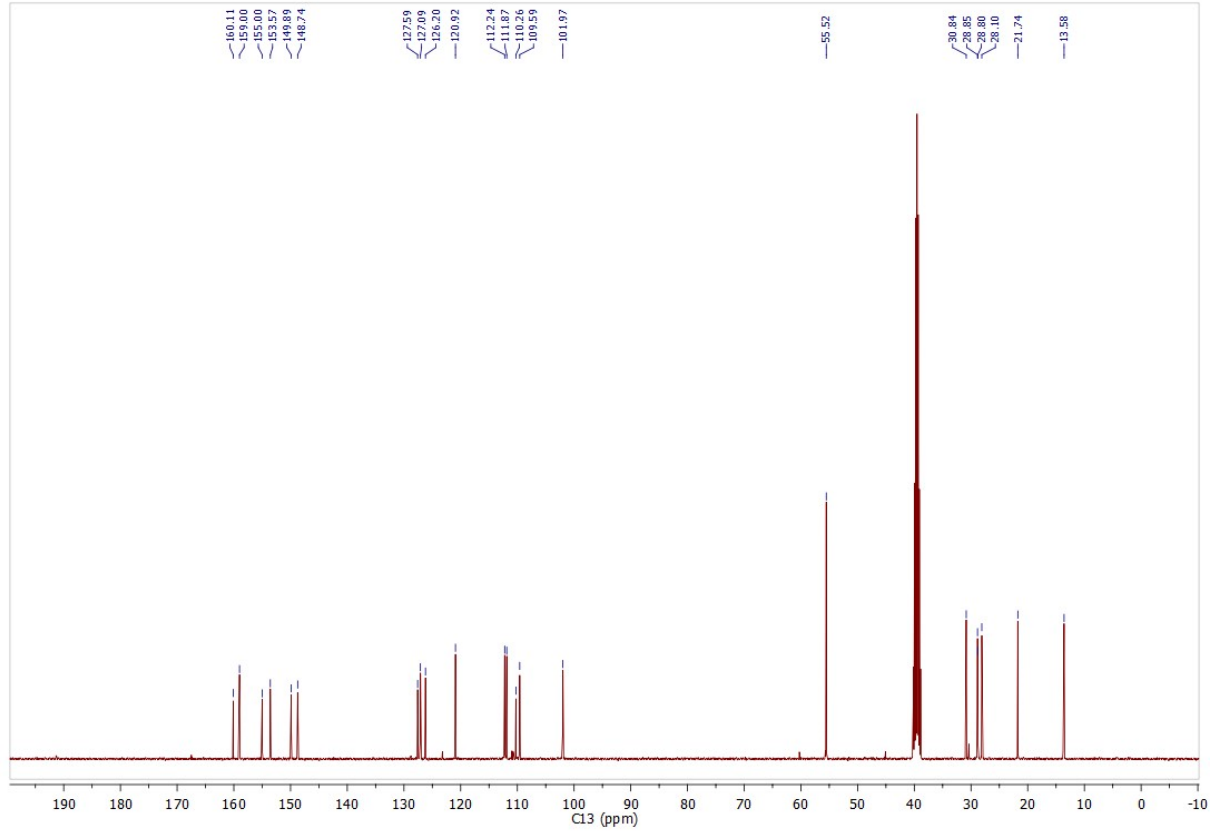

Figure S30. ^{13}C NMR spectrum of 3u

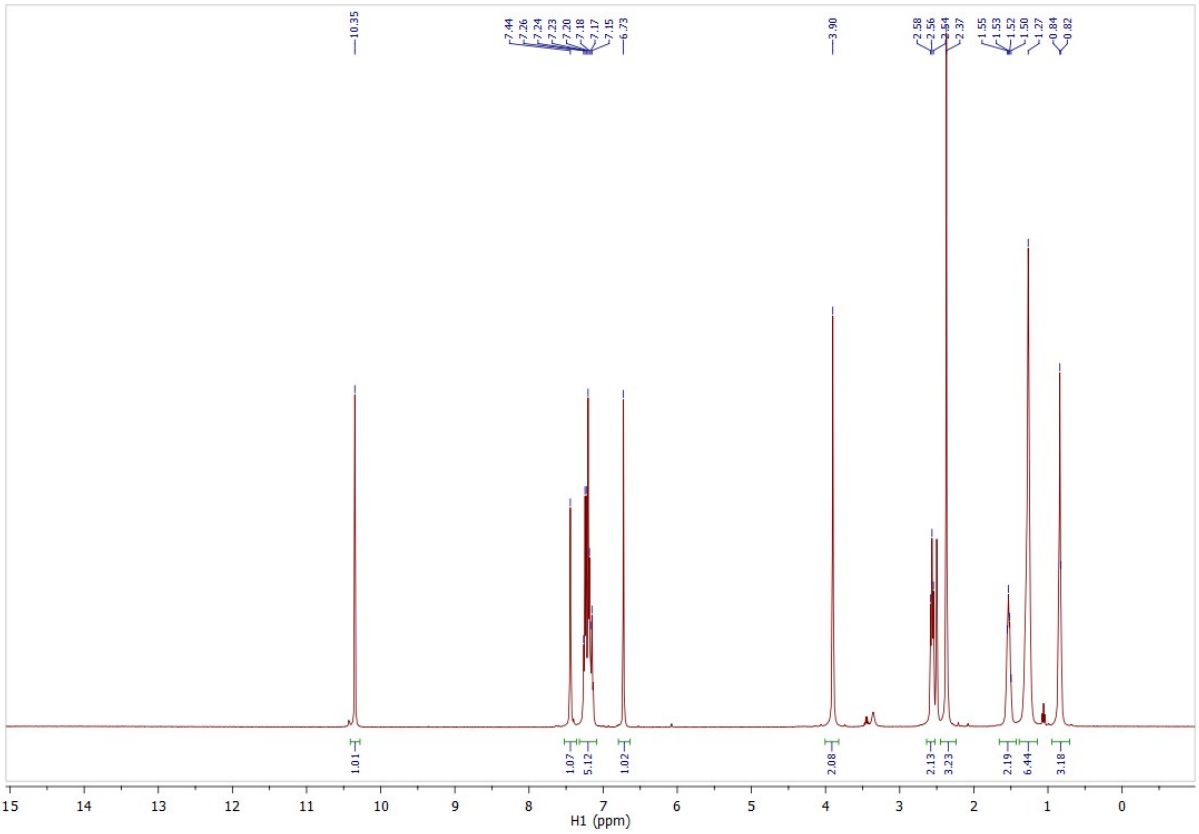

Figure S31. ^{1}H NMR spectrum of 3v

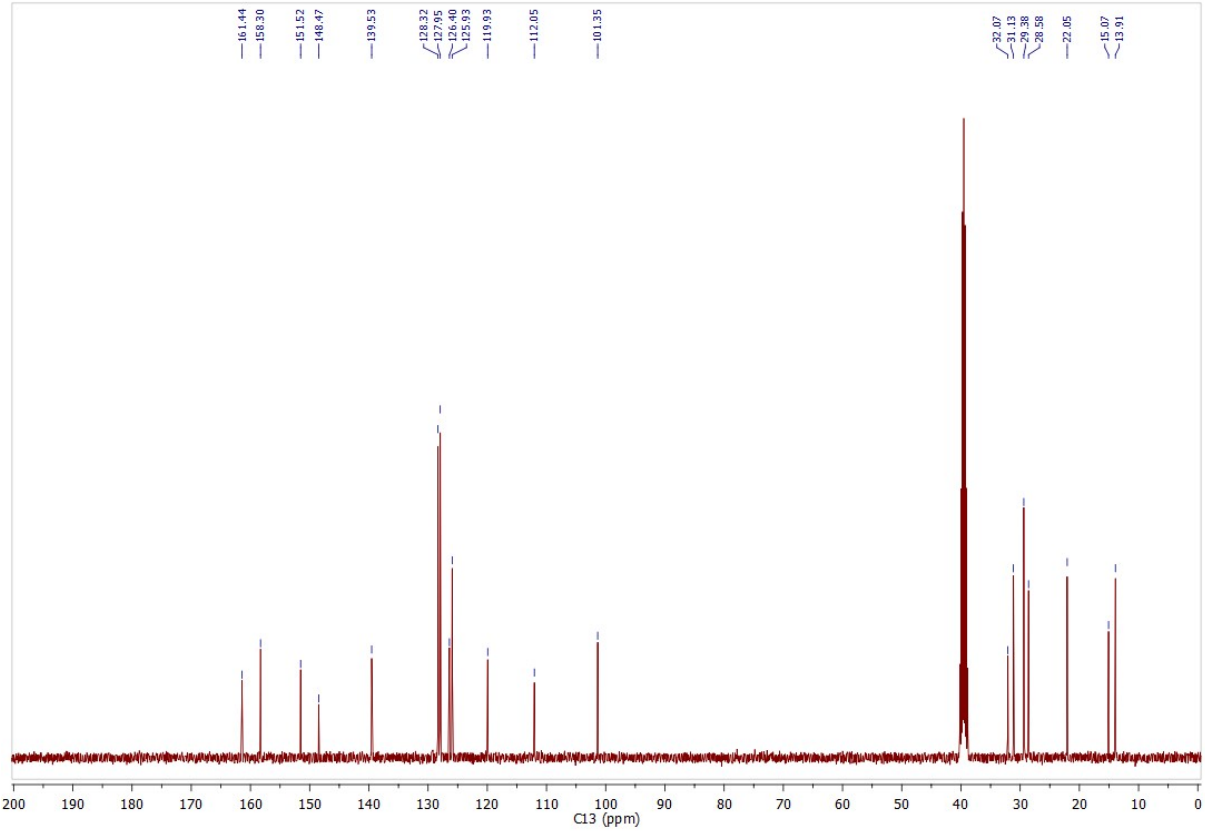

Figure S32. ^{13}C NMR spectrum of 3v

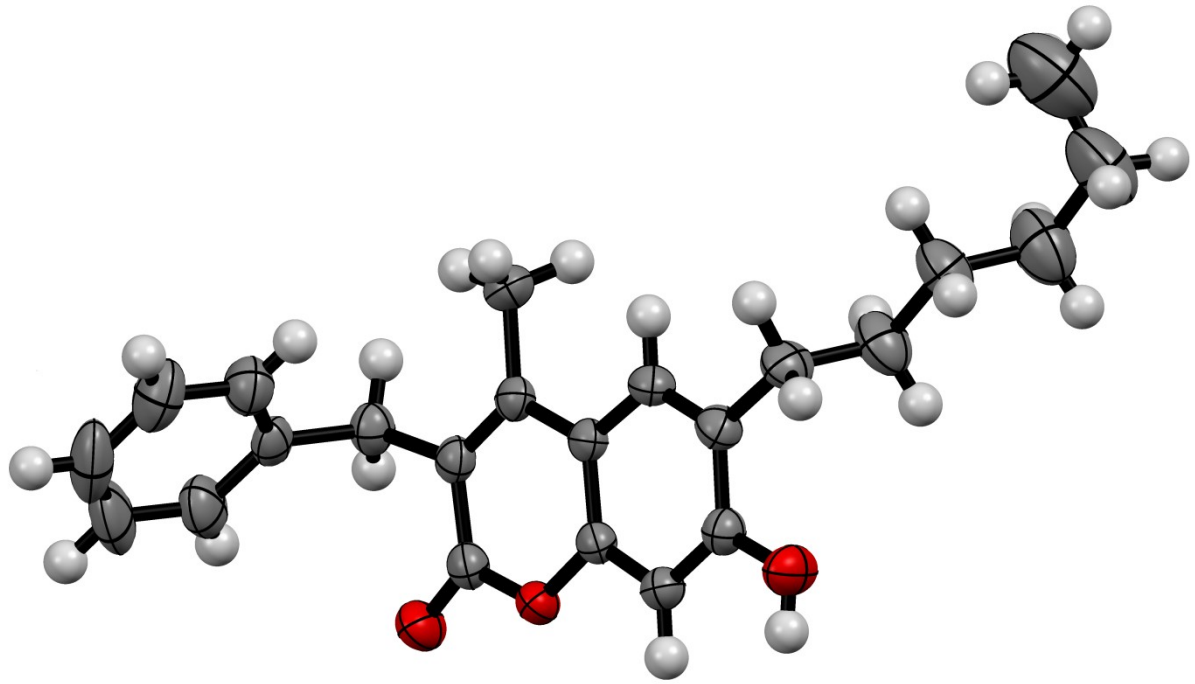

Figure S33. Thermal ellipsoid plot of compound 3v; ellipsoid contour at the 30% probability level. carbon (gray), hydrogen (light gray), and oxygen (red). Single crystal was grown by the slow evaporation of the solution of compound 2v in EtOAc.

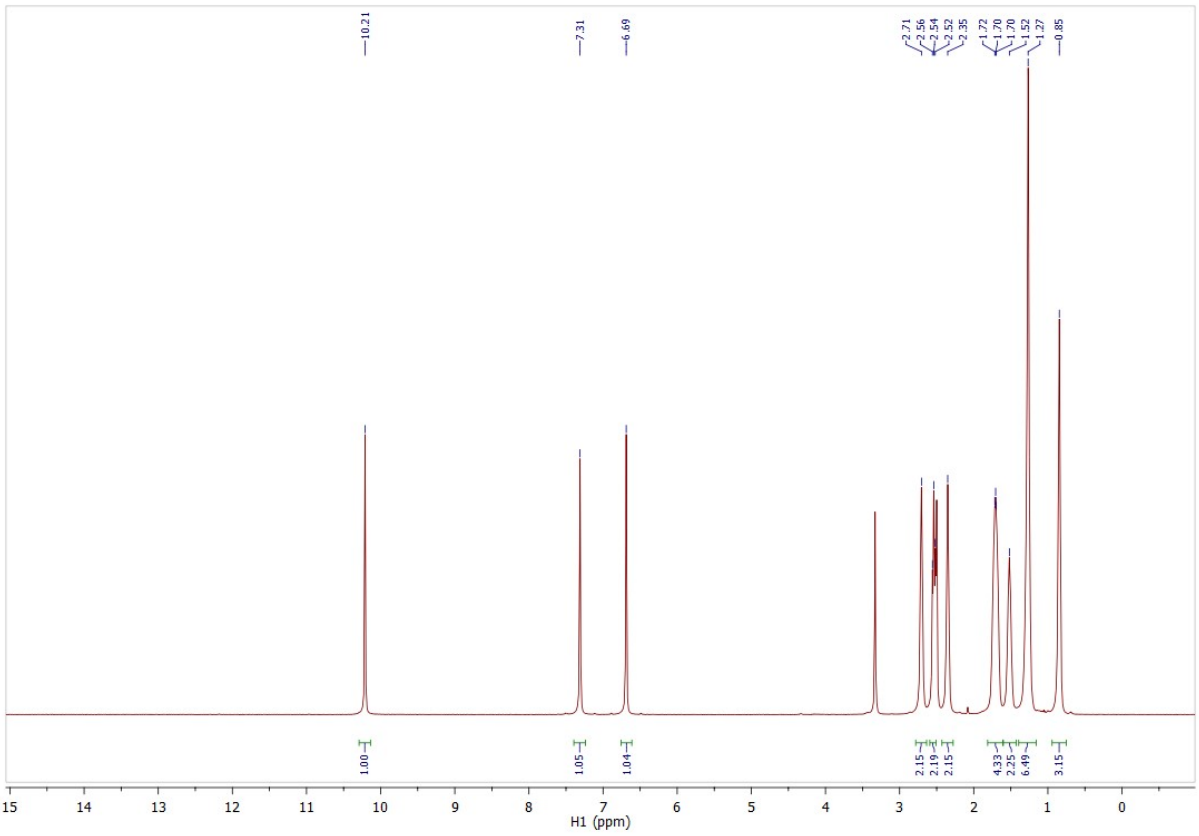

Figure S34. ^{1}H NMR spectrum of 3w

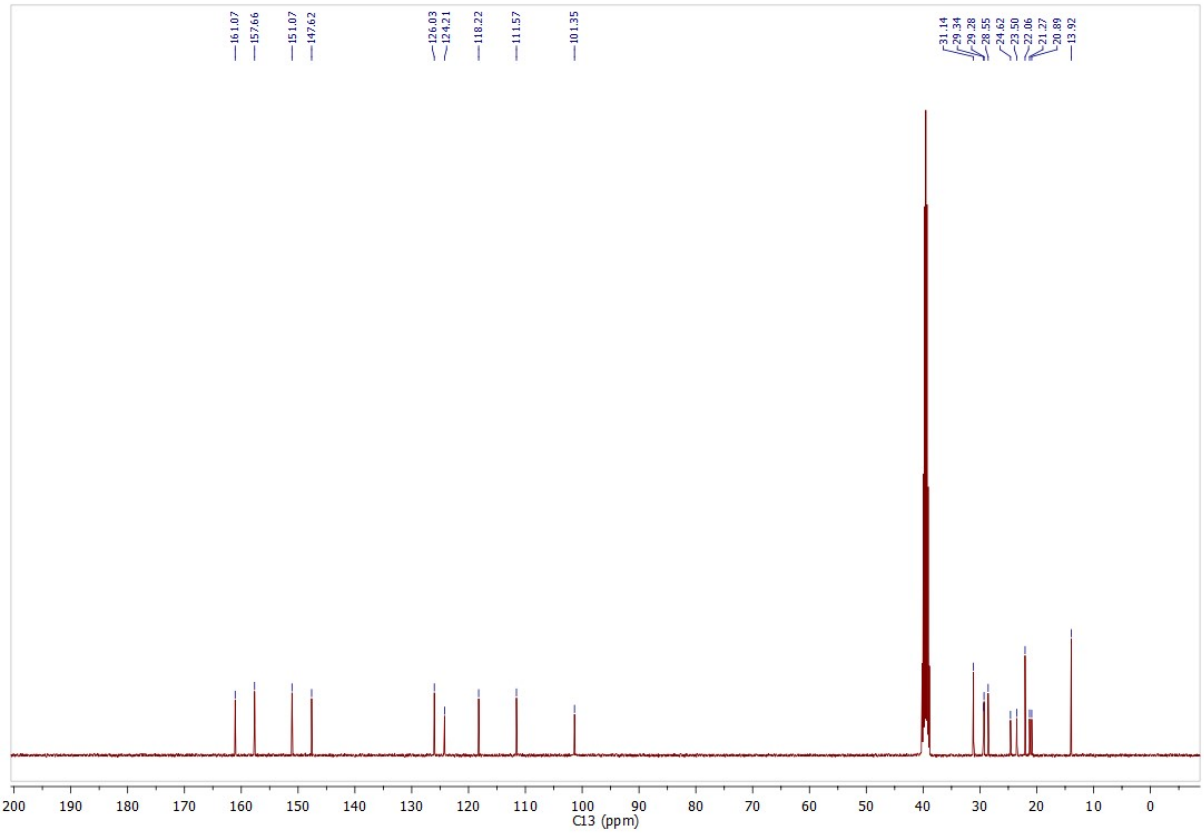

Figure S35. ^{13}C NMR spectrum of 3w

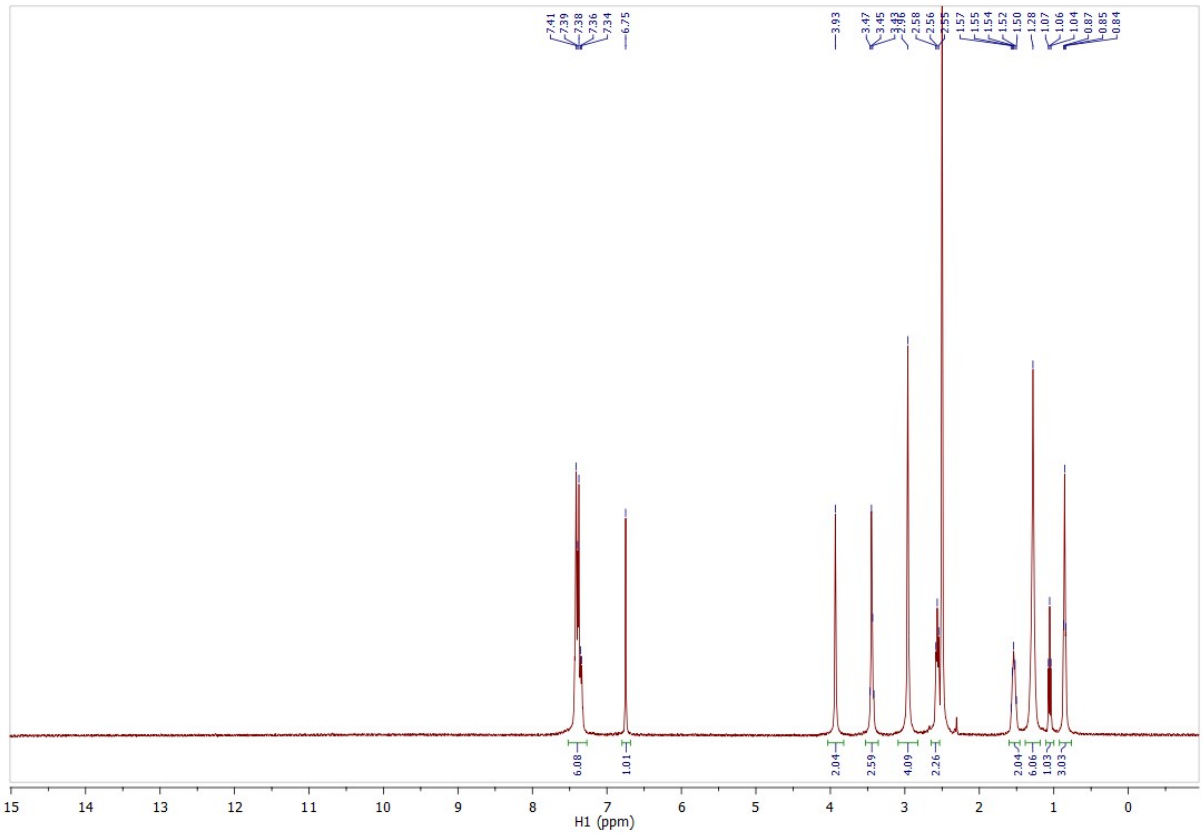

Figure S36. ^{1}H NMR spectrum of 3x

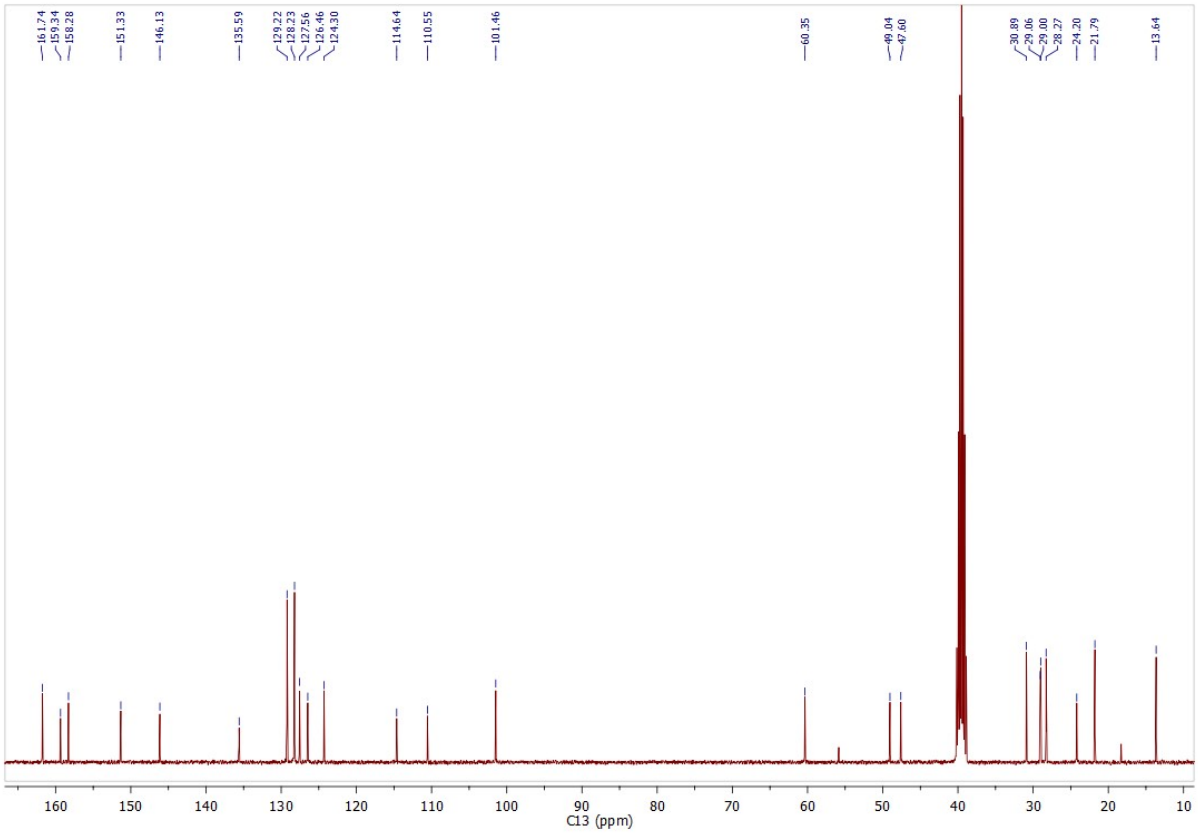

Figure S37. ^{13}C NMR spectrum of 3x

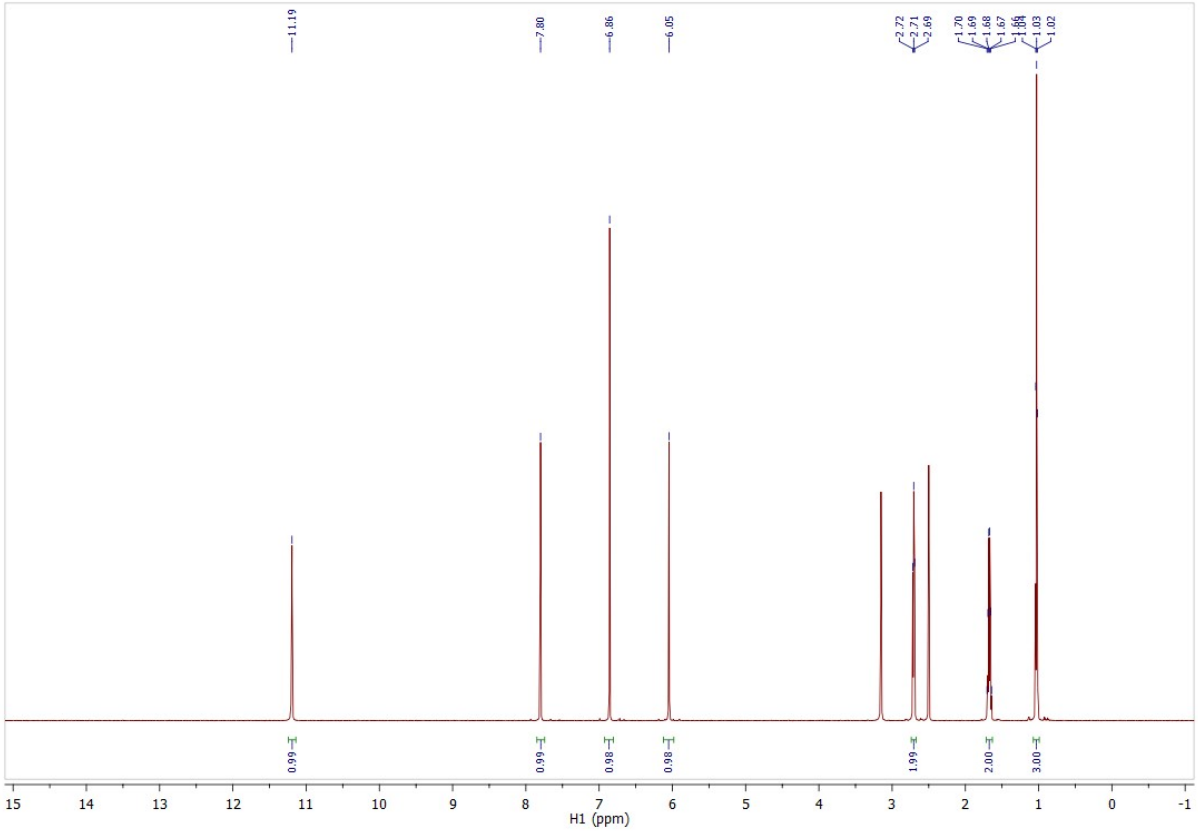

Figure S38. ^{1}H NMR spectrum of 3y

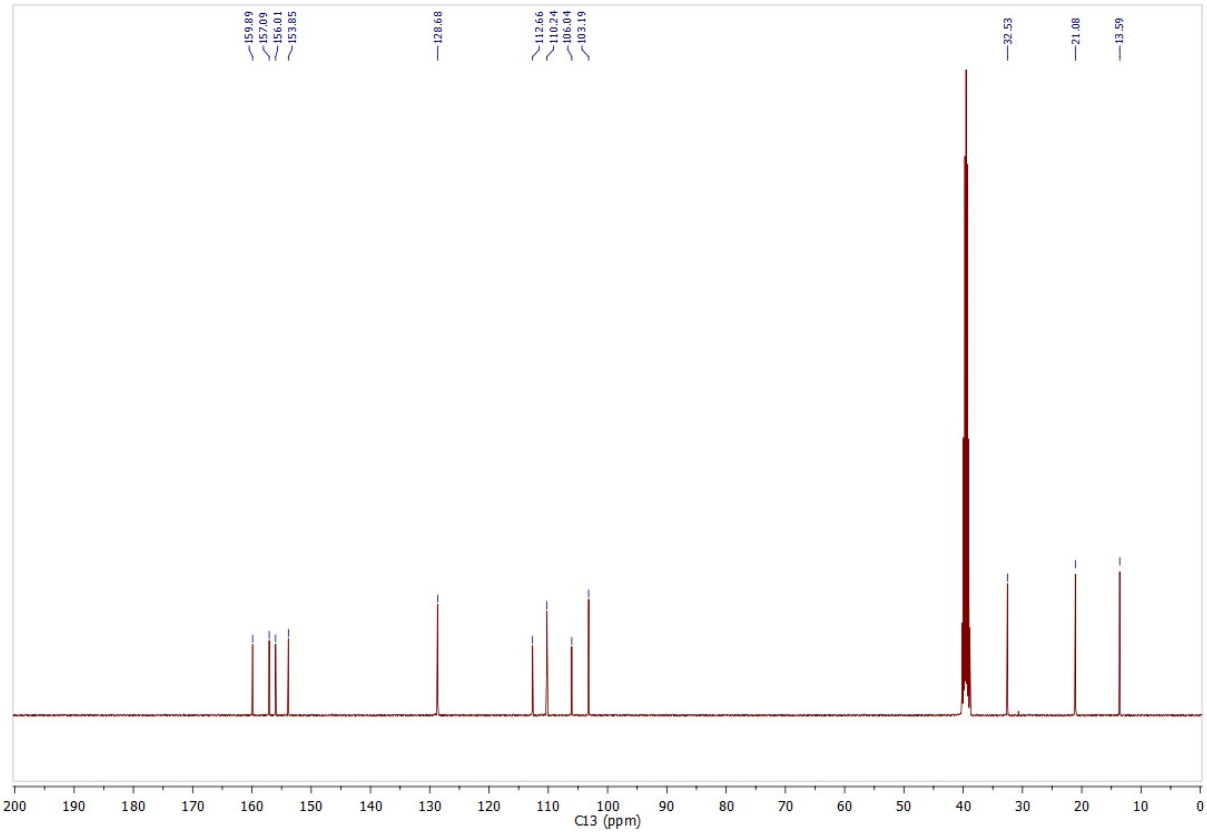

Figure S39. ^{13}C NMR spectrum of 3y

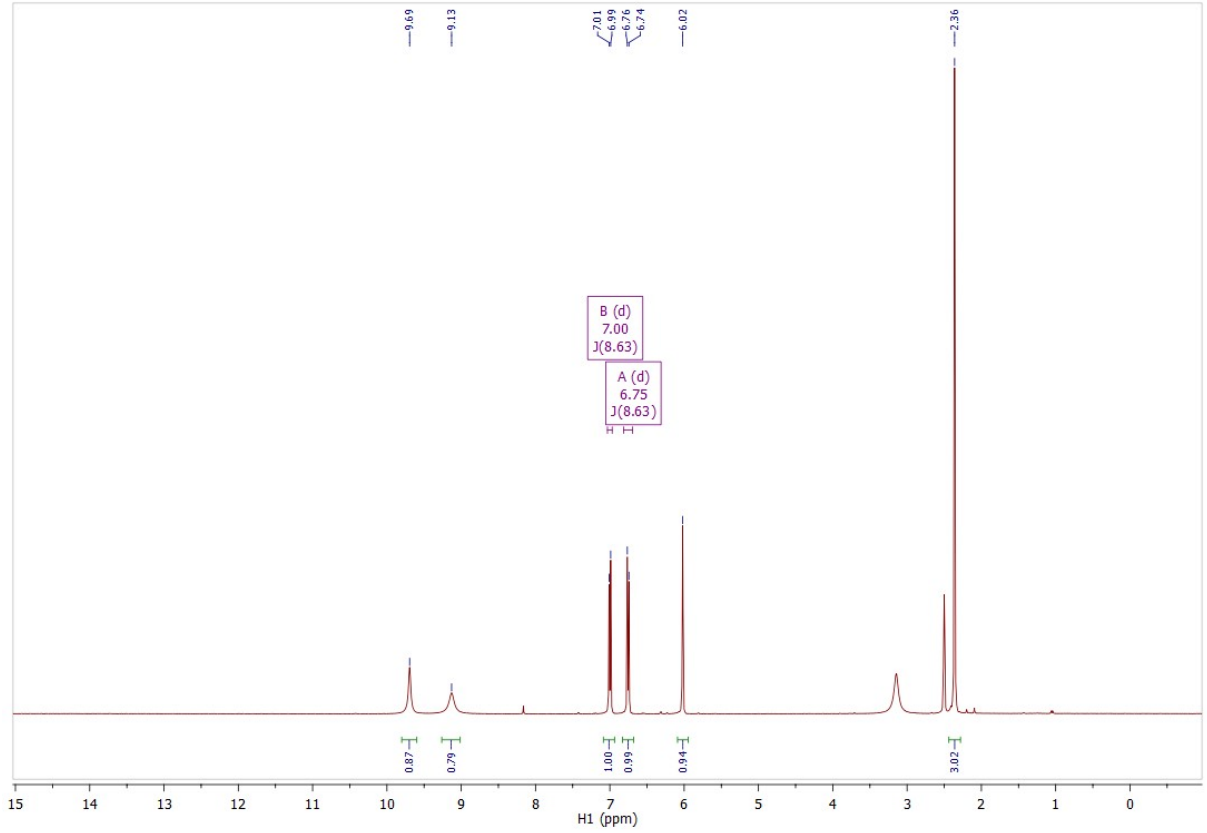

Figure S40. ^{1}H NMR spectrum of 3z

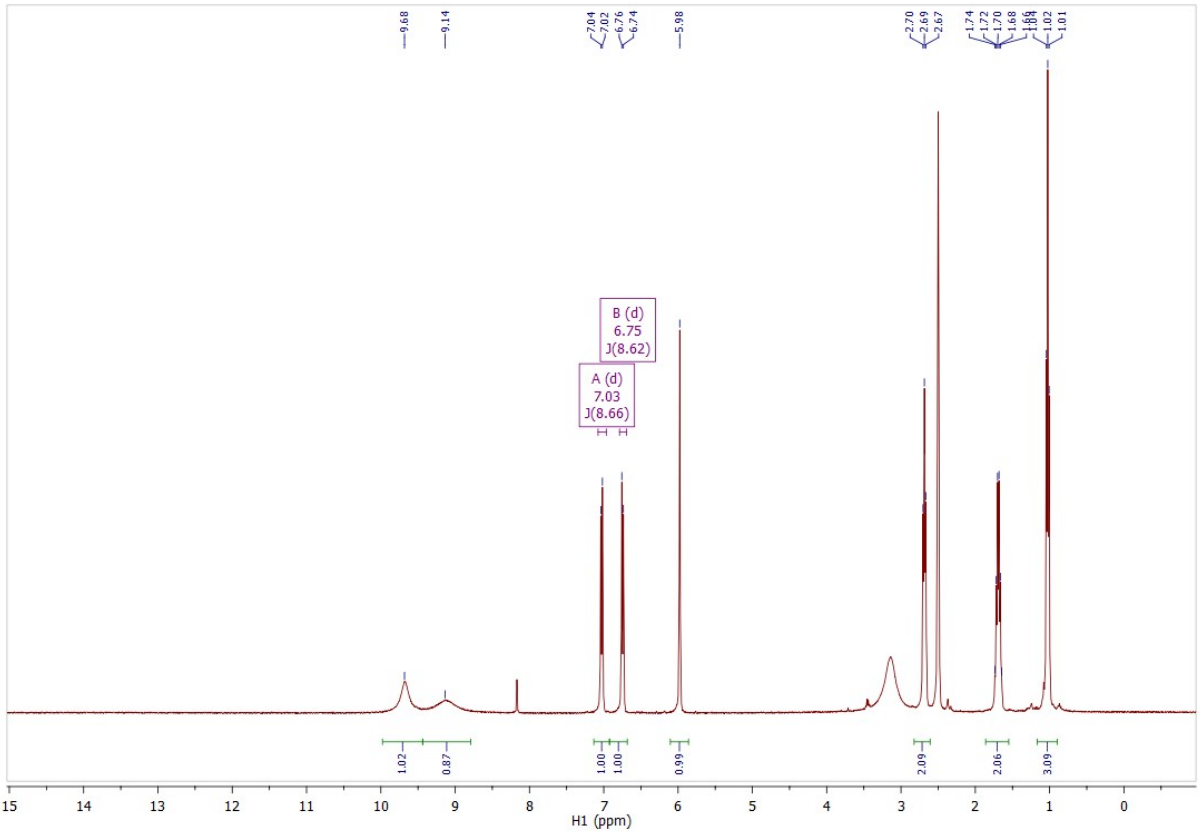

Figure S41. ^{1}H NMR spectrum of 3aa

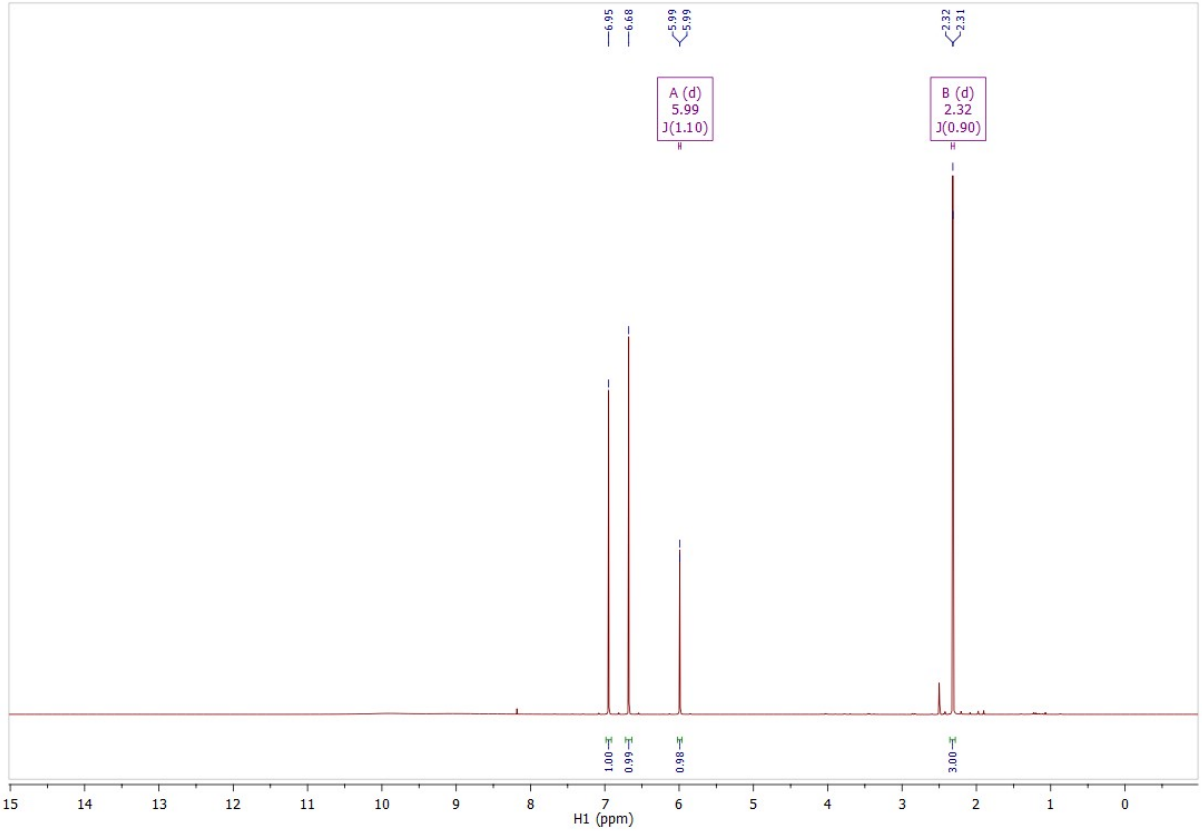

Figure S42. ^{1}H NMR spectrum of 3ab

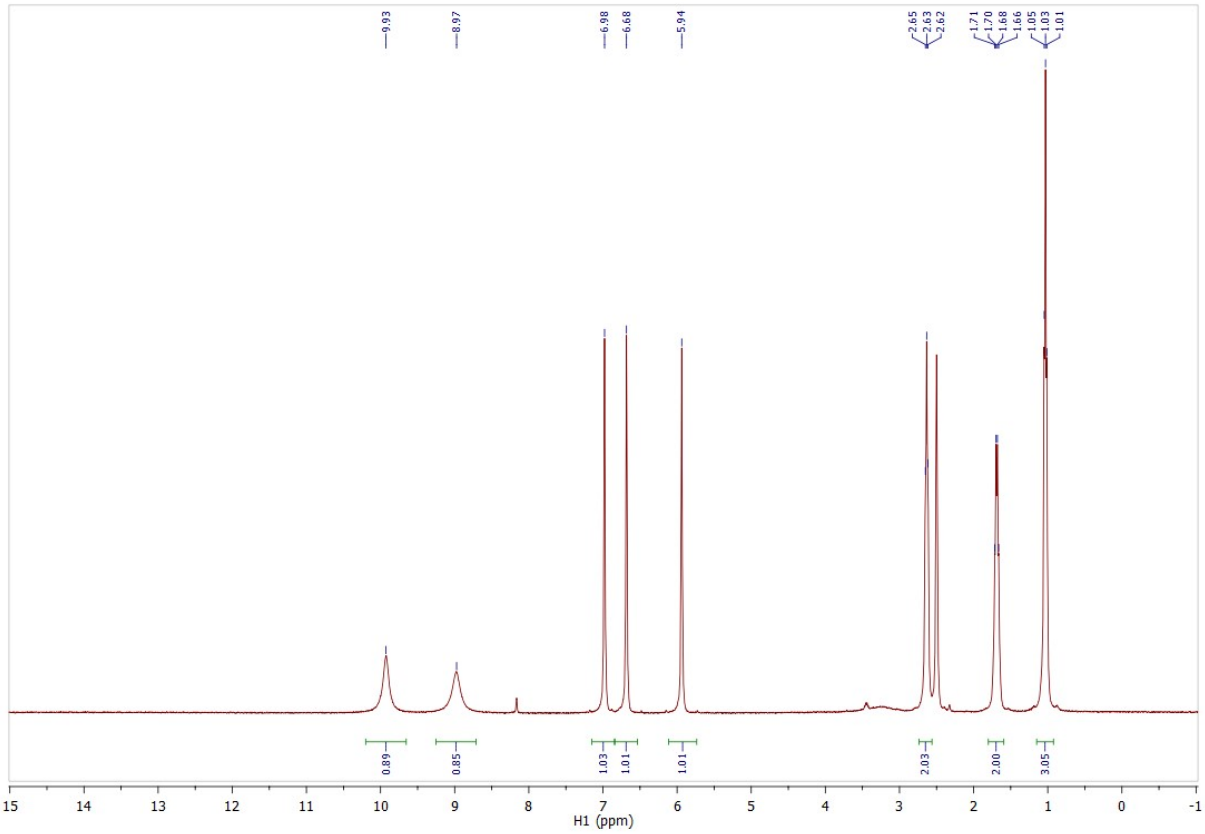

Figure S43. ^{1}H NMR spectrum of 3ac

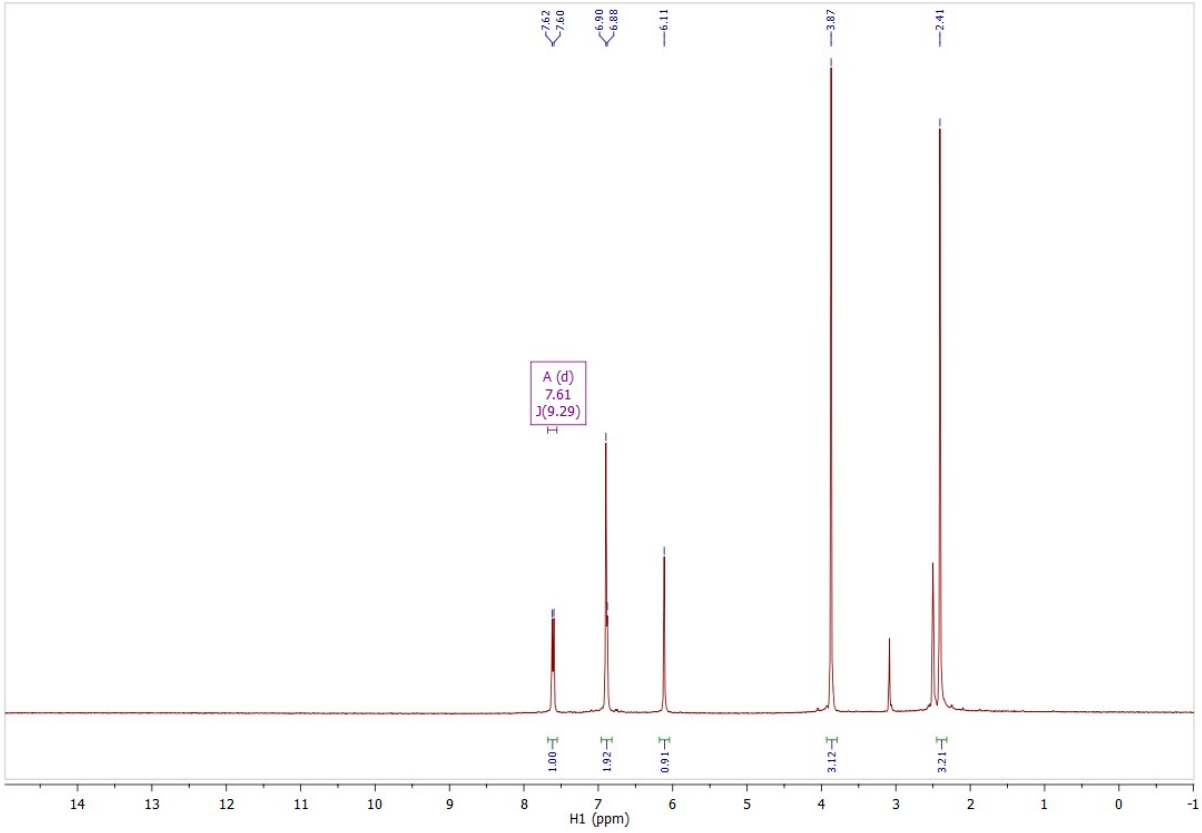

Figure S44. ^{1}H NMR spectrum of 3ad

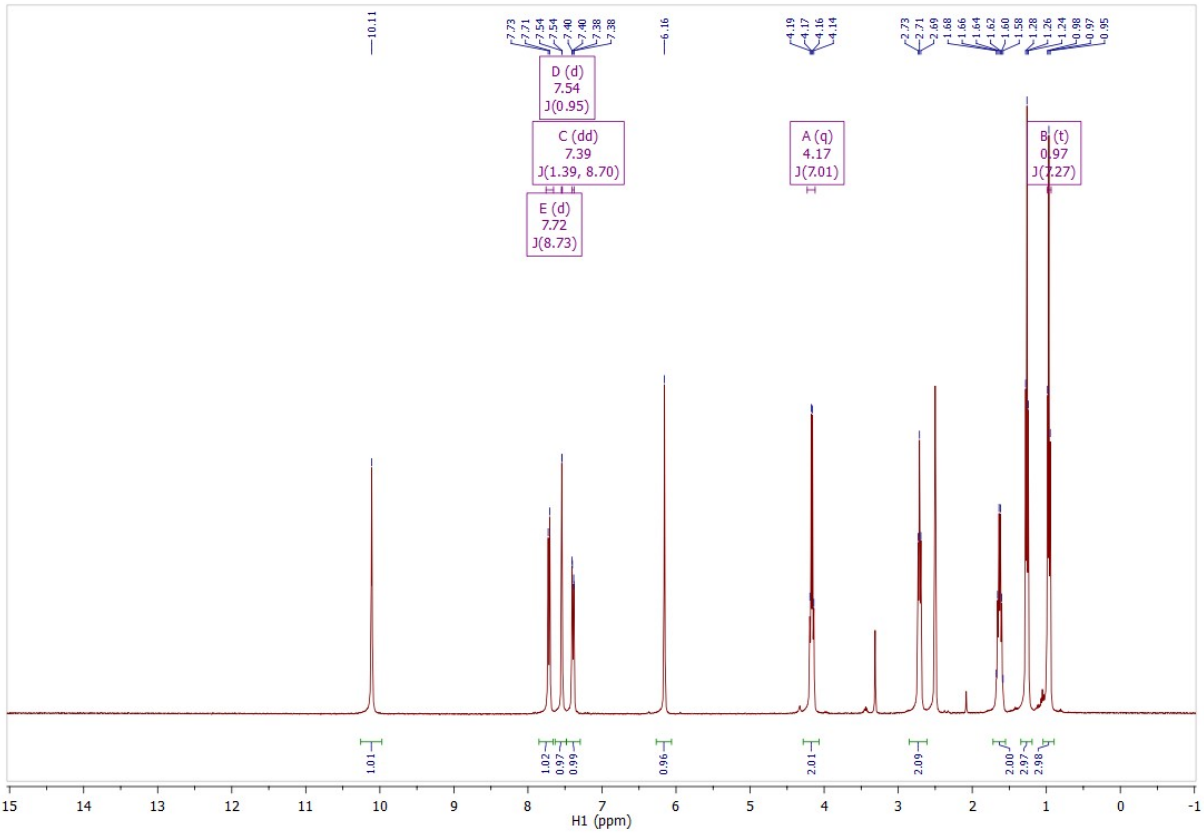

Figure S45. ^{1}H NMR spectrum of 3ae

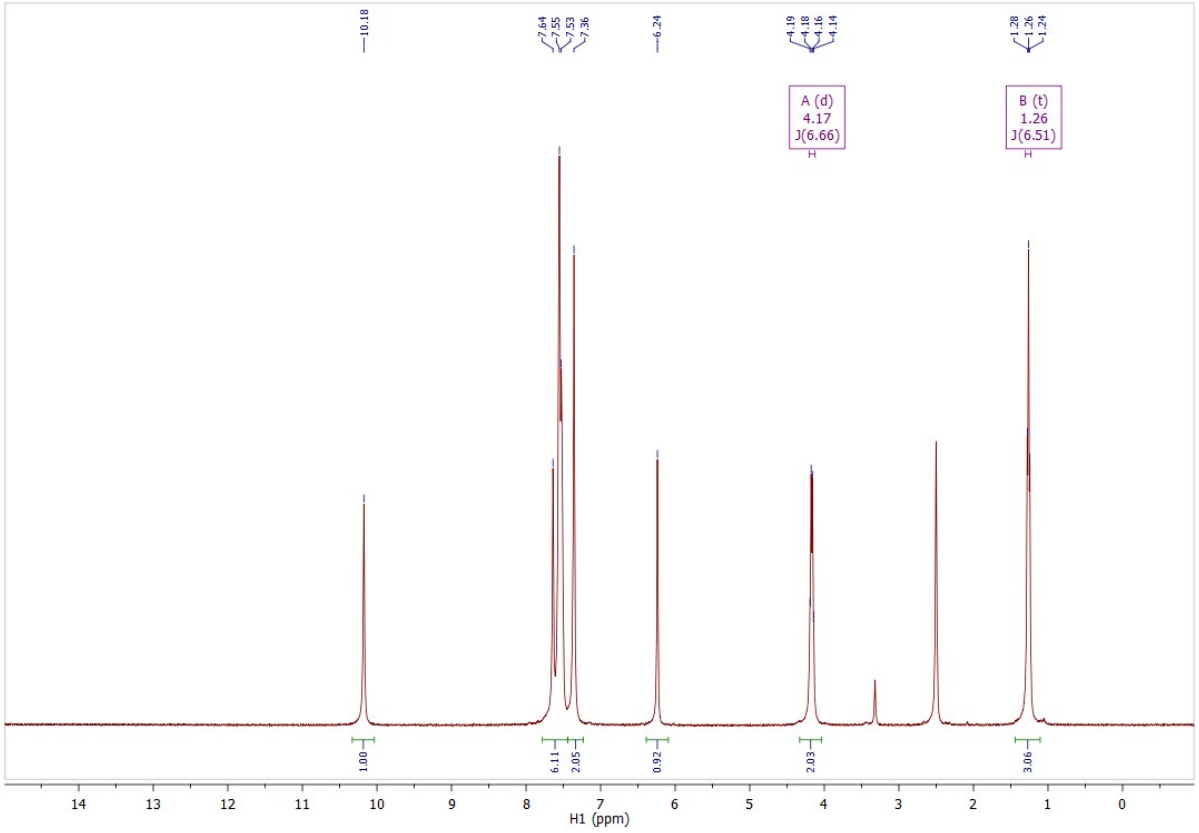

Figure S46. ^{1}H NMR spectrum of 3af

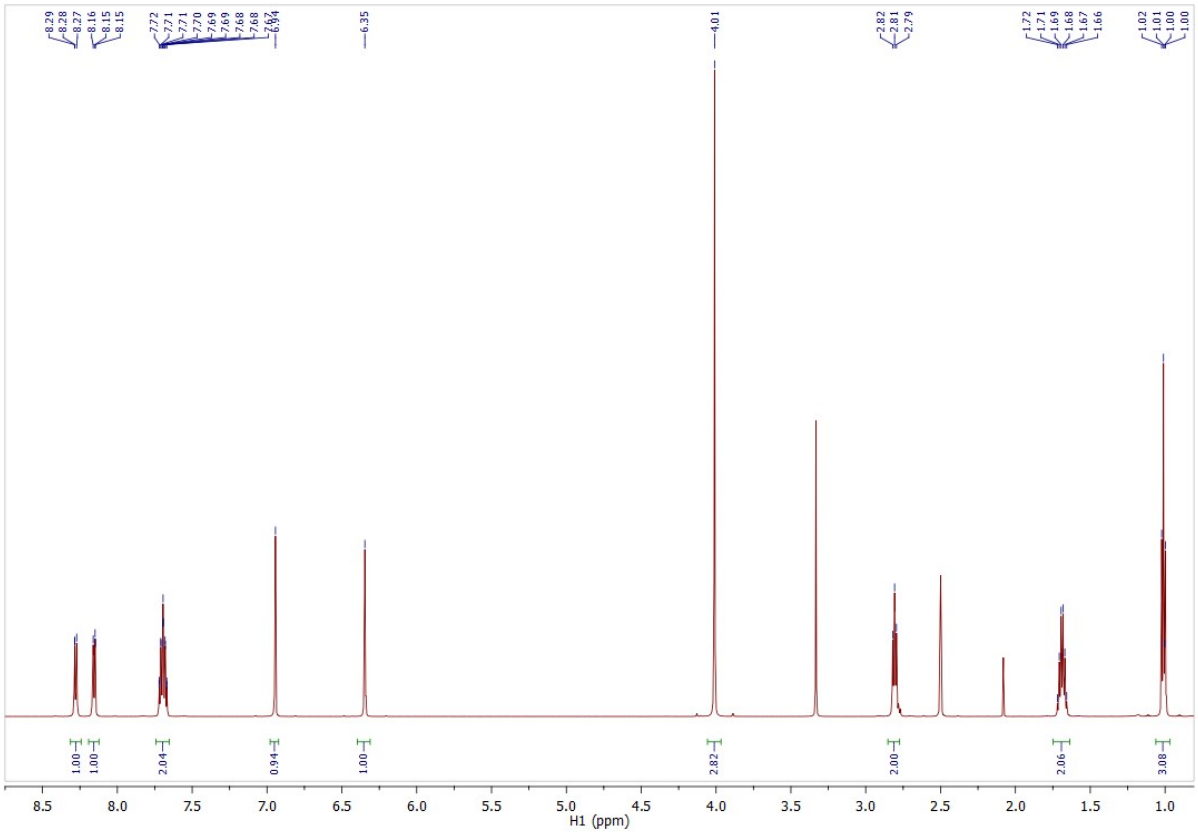

Figure S47. ^{1}H NMR spectrum of 3ag

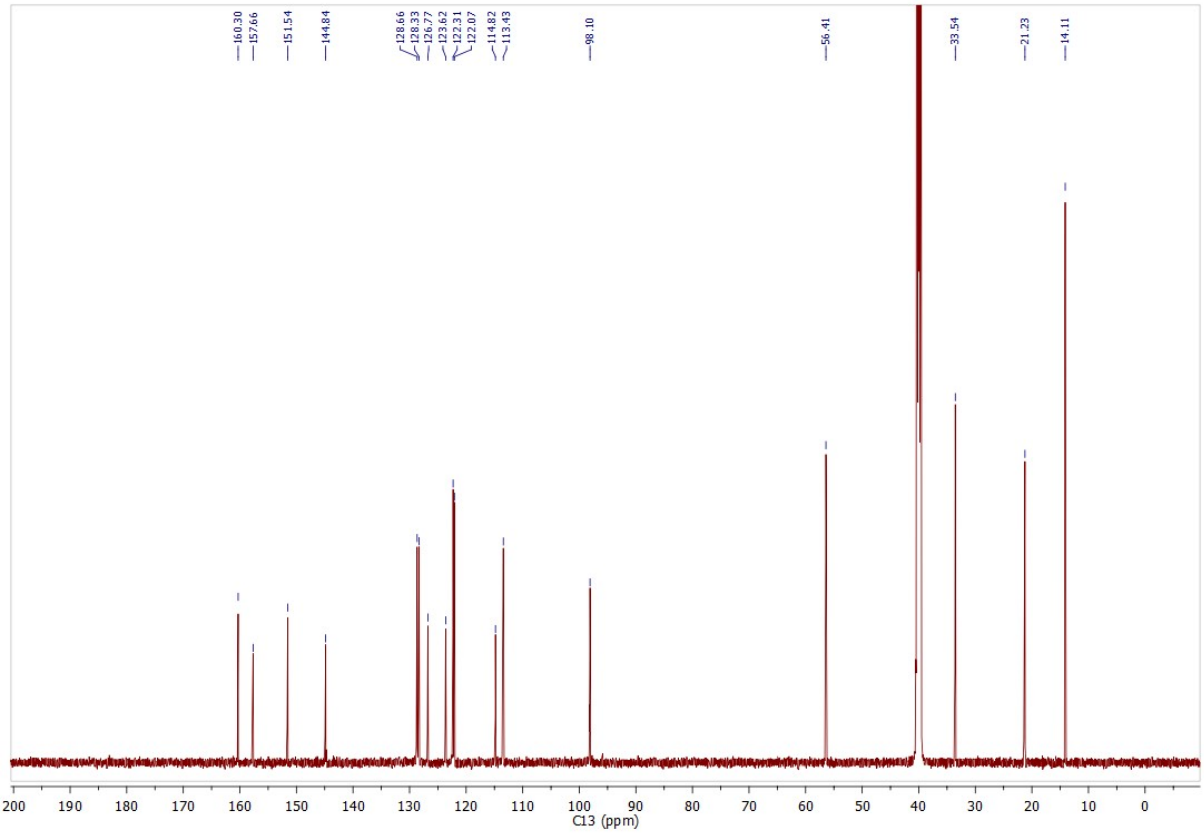

Figure S48. ^{13}C NMR spectrum of 3ag

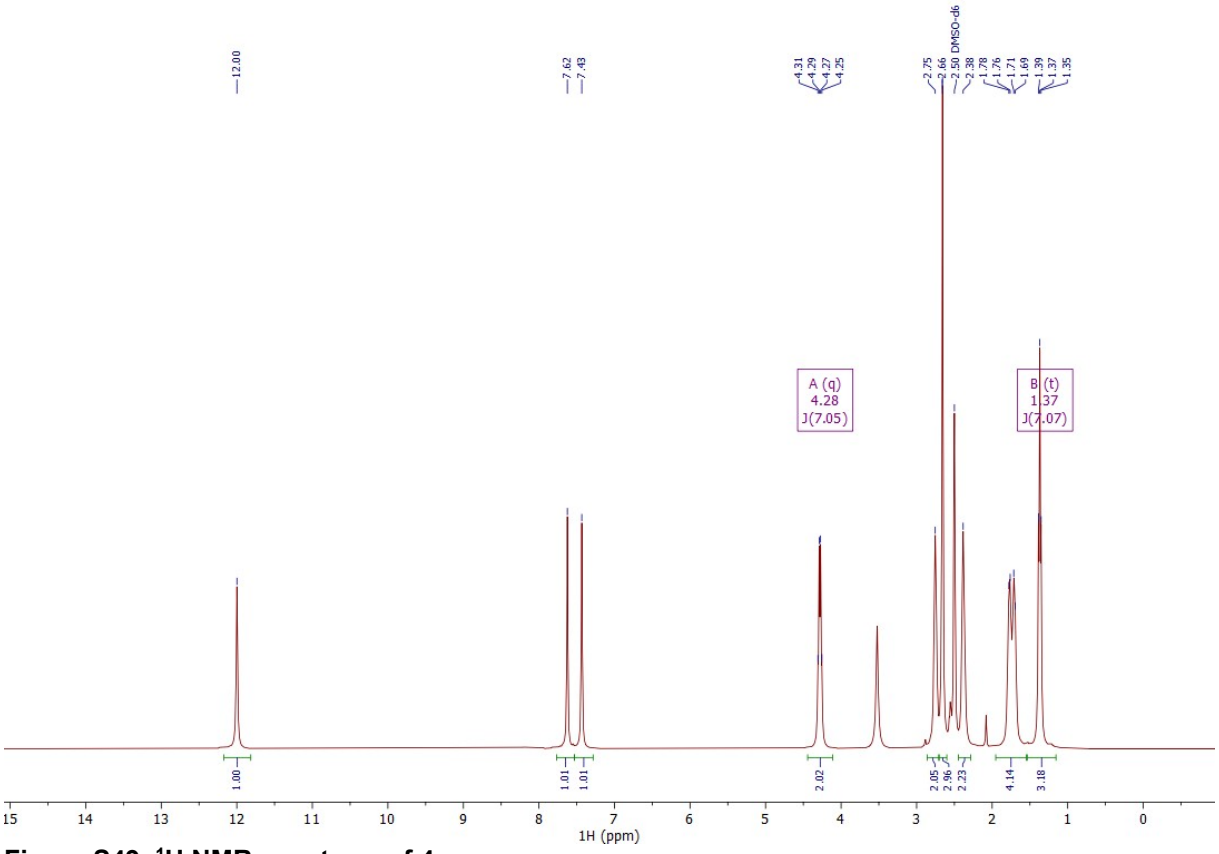

Figure S49. ^{1}H NMR spectrum of 4a

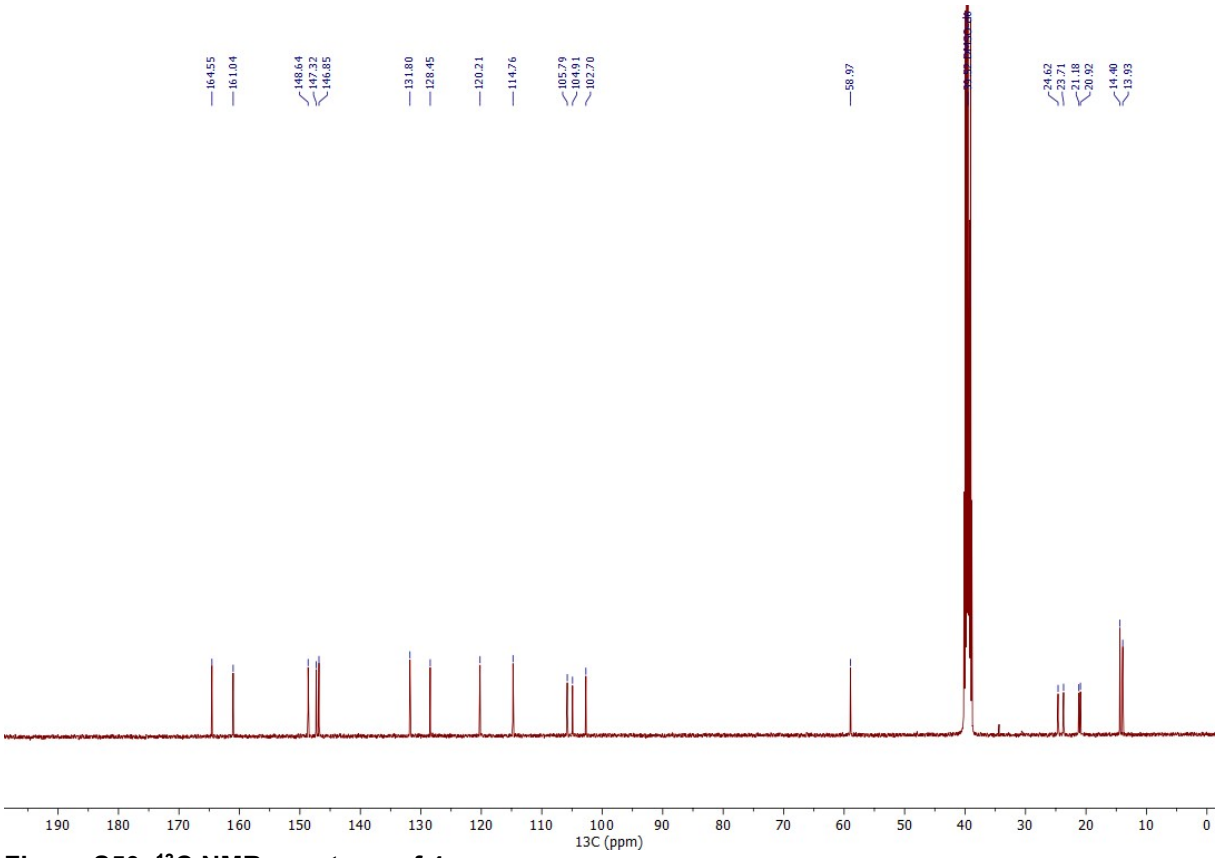

Figure S50. ^{13}C NMR spectrum of 4a

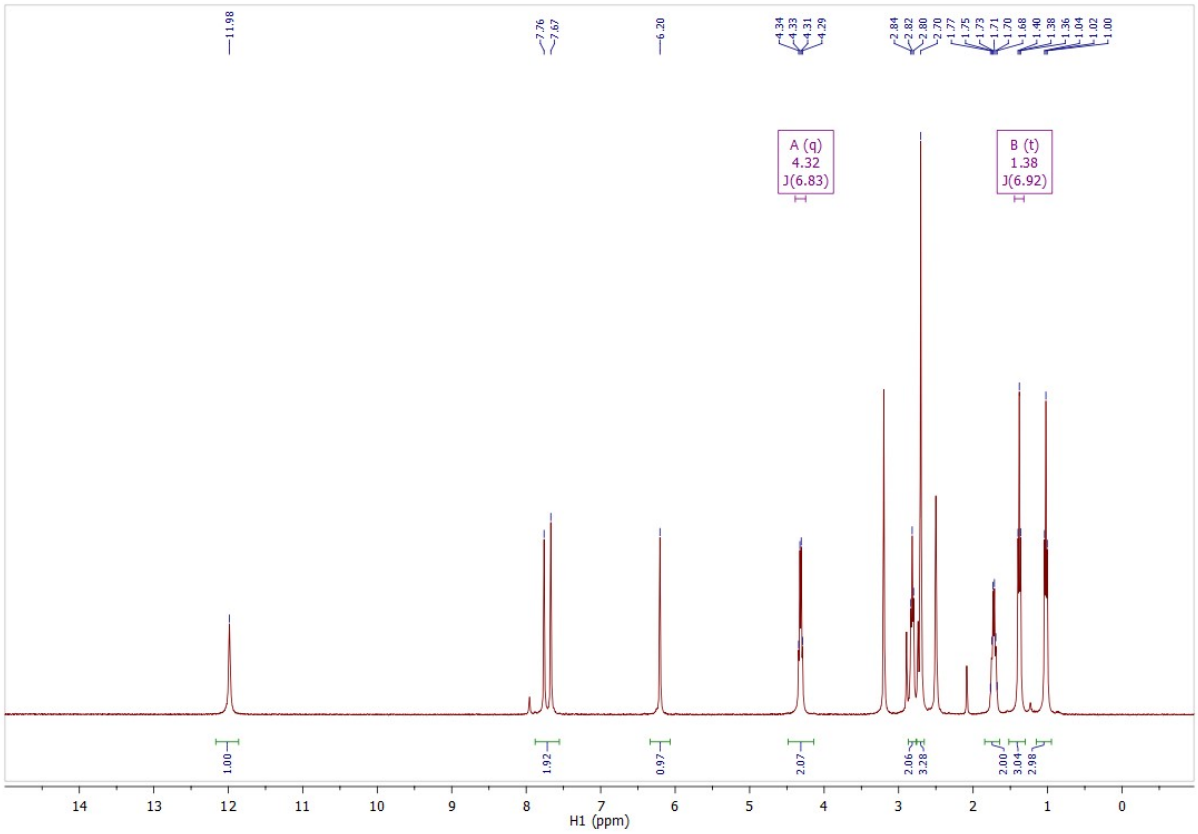

Figure S51. ^{1}H NMR spectrum of 4b

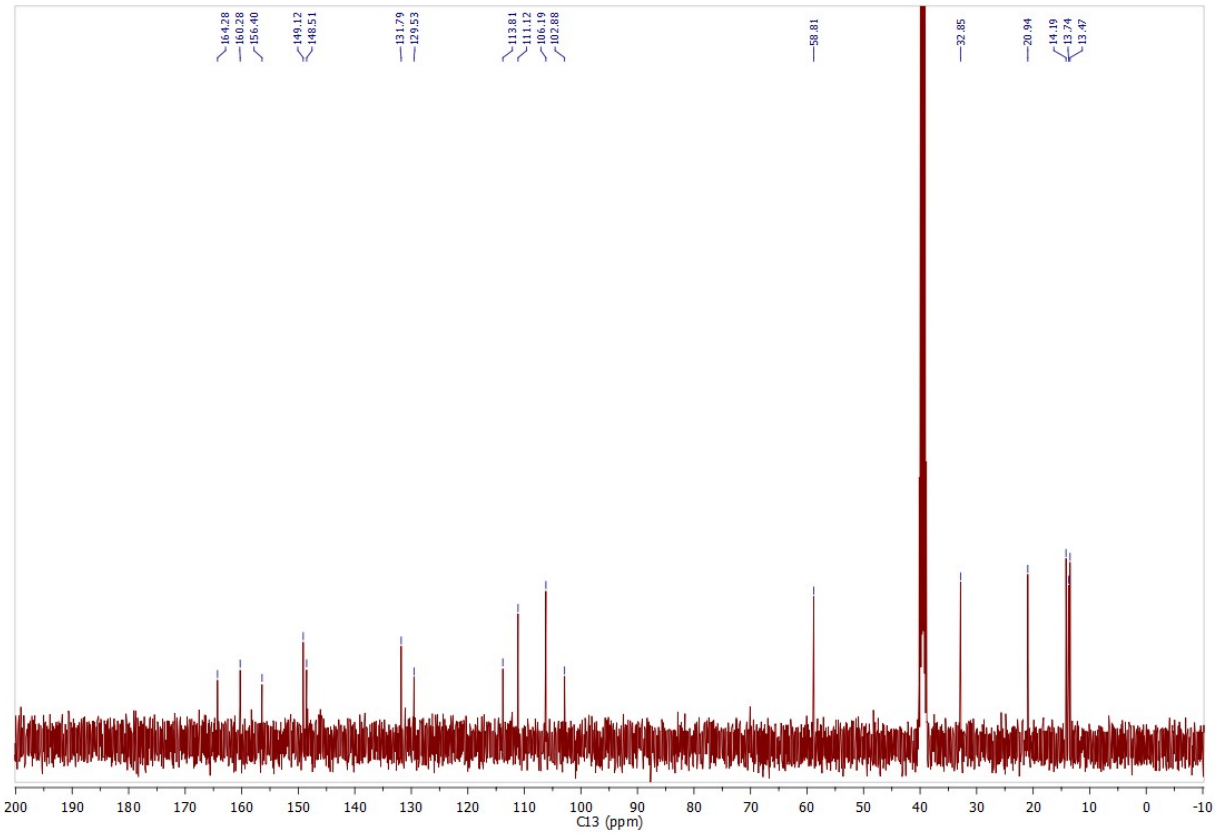

Figure S52. ^{13}C NMR spectrum of 4b

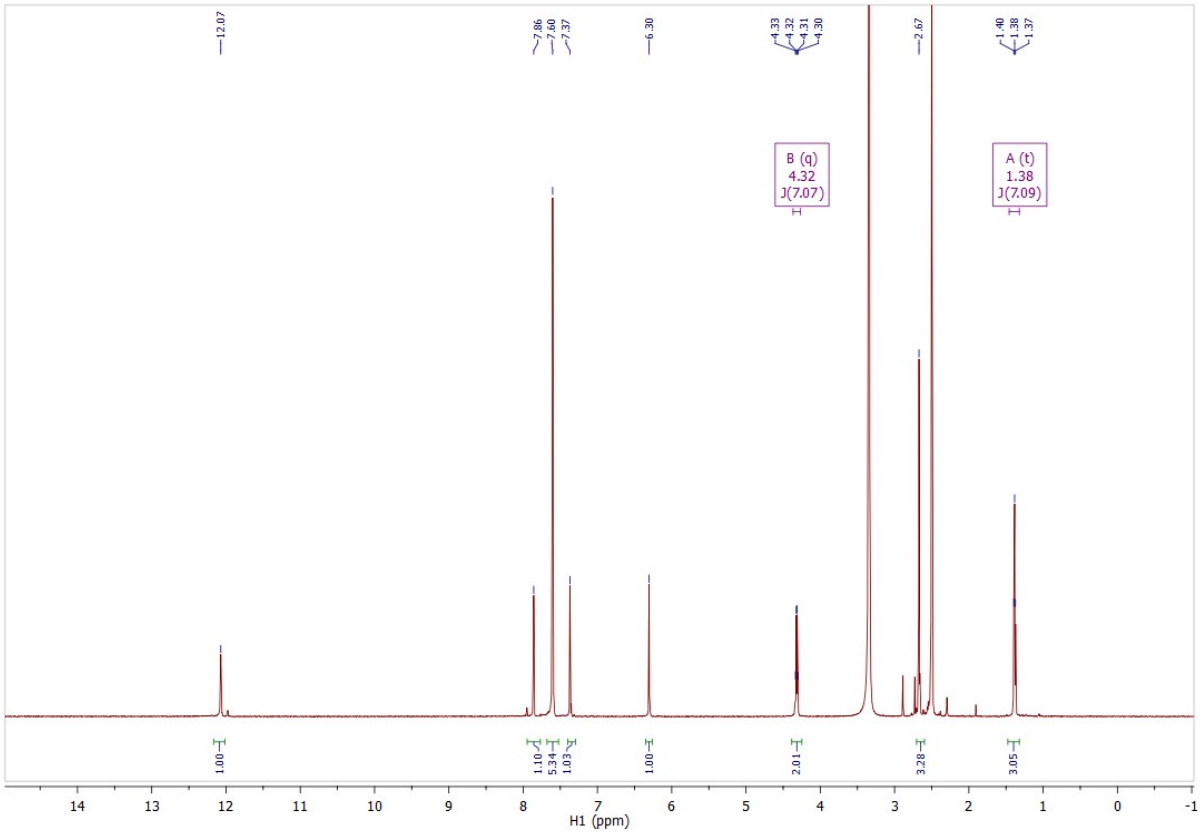

Figure S53. ^{1}H NMR spectrum of 4c

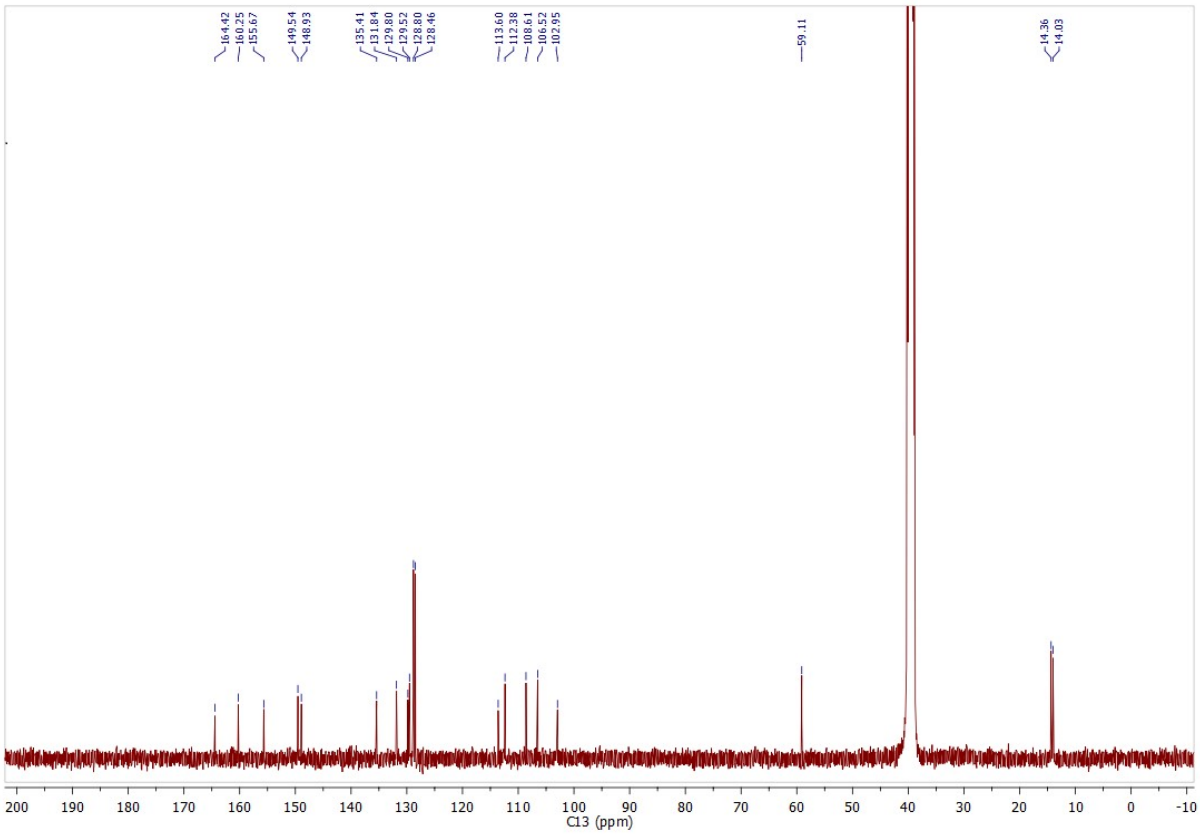

Figure S54. ^{13}C NMR spectrum of 4c

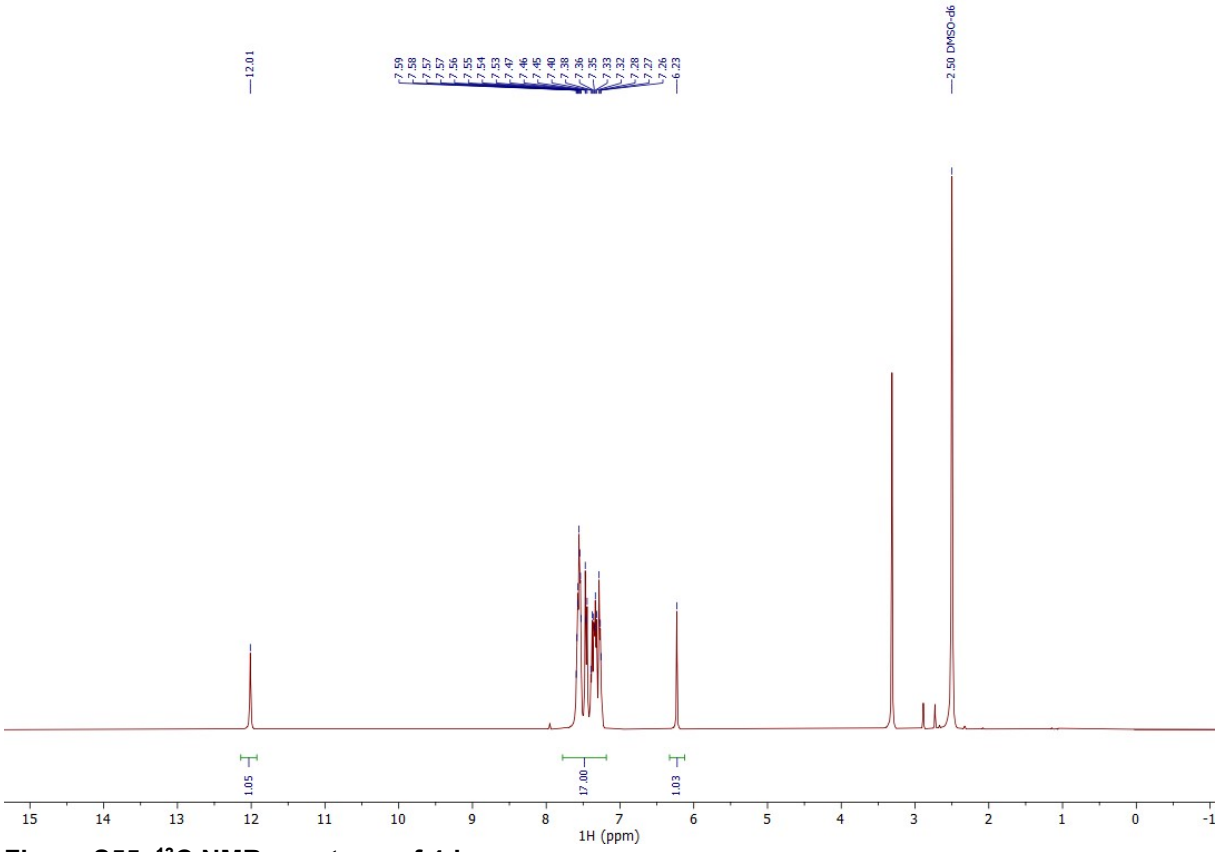

Figure S55. ^{13}C NMR spectrum of 4d

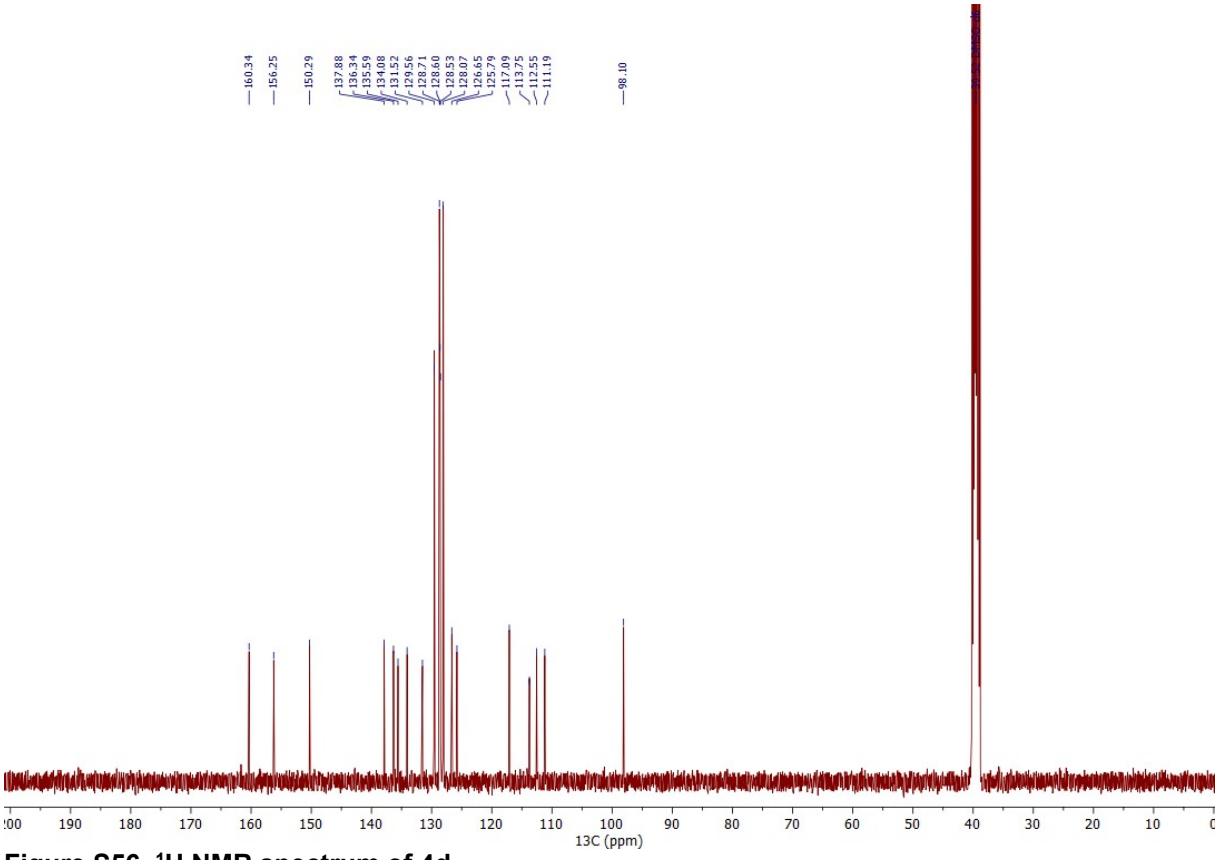

Figure S56. ^{1}H NMR spectrum of 4d

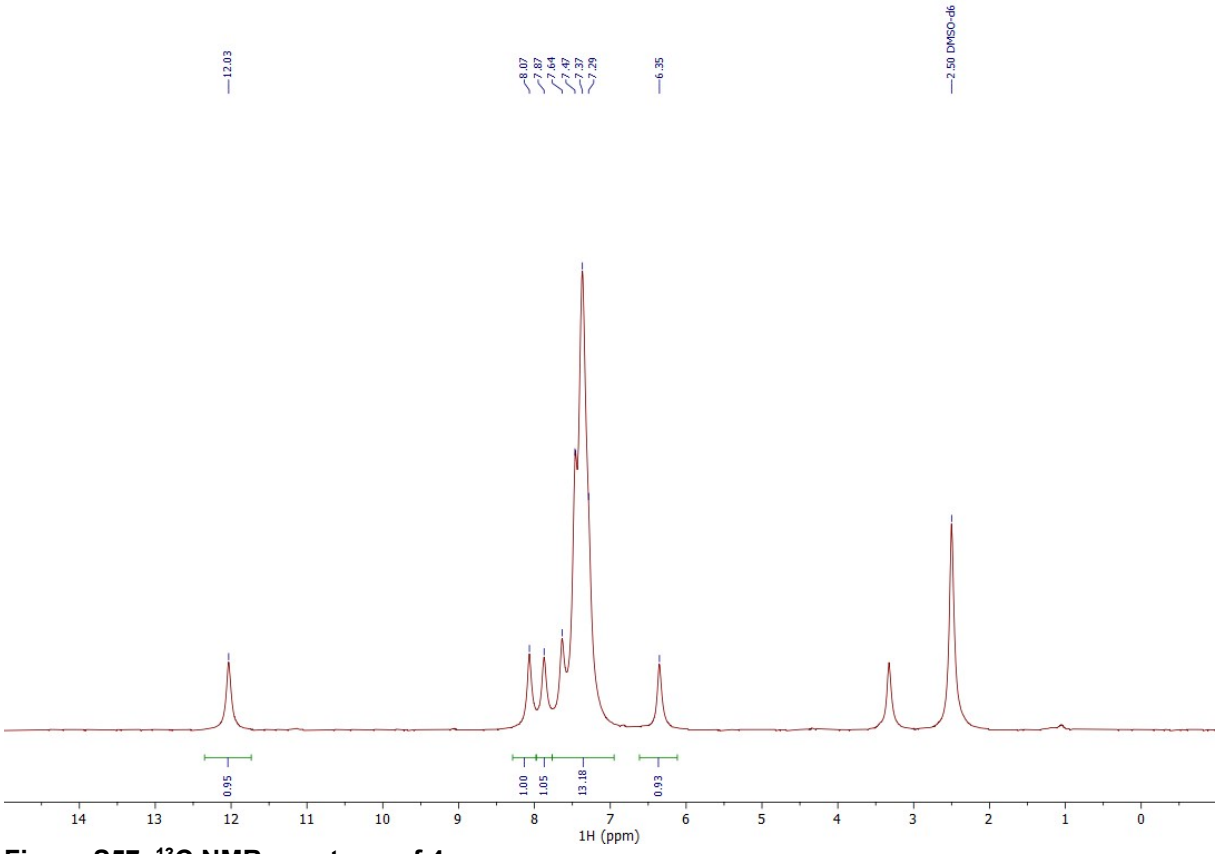

Figure S57. ^{13}C NMR spectrum of 4e

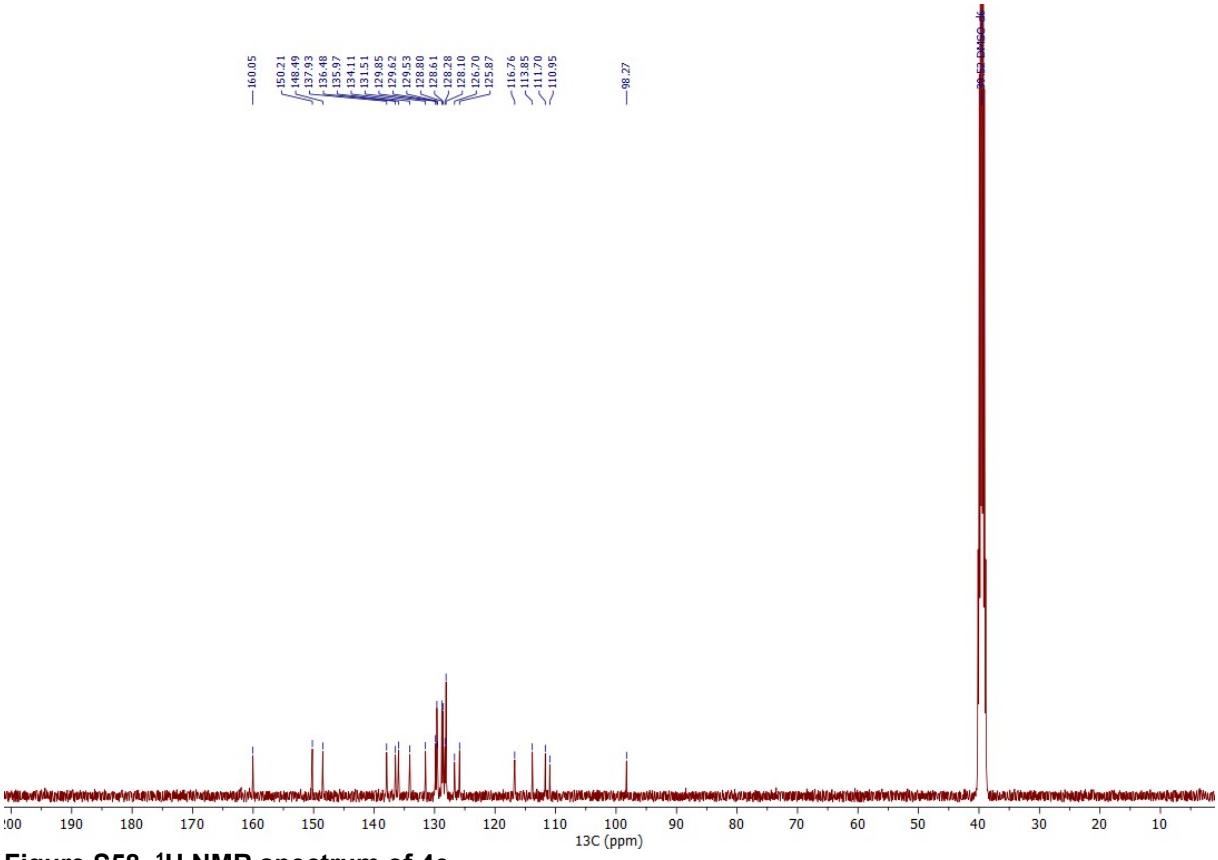

Figure S58. ^{1}H NMR spectrum of 4e

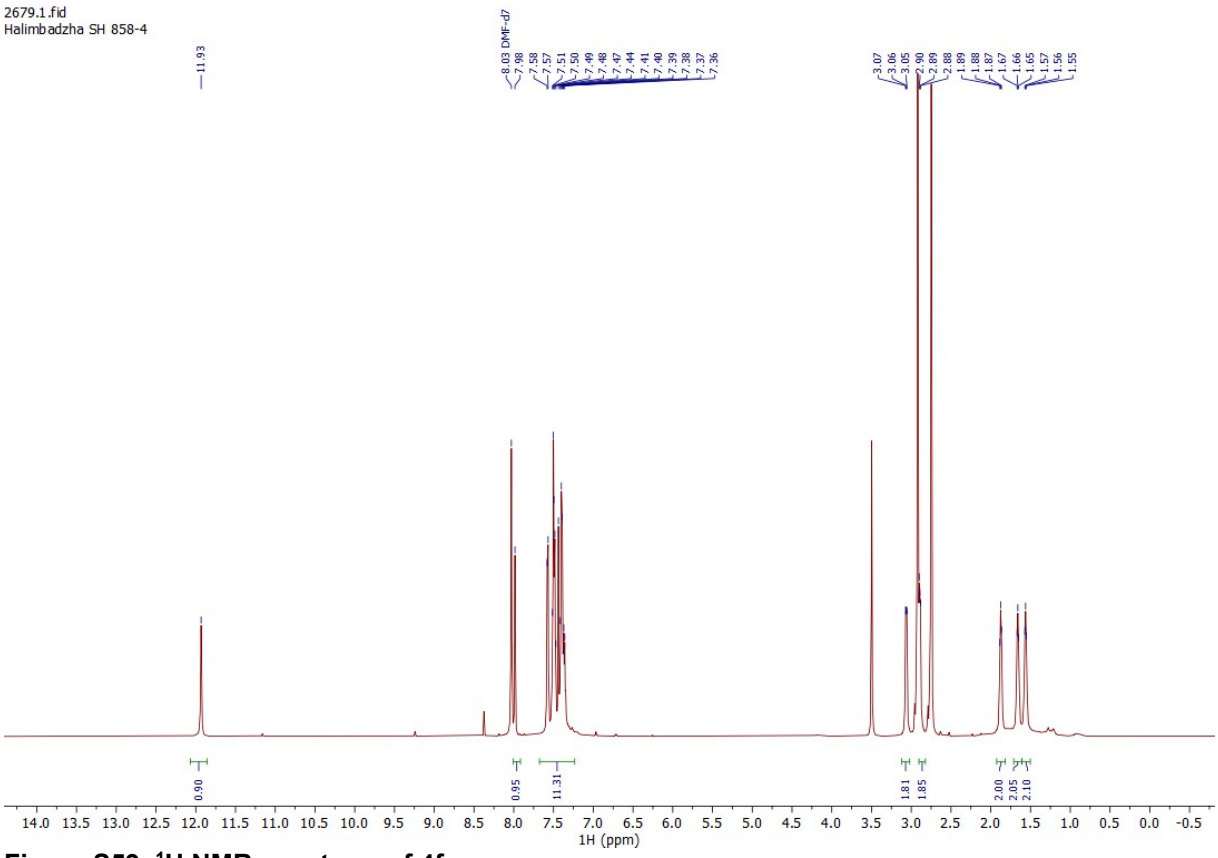

Figure S59. ^{1}H NMR spectrum of 4f

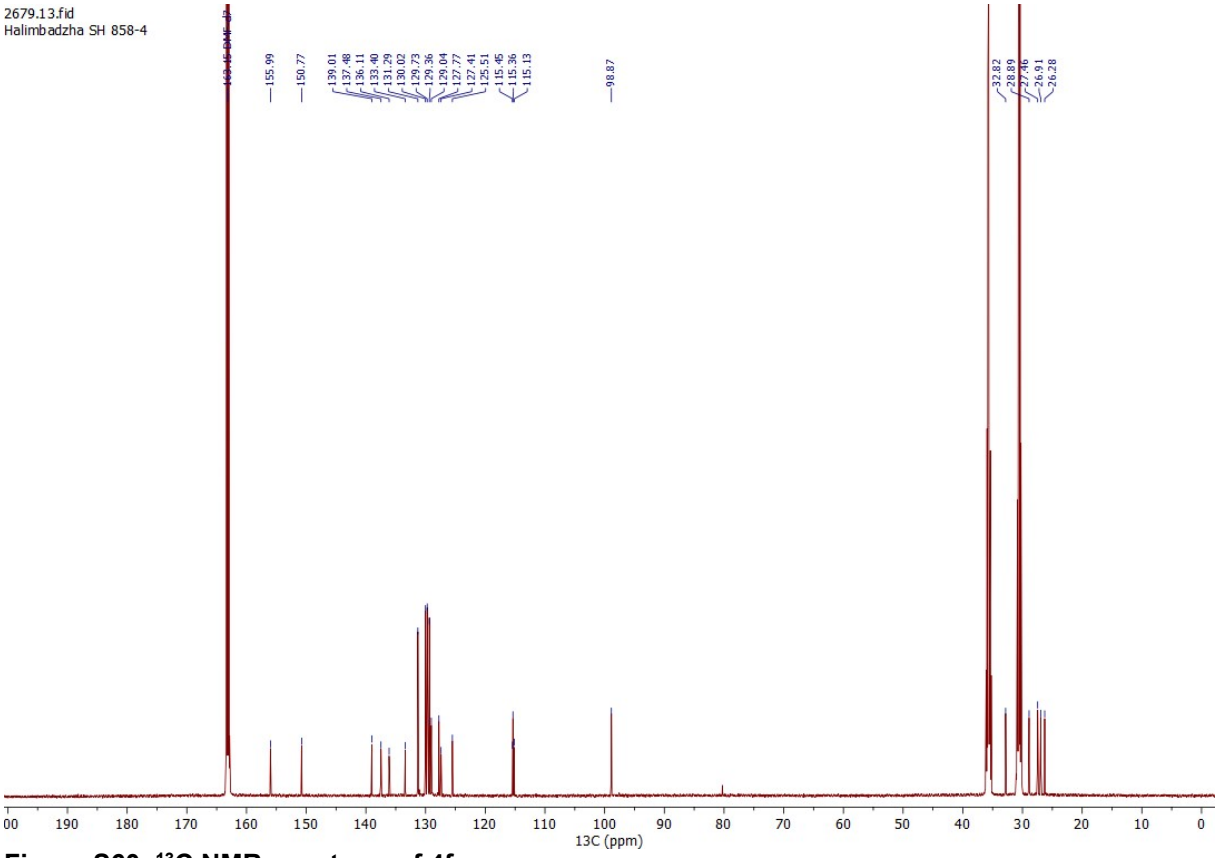

Figure S60. ^{13}C NMR spectrum of 4f

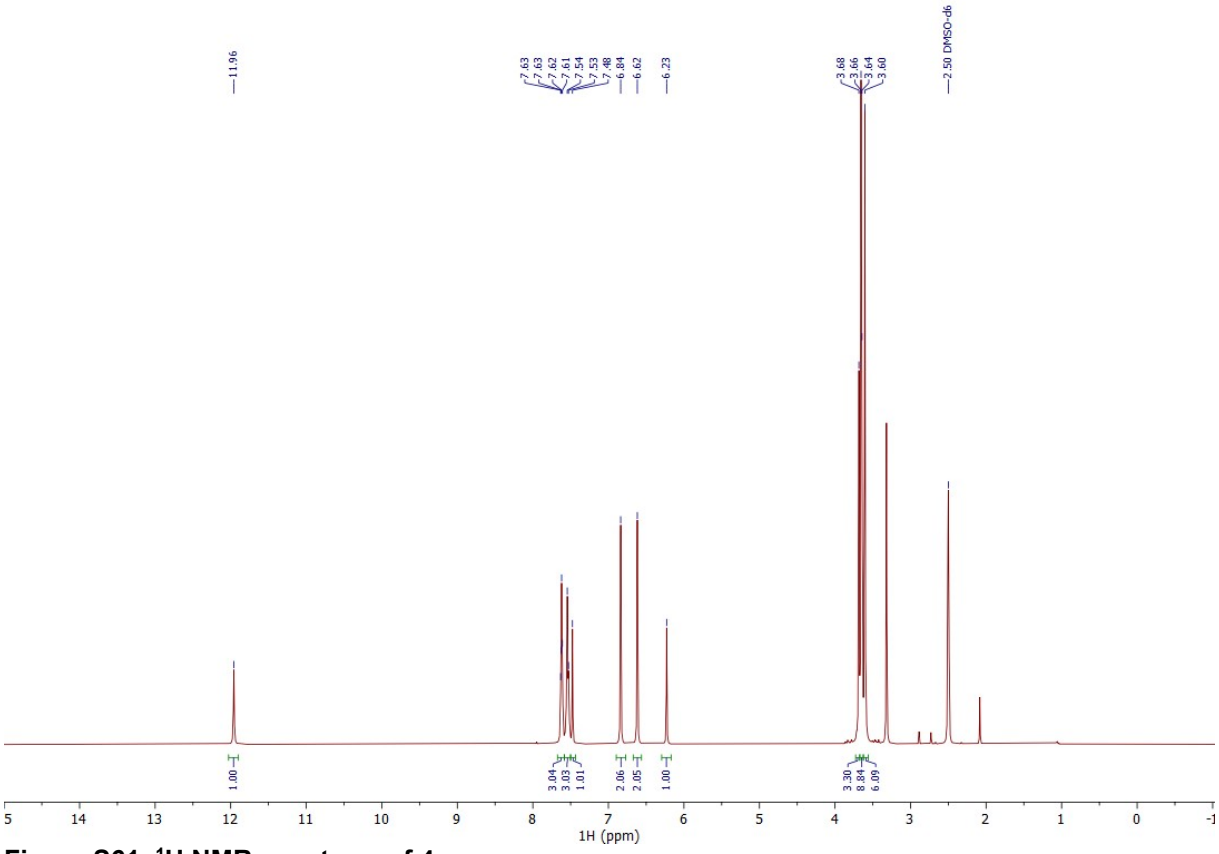

Figure S61. ^{1}H NMR spectrum of 4g

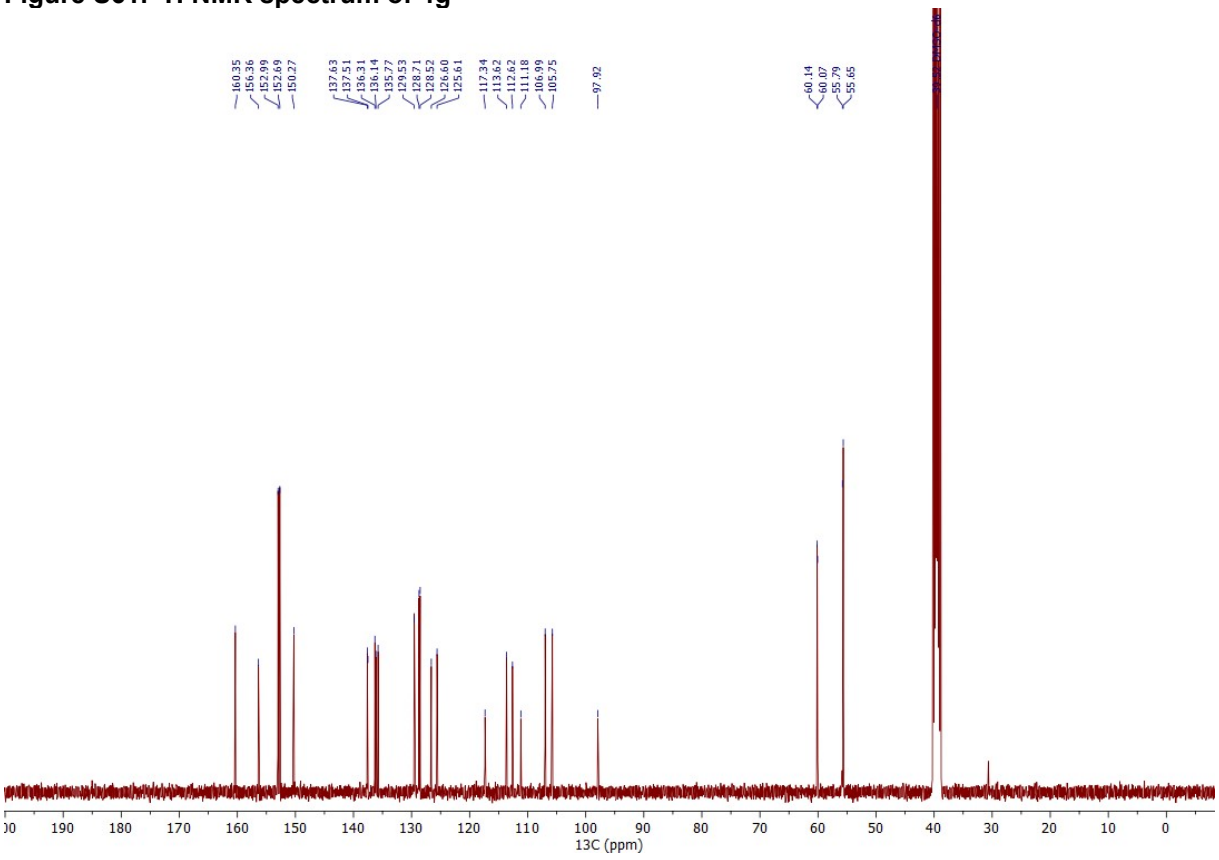

Figure S62. ^{13}C NMR spectrum of 4g

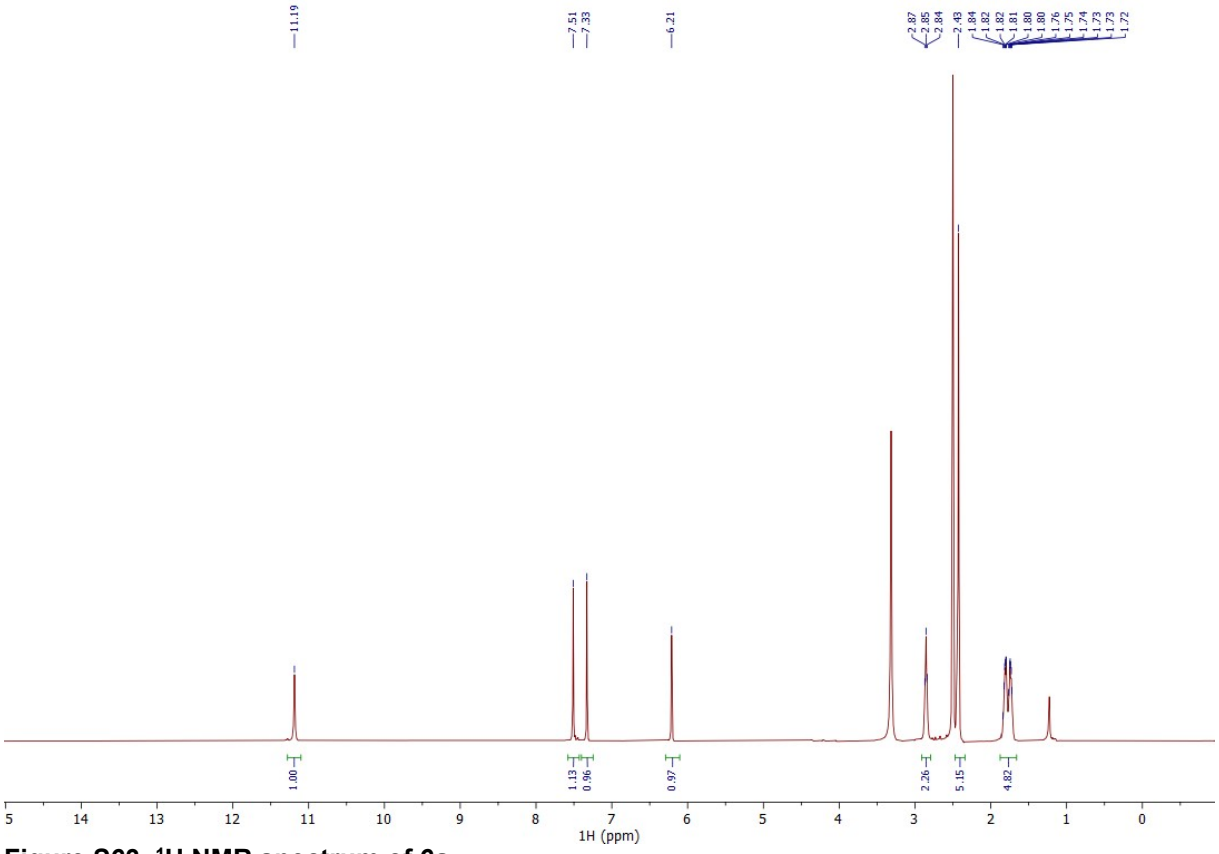

Figure S63. ^{1}H NMR spectrum of 6a

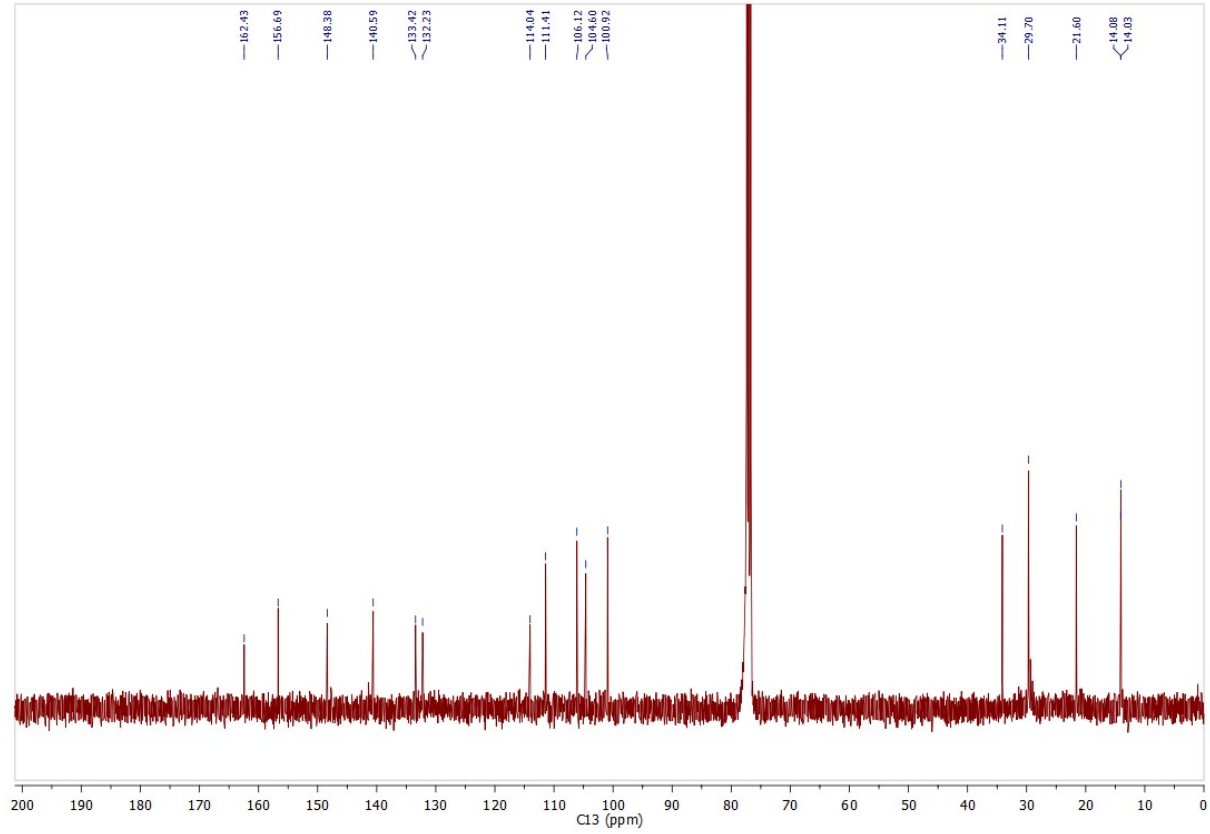

Figure S64. ^{13}C NMR spectrum of 6a

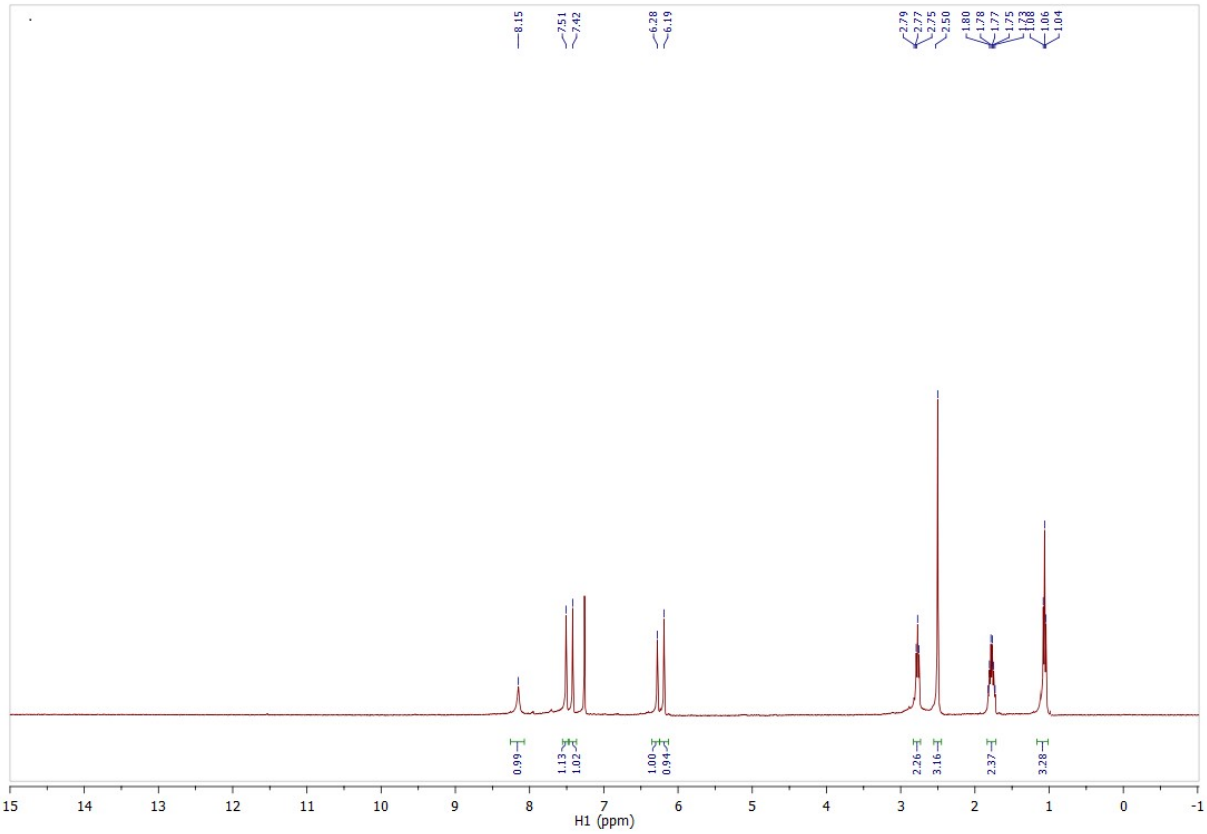

Figure S65. ^{1}H NMR spectrum of 6b

Figure S66. ^{13}C NMR spectrum of 6b