

Supporting Information

Efficient synthesis of 1,5-disubstituted carbohydrazones using K₂CO₃ as carbonyl donor

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General information:

All reagents were purchased from commercial suppliers and used without further purification. Solvents were freshly distilled prior to use.¹H-NMR, ¹³C-NMR spectra were measured on a Bruker AM400 NMR spectrometer (400 MHz or 100MHz, respectively) with *d*6-DMSO as solvent. ESI-MS spectral data were recorded on a Finnigan LCQDECA mass spectrometer.

General procedure for the sulfonylhydrazones.

To a rapidly stirred suspension of sulfonylhydrazide (2.5 mmol) in methanol (10 mL) was added aldehyde or ketone (2 mmol) dropwise (added as a methanol solution). When ketone was used, concentrated hydrochloric acid (0.1 ml) was added to reaction medium. After reflux for 1 hour, the mixture was cooled to 0 °C. The crystalline precipitate was collected by filtration, washed with a small quantity of methanol, dried in vacuo.

General procedure for the carbonylation of various tosylhydrazone derivatives

A reflux tube equipped with a magnetic stir bar charged with tosylhydrazone (0.5mmol), K₂CO₃ (0.75 mmol), diethyl phosphite (0.5 mmol), DMSO (2 mL), and the reaction vessel was placed in a 60°C oil bath. After stirring at this temperature for 10 h, the reaction mixture was then allowed to cool to ambient temperature, and diluted with 20 mL of ethyl acetate, and washed with brine (15

mL), water (15 mL), and then the organic layer was dried over Na_2SO_4 . After concentrated in vacuo, the crude product was purified by column chromatography (column-layer chromatographic silica gel, 37-54 μm , $\text{CH}_2\text{Cl}_2/\text{EtOAc} = 5/1$). The identity and purity of the known product was confirmed by $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and ESI-MS.

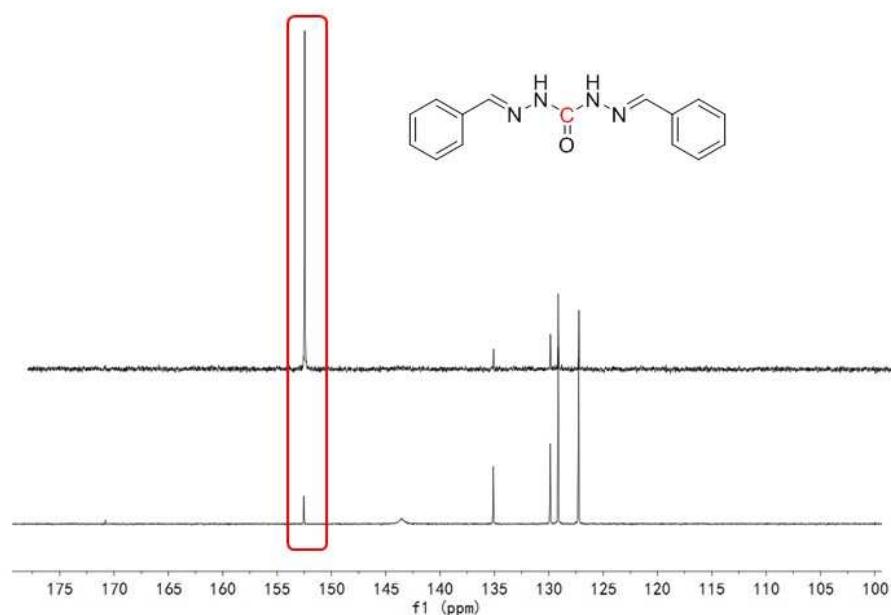
General procedure for one-pot carbonylation reactions

A reflux tube equipped with a magnetic stir bar charged with aldehyde (0.5mmol), tosyl hydrazide (0.6mmol), K_2CO_3 (0.75 mmol), diethyl phosphite (0.5 mmol), DMSO (2 mL), and the reaction vessel was placed in a 60°C oil bath. After stirring at this temperature for 10 h, the reaction mixture was then allowed to cool to ambient temperature, and diluted with 20 mL of ethyl acetate, and washed with brine (15 mL), water (15 mL), and then the organic layer was dried over Na_2SO_4 . After concentrated in vacuo, the crude product was purified by column chromatography (column-layer chromatographic silica gel, 37-54 μm , $\text{CH}_2\text{Cl}_2/\text{EtOAc} = 5/1$). The identity and purity of the known product was confirmed by $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and ESI-MS.

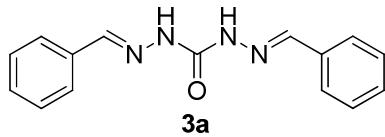
Investigation of carbonylation reaction using K_2CO_3 - ^{13}C as the base

A reflux tube equipped with a magnetic stir bar charged with tosylhydrazone **1a** (0.5mmol), K_2CO_3 - ^{13}C (0.75 mmol), diethyl phosphite (0.5 mmol), DMSO (2 mL), and the reaction vessel was placed in a 60°C oil bath. After stirring at this temperature for 10 h, the reaction mixture was then allowed to cool to ambient temperature, and diluted with 20 mL of ethyl acetate, and washed with brine (15 mL), water (15 mL), and then the organic layer was dried over Na_2SO_4 . After concentrated in vacuo, the crude product was purified by column chromatography (column-layer chromatographic silica gel, 37-54 μm , $\text{CH}_2\text{Cl}_2/\text{EtOAc} = 5/1$). The isolated product was monitored by $^{13}\text{C-NMR}$.

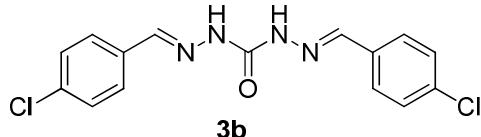
Figure S1: The $^{13}\text{C-NMR}$ spectrum contrast of carbonylation product using different K_2CO_3



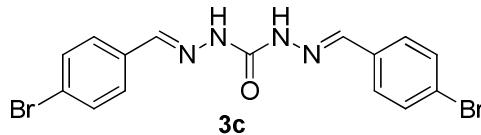
Spectroscopic data of products



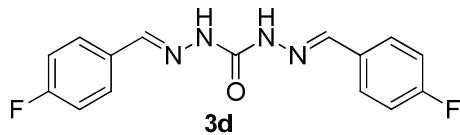
White solid, ^1H -NMR (400 MHz, *d*6-DMSO) δ = 10.72 (s, 2H), 8.21 (s, 2H), 7.75-7.77 (d, J =7.2, 4H), 7.39-7.46 (m, 6H). ^{13}C -NMR (100 MHz, *d*6-DMSO), δ =152.5, 135.1, 129.8, 129.1, 127.2. HRMS (ESI): m/z = 289.1055 [M+Na] $^+$.



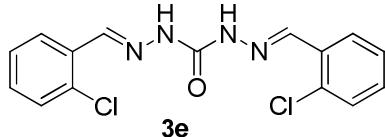
White solid, ^1H -NMR (400 MHz, *d*6-DMSO) δ = 10.79 (s, 2H), 8.17 (s, 2H), 7.77-7.79 (d, J =8.4, 4H), 7.49-7.51 (d, J =8.4, 4H). ^{13}C -NMR (100 MHz, *d*6-DMSO), δ =152.3, 134.2, 134.0, 130.4, 129.2, 128.8. HRMS (ESI): m/z = 357.0253 [M+Na] $^+$.



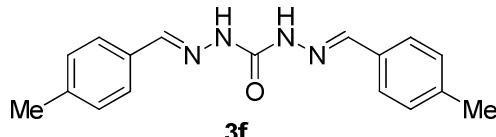
White solid, ^1H -NMR (400 MHz, *d*6-DMSO) δ = 10.80 (s, 2H), 8.15 (s, 2H), 7.70-7.72 (d, J =8.4, 4H), 7.62-7.64 (d, J =8.4, 4H). ^{13}C -NMR (100 MHz, *d*6-DMSO), δ =152.3, 134.3, 132.1, 129.1, 123.0. HRMS (ESI): m/z = 444.9262 [M+Na] $^+$.



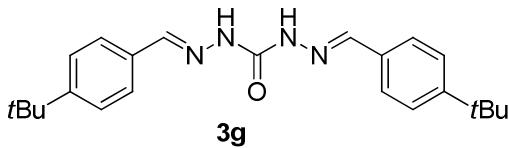
White solid, ^1H -NMR (400 MHz, *d*6-DMSO) δ = 10.70 (s, 2H), 8.18 (s, 2H), 7.79-7.83 (m, 4H), 7.25-7.30 (m, 4H). ^{13}C -NMR (100 MHz, *d*6-DMSO), δ =164.4, 161.9, 152.5, 131.7, 131.6, 129.4, 129.3, 116.2, 116.0. HRMS (ESI): m/z = 325.0845 [M+Na] $^+$.



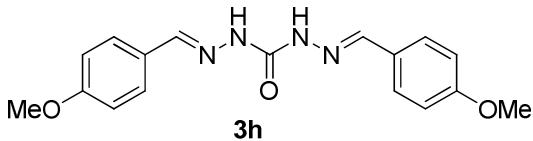
White solid, ^1H -NMR (400 MHz, *d*6-DMSO) δ = 11.06 (s, 2H), 8.59 (s, 2H), 8.18 (s, 2H) 7.41-7.53 (m, 6H). ^{13}C -NMR (100 MHz, *d*6-DMSO), δ =157.1, 144.2, 137.8, 137.0, 136.0, 134.9, 132.5, 132.3. HRMS (ESI): m/z = 357.0257 [M+Na] $^+$.



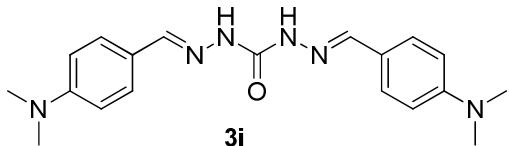
White solid, ^1H -NMR (400 MHz, *d*6-DMSO) δ = 10.58 (s, 2H), 8.14 (s, 2H), 7.63-7.65 (d, J =8.0, 4H), 7.24-7.26 (d, J =8.0, 4H), 2.34 (s, 6H). ^{13}C -NMR (100 MHz, *d*6-DMSO), δ =152.5, 139.5, 132.4, 129.7, 127.2, 21.4. HRMS (ESI): m/z = 317.1330 [M+Na] $^+$.



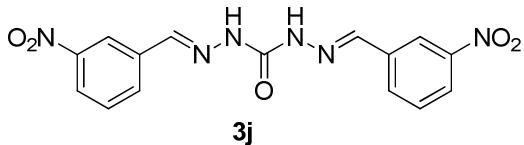
colorless oil, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 10.63 (s, 2H), 8.18 (s, 2H), 7.67-7.69 (d, J =8.4, 4H), 7.43-7.45 (d, J =8.4, 4H), 1.29 (s, 18H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =152.5, 143.3, 132.4, 127.0, 125.8, 34.9, 31.4. HRMS (ESI): m/z = 401.2282 [M+Na] $^+$.



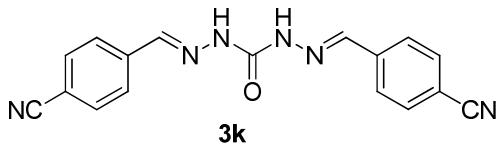
White solid, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 10.48 (s, 2H), 8.11 (s, 2H), 7.67-7.69 (d, J =8.4, 4H), 6.98-7.01 (d, J =8.8, 4H), 3.80 (s, 6H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =160.7, 152.5, 128.7, 127.7, 114.6, 55.7. HRMS (ESI): m/z = 349.1243 [M+Na] $^+$.



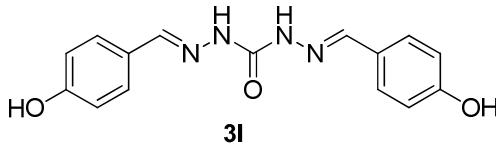
Yellow solid, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 10.23 (s, 2H), 8.02 (s, 2H), 7.53-7.55 (d, J =8.8, 4H), 6.73-6.75 (d, J =8.8, 4H), 2.96 (s, 12H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =152.6, 151.5, 128.4, 122.7, 112.2, 40.3. HRMS (ESI): m/z = 375.1868 [M+Na] $^+$.



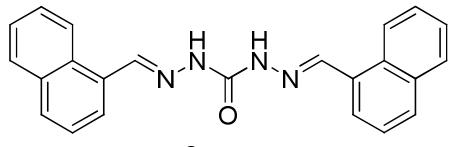
Yellow solid, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 11.21 (s, 2H), 8.60 (s, 2H), 8.27 (s, 2H), 8.04-8.06 (m, 2H), 7.79-7.83 (m, 2H), 7.62-7.67 (m, 2H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =152.1, 148.4, 138.8, 133.9, 130.6, 129.2, 128.4, 124.9. HRMS (ESI): m/z = 379.0725 [M+Na] $^+$.



White solid, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 11.09 (s, 2H), 8.24 (s, 2H), 7.89-7.93 (m, 8H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =152.1, 139.5, 133.0, 127.8, 119.2, 111.7. HRMS (ESI): m/z = 339.0971 [M+Na] $^+$.

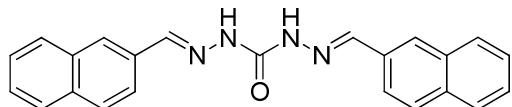


White solid, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 10.36 (s, 2H), 9.80 (s, 2H), 8.05 (s, 2H), 7.55-7.57 (d, J =8.4, 4H), 6.80-6.82 (d, J =8.4, 4H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =159.2, 152.6, 128.8, 126.2, 115.9. HRMS (ESI): m/z = 321.0933 [M+Na] $^+$.



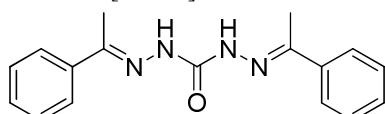
3m

White solid, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 10.88 (s, 2H), 9.01 (s, 2H), 8.59 (s, 2H), 8.14 (s, 2H), 8.00-8.02 (d, J =8.0, 4H), 7.58-7.69 (m, 6H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =152.5, 133.9, 130.8, 130.3, 130.2, 129.2, 127.5, 126.6, 126.1, 126.0, 123.9. HRMS (ESI): m/z = 389.1340 [M+Na] $^+$.



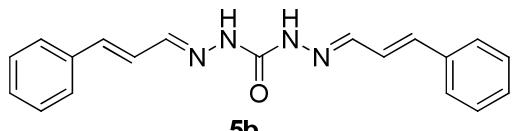
3n

White solid, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 10.87 (s, 2H), 8.38 (s, 2H), 8.11-8.13 (d, J =10.0, 4H), 7.94-8.00 (m, 6H), 7.55-7.58 (m, 4H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =152.5, 133.9, 133.4, 132.9, 128.7, 128.6, 128.3, 128.2, 127.7, 127.2, 127.1, 123.4. HRMS (ESI): m/z = 389.1348 [M+Na] $^+$.



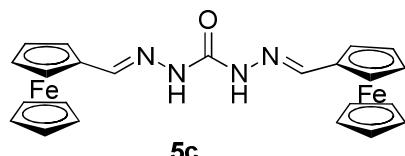
5a

White solid, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 9.86 (s, 2H), 7.80-7.83 (m, 4H), 7.39-7.45 (m, 6H), 2.28 (s, 6H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =152.6, 138.6, 129.3, 128.8, 126.4, 13.8. HRMS (ESI): m/z = 317.1346 [M+Na] $^+$.



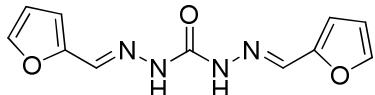
5b

White solid, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 10.57 (s, 2H), 7.95-7.96 (d, J =5.6, 2H), 7.56-7.58 (d, J =7.6, 4H), 7.37-7.41 (m, 4H), 7.30-7.33 (m, 2H), 6.94-6.96 (d, J =6.8, 2H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =152.2, 137.4, 136.5, 129.3, 129.0, 127.2, 126.1. HRMS (ESI): m/z = 341.1344 [M+Na] $^+$.



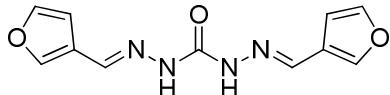
5c

Red solid, $^1\text{H-NMR}$ (400 MHz, *d*6-DMSO) δ = 10.20 (s, 2H), 7.95 (s, 2H), 4.67 (s, 4H), 4.40 (s, 4H), 4.22 (s, 10H). $^{13}\text{C-NMR}$ (100 MHz, *d*6-DMSO), δ =152.2, 80.3, 70.0, 69.5, 69.3, 67.6, 60.2. HRMS (ESI): m/z = 505.0345 [M+Na] $^+$.



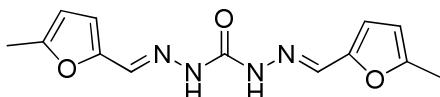
5d

White solid, $^1\text{H-NMR}$ (400 MHz, d_6 -DMSO) δ = 10.61 (s, 2H), 8.08 (s, 2H), 7.79 (d, $J=1.2$, 2H), 6.83-6.84 (d, $J=3.2$, 2H), 6.61 (m, 2H). $^{13}\text{C-NMR}$ (100 MHz, d_6 -DMSO), δ =152.2, 150.2, 144.8, 133.8, 112.5, 112.1. HRMS (ESI): m/z = 269.0643 [M+Na] $^+$.



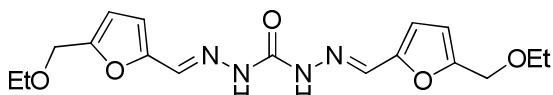
5e

White solid, $^1\text{H-NMR}$ (400 MHz, d_6 -DMSO) δ = 10.48 (s, 2H), 8.10 (s, 2H), 8.05 (s, 2H), 7.74 (s, 2H), 6.91 (s, 2H). $^{13}\text{C-NMR}$ (100 MHz, d_6 -DMSO), δ =152.4, 144.9, 144.6, 123.3, 107.9. HRMS (ESI): m/z = 269.0635 [M+Na] $^+$.



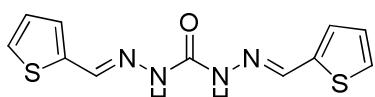
5f

White solid, $^1\text{H-NMR}$ (400 MHz, d_6 -DMSO) δ = 10.46 (s, 2H), 7.98 (s, 2H), 6.69-7.70 (d, $J=3.2$, 2H), 6.22-6.23 (m, 2H), 2.33 (s, 6H). $^{13}\text{C-NMR}$ (100 MHz, d_6 -DMSO), δ =154.1, 152.3, 148.6, 113.9, 108.8, 13.9. HRMS (ESI): m/z = 297.0947 [M+Na] $^+$.



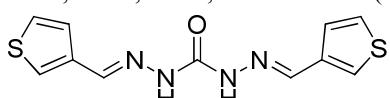
5g

White solid, $^1\text{H-NMR}$ (400 MHz, d_6 -DMSO) δ = 10.62 (s, 2H), 8.03 (s, 2H), 6.78-6.79 (d, $J=3.2$, 2H), 6.54-6.50 (d, $J=3.6$, 2H), 4.42 (s, 4H), 3.45-3.50 (m, 4H), 1.11-1.14 (m, 6H). $^{13}\text{C-NMR}$ (100 MHz, d_6 -DMSO), δ =153.8, 152.2, 150.0, 113.1, 111.8, 65.3, 64.1, 15.4. HRMS (ESI): m/z = 385.1463 [M+Na] $^+$.



5h

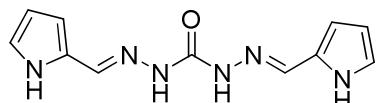
Yellow solid, $^1\text{H-NMR}$ (400 MHz, d_6 -DMSO) δ = 10.56 (s, 2H), 8.36 (s, 2H), 7.61-7.63 (d, $J=5.2$, 2H), 7.37-7.38 (m, 2H), 7.10-7.12 (m, 2H). $^{13}\text{C-NMR}$ (100 MHz, d_6 -DMSO), δ =152.1, 139.7, 138.9, 130.0, 128.4, 128.1. HRMS (ESI): m/z = 301.0155 [M+Na] $^+$.



5i

Yellow solid, $^1\text{H-NMR}$ (400 MHz, d_6 -DMSO) δ = 10.53 (s, 2H), 8.20 (s, 2H), 7.81-7.82 (m, 2H), 7.60-7.63 (m, 4H). $^{13}\text{C-NMR}$ (100 MHz, d_6 -DMSO), δ =152.5, 138.3, 127.6, 127.0, 125.5. HRMS

(ESI): m/z = 301.0187 [M+Na]⁺.

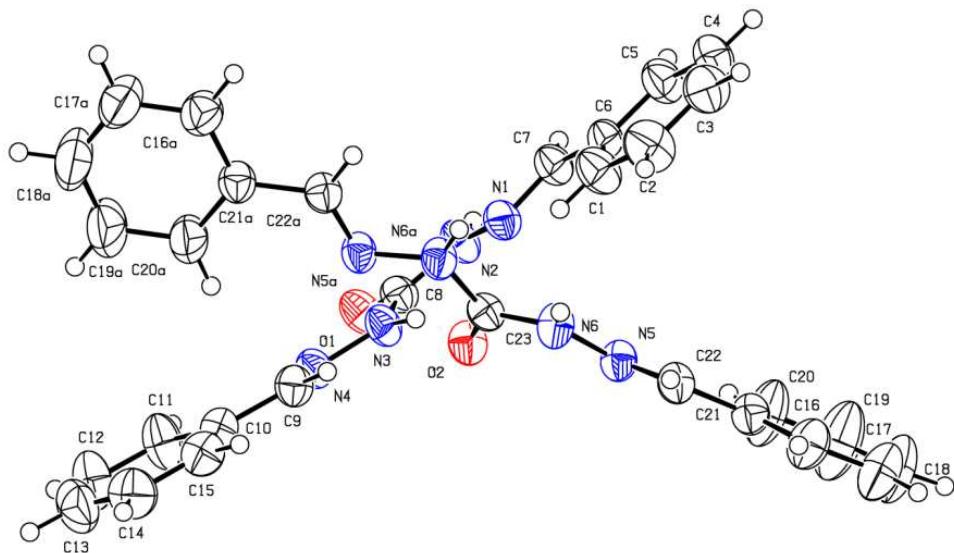


5j

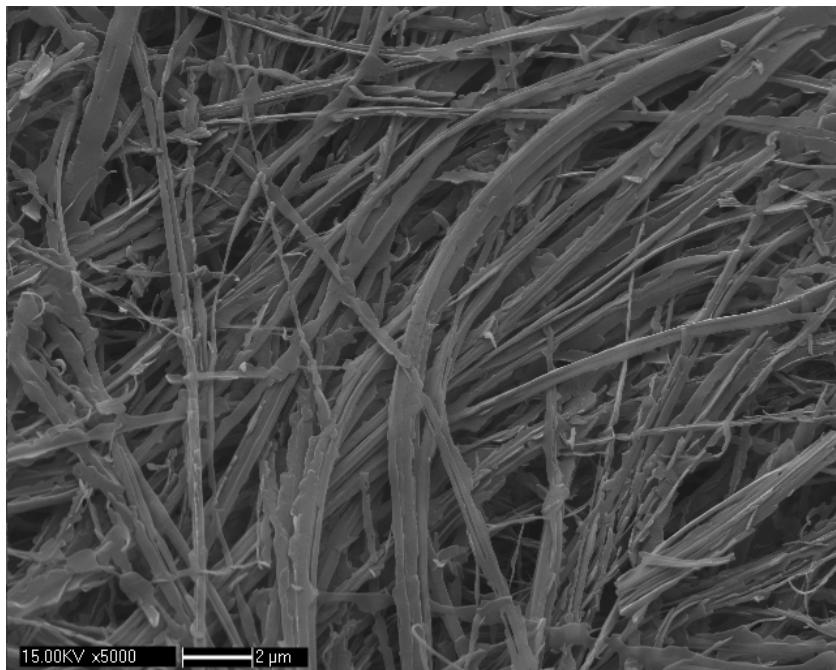
Yellow solid, ¹H-NMR (400 MHz, *d*6-DMSO) δ= 11.36 (s, 2H), 10.29 (s, 2H), 7.92 (s, 2H), 6.94 (s, 2H), 6.38 (s, 2H), 6.11-6.12 (d, J=2.8, 2H). ¹³C-NMR (100 MHz, *d*6-DMSO), δ=179.6, 152.6, 128.0, 121.8, 112.2, 109.4. HRMS (ESI): m/z = 267.0938 [M+Na]⁺.

Crystallographic Data of 3a

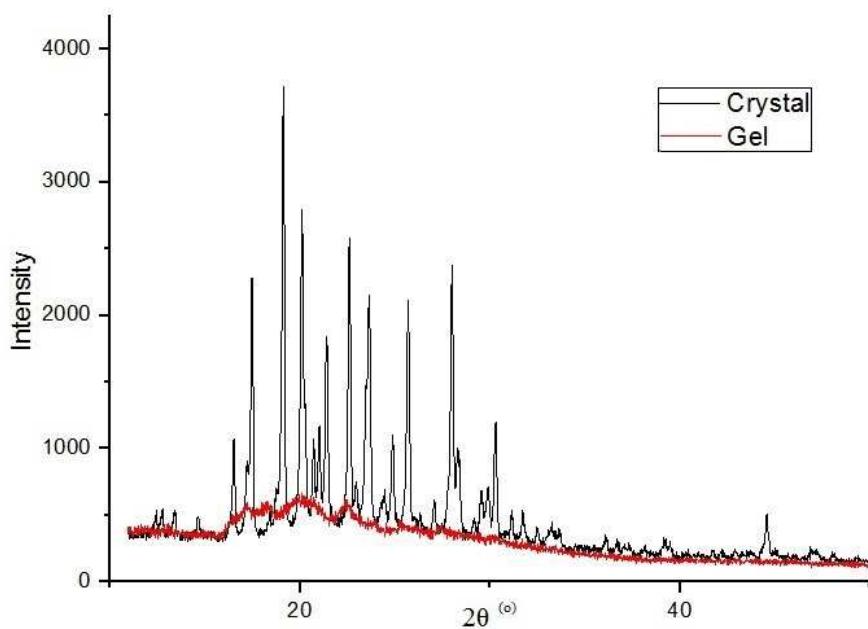
Chemical formula	C ₁₅ H ₁₄ N ₄ O
formula weight	266.30
temperature/K	296
crystal system	monoclinic
space group	P 2/c
a (Å)	14.3095(6)
b (Å)	8.5597(4)
c (Å)	17.1468(8)
α(deg)	90
β (deg)	97.135(3)
γ (deg)	90
V, Å ³	2083.96(16)
Z	6
ρ, g/cm ³	1.273



SEM image of the xerogel obtained from the gel of 3a in CHCl₃



Powder X-ray diffraction patterns of the single crystal and gel (red line) of 3a



¹H-NMR and ¹³C-NMR spectra

