Regioselective Synthesis of Vitamin K_3 Based Dihydrobenzophenazine Derivative: Their Novel Crystal Structure and DFT Studies

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Supplementary material

Synthesis of 1

1 g of menadione (5.80 mM) was taken in a round bottom flask. About 30 ml methanol was added to it just so that it dissolves. After stirring the solution on a magnetic stirrer for about 15 minutes, about 0.625 g of o-phenylenediamine (5.80 mM) was added to it. The reaction was refluxed for 30 hrs with constant stirring at 60-70°C. During this time the progress of the reaction was monitored using thin layer chromatography. The reaction mixture was transferred to a beaker and kept for 5 days for the solvent to evaporate. The solid crude product was obtained by evaporation. The crude product was purified by column chromatography using toluene: methanol (9.5:0.5) as eluent. Dark orange colored crystals obtained by slow evaporation the solvent (toluene).

General Materials and Methods

The materials used viz vitamin K3 (2-methyl-1,4-naphthoquinone), 2-aminophenol, O-phenelenediamine were purchased from Sigma-Aldrich. The solvents used such as toluene, methanol are of analytical grade were purchased from Merck Chemicals. Solvents were distilled by standard methods and dried wherever necessary. The FT-IR spectra of the compounds were recorded between 4000-400 cm^{-1} as KBr pellets on SHIMADZU FT 8400 spectrometer. Mass of compound was determined by GC-MS 2010-eV (Make SHIMADZU). Melting points of compound were determined using melting point apparatus (Make-METTLER) and were corrected using DSC (Differential Scanning Calorimetry) (Make- TA Q2000). UV-Visible spectra of compound were recorded on SHIMADZU UV 1650 in DMSO between 200 to 800 nm. ^{1}H, $^{13}CNMR$ and 2D gHSQCAD of compounds was recorded in $CDCl_3$ on Varian mercury

500 MHz NMR instrument; TMS (tetramethylsilane) was used as the internal reference. Elemental analysis was performed on Elementar Vario EL III.

Figure legends

Fig.S1 LC-MS spectra of **1**

Fig.S2 FT-IR spectrums of vitamin K3 in region 4000 cm^{-1} to 400 cm^{-1} (vitamin K3 = 2-methyl-1,4-naphthaquinone)

Fig.S3 FT-IR spectrums of **1** in region 4000 cm^{-1} to 400 cm^{-}

Fig.S4 [1]Characteristic FT-IR frequencies of vitamin K3 and **1**. (a) ν_{N-H} region (b) $\nu_{C=O}$ and ν_{C-N} region

Fig.S5 DSC plot of **1**

Fig.S6 a) ^{1}H, b) ^{13}C NMR spectra of **1**

Fig.S7 2D gHSQCAD NMR spectra of **1** of saturated carbon

Fig.S8 2D gHSQCAD NMR spectra of **1** in aromatic region

Fig.S9 UV-Visible spectra of vitamin K3 and **1** in DMSO with concentration ~ 1×10^{-4} M

Fig.S10 HOMO and LUMO orbitals of **1** (Isosurface value of -17.5 kJ mol^{-1})

Fig.S11 Observed and optimized IR spectra of **1**

Table legends

Table S1 Crystallographic data of **1**

Table S2 Selected bond lengths (Å) and angles (°) for **1**

LCMS REPORT

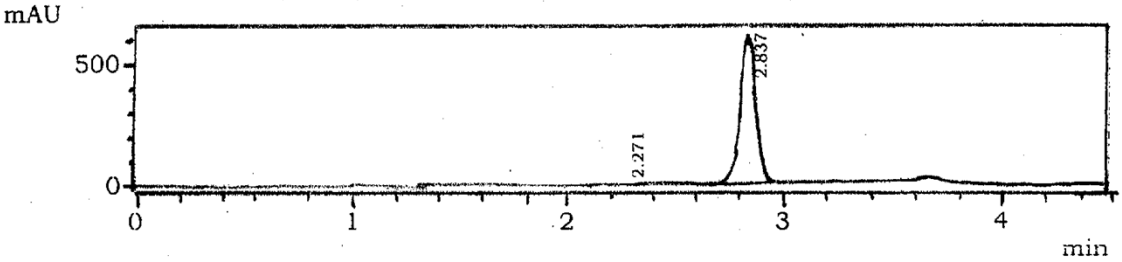
Sample Information

Acquired by	: Admin
Date Acquired	: 9/17/2014 7:06:47 PM
Sample Name	: AP TT1-5
Sample ID	: MD-12DA
Data File	: 075.lcd
Method File	: LCMS METHOD
AR number	:
Analysed By	: LCMS-03-170914-75

Method:-METHOD
Column :YMC TRIART ,50mm X4.6 mm.3 µ
Mobile Phase: A. 5mM Ammonium Formate in water + 0.1% Ammonia
B. Acetonitrile + 5% Solvent A + 0.1% Ammonia
Inj Volume; .5µL, Flow Rate: 1.400 mL/minute
Gradient program:
10% B to 95% B in 2.5 minute, Hold till 3.00 min
At 4.00min B conc is 10 % hold up to 4.5 min

Chromatogram

AP TT1-5 E:\AMC\LCMS 03\DATA\2014\SEPT\17\Sample\075.lcd



1 PDA Multi 1 / 210nm - 400nm 4nm

MS Chromatogram

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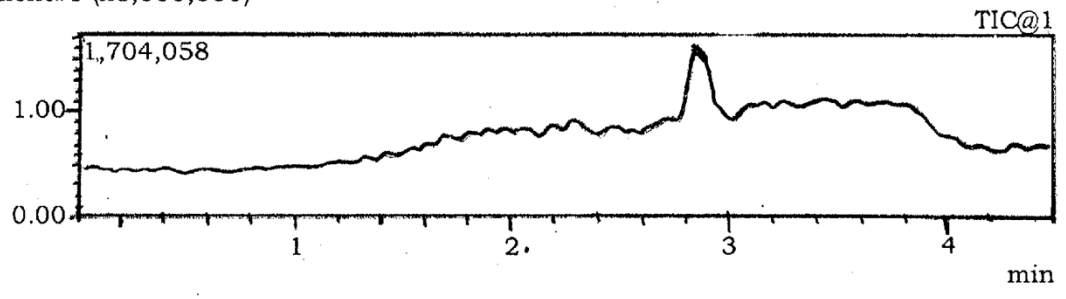
Segment#1 (x1,000,000)



MS Spectrum Graph

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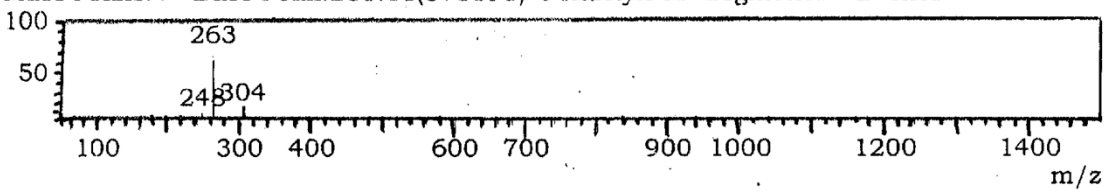
Mass Peaks:4 Base Peak:263.11(378398) Polarity:Pos Segment1 - Event1



PeakTable

PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %
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2	3.810	193068	98.537
3	3.915	1362	0.695
Total		195933	100.000

Fig.S1LC-MS spectra of **1**

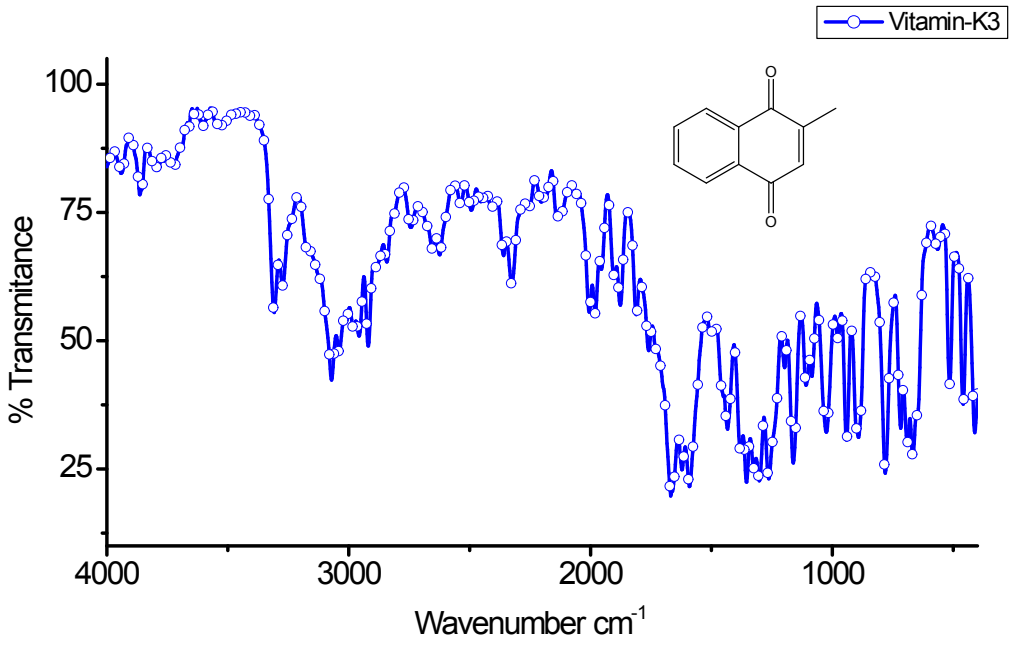


Fig.S2 FT-IR spectrums of Vitamin-K3 in region 4000 cm^{-1} to 400 cm^{-1}

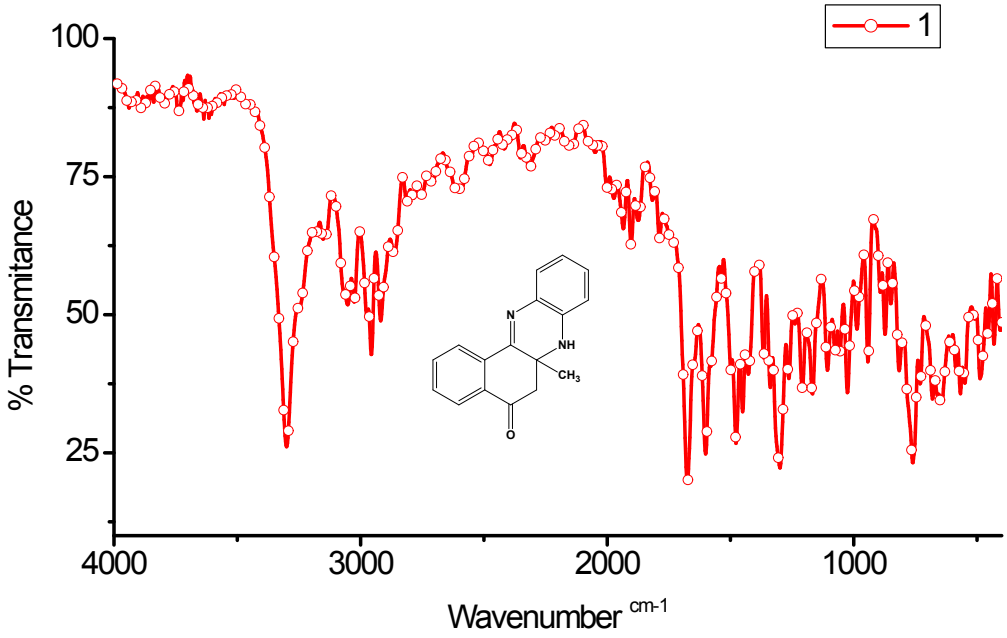


Fig.S3 FT-IR spectrums of **1** in region 4000 cm^{-1} to 400 cm^{-1}

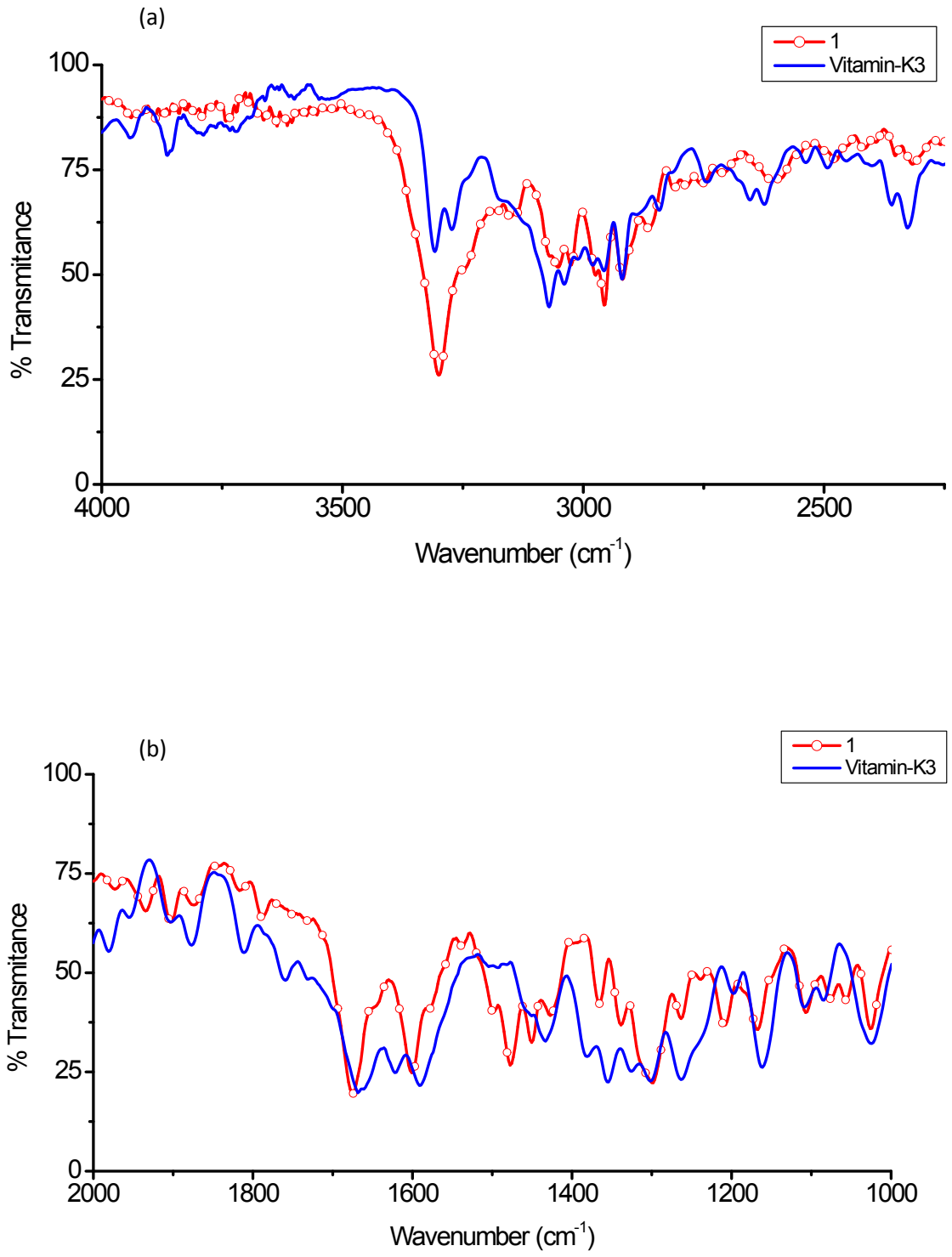


Fig.S4 Characteristic FT-IR frequencies of vitamin K3 and **1**. (a) ν_{N-H} region (b) $\nu_{C=O}$ and ν_{C-N} region

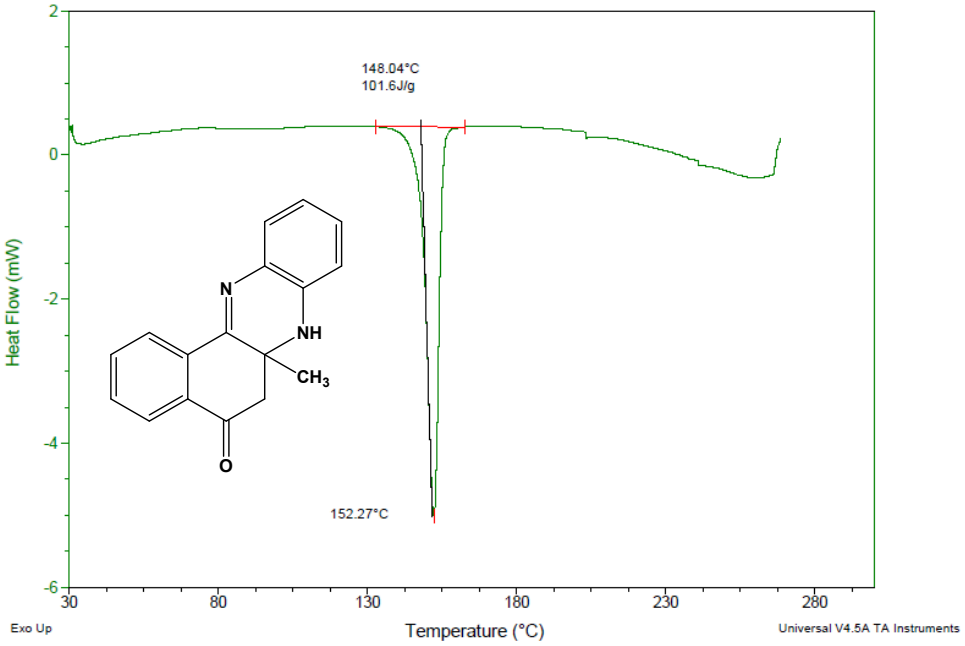
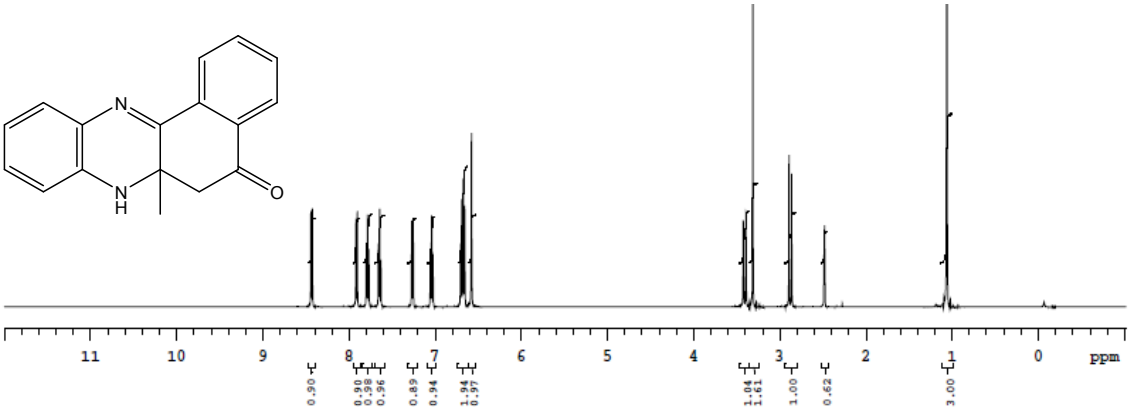
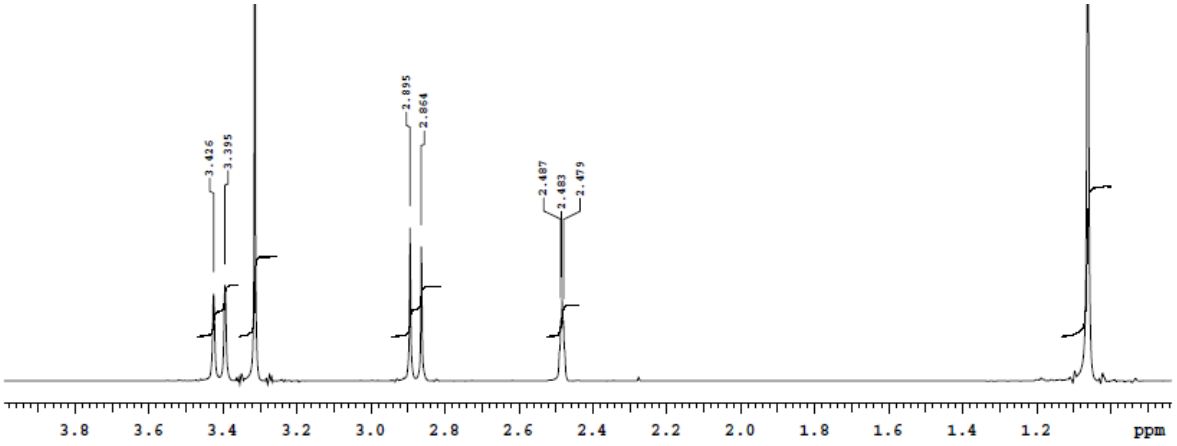


Fig.S5DSC plot of **1**

(a)


N
N
H
O
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.90
0.90
0.98
0.96
0.89
0.94
1.94
0.97
1.04
1.61
1.00
0.62
3.00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2.895
2.864
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2.483
2.479
3.8
3.6
3.4
3.2
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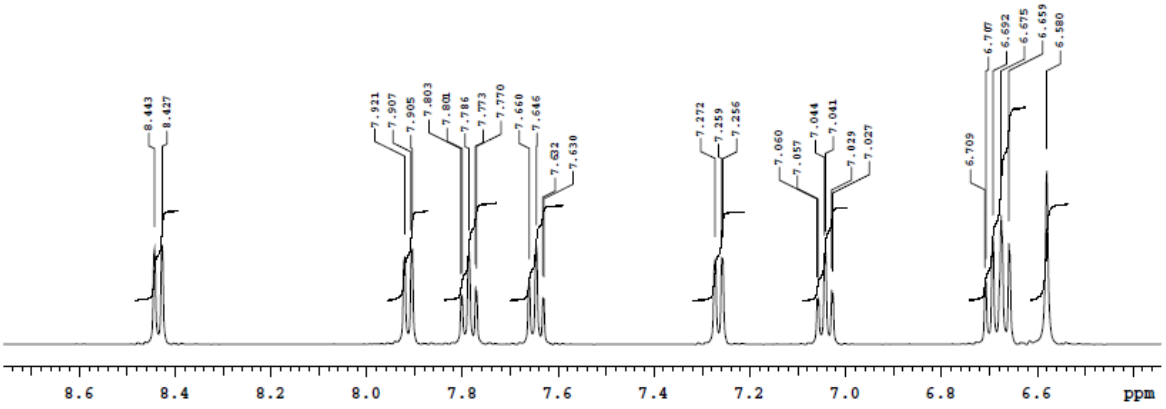
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
ppm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7.907
7.905
7.803
7.801
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7.773
7.770
7.660
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7.632
7.630
7.272
7.259
7.256
7.060
7.057
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7.041
7.029
7.027
6.709
6.707
6.692
6.675
6.659
6.580
8.6
8.4
8.2
8.0
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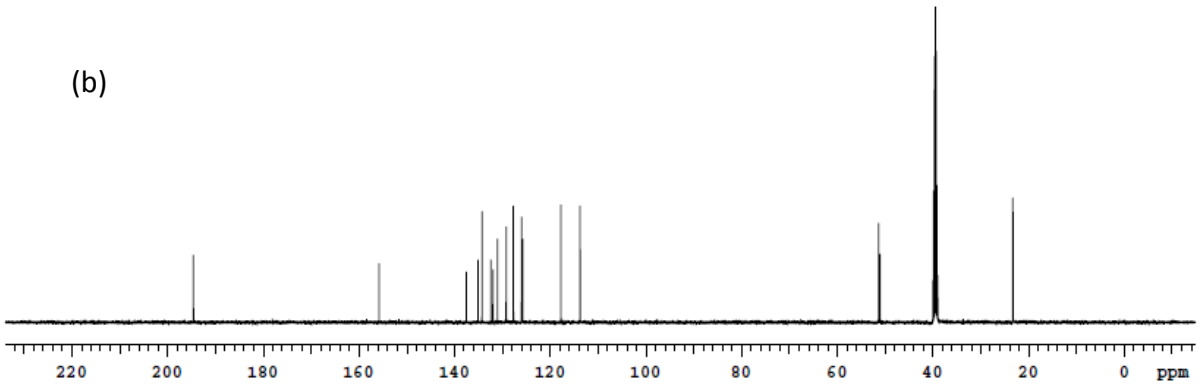
7.4
7.2
7.0
6.8
6.6
ppm

(b)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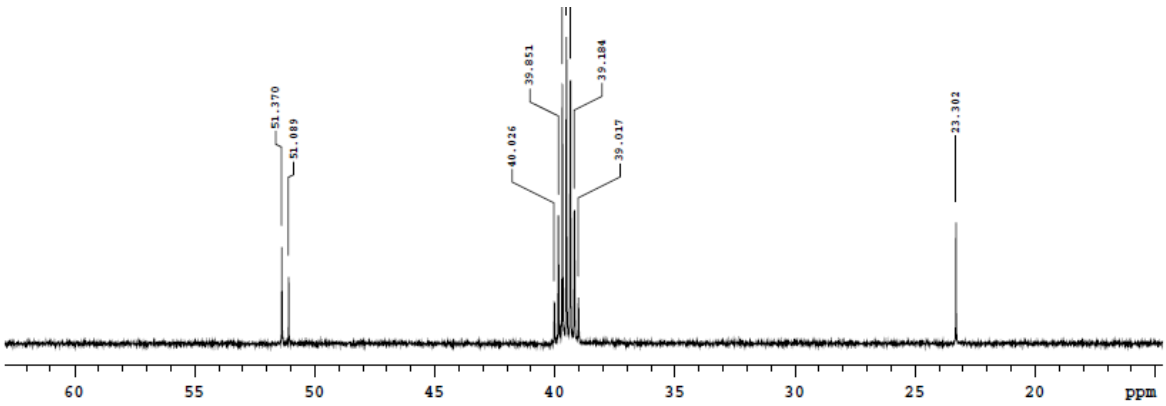
120
100
80
60
40
20
0
ppm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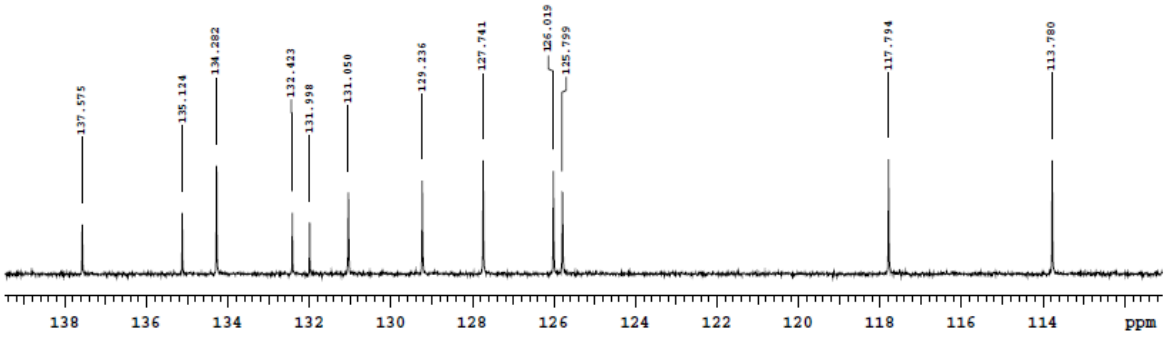
60
55
50
45
40
35
30
25
20
ppm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118
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114
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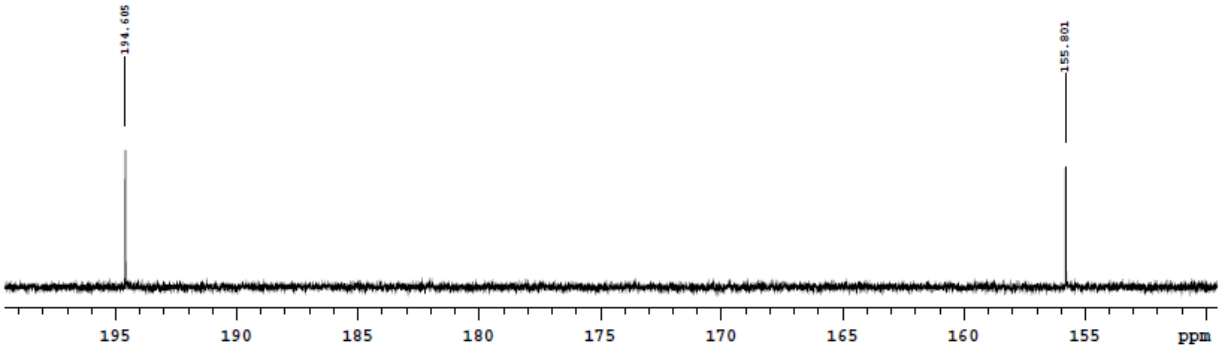
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165
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155
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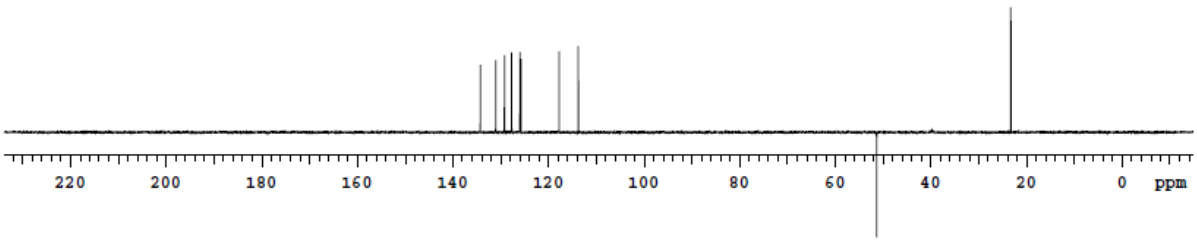
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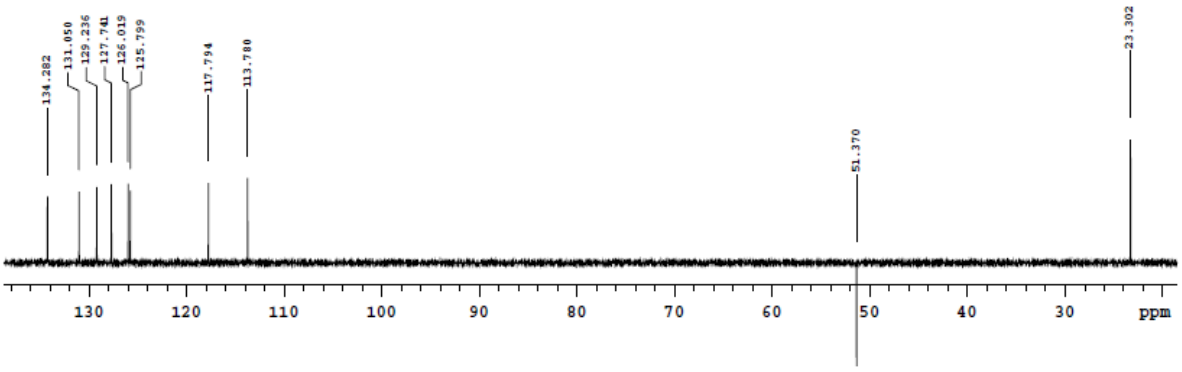


Fig.S6 a) ^{1}H, b) ^{13}C NMR spectra of **1**

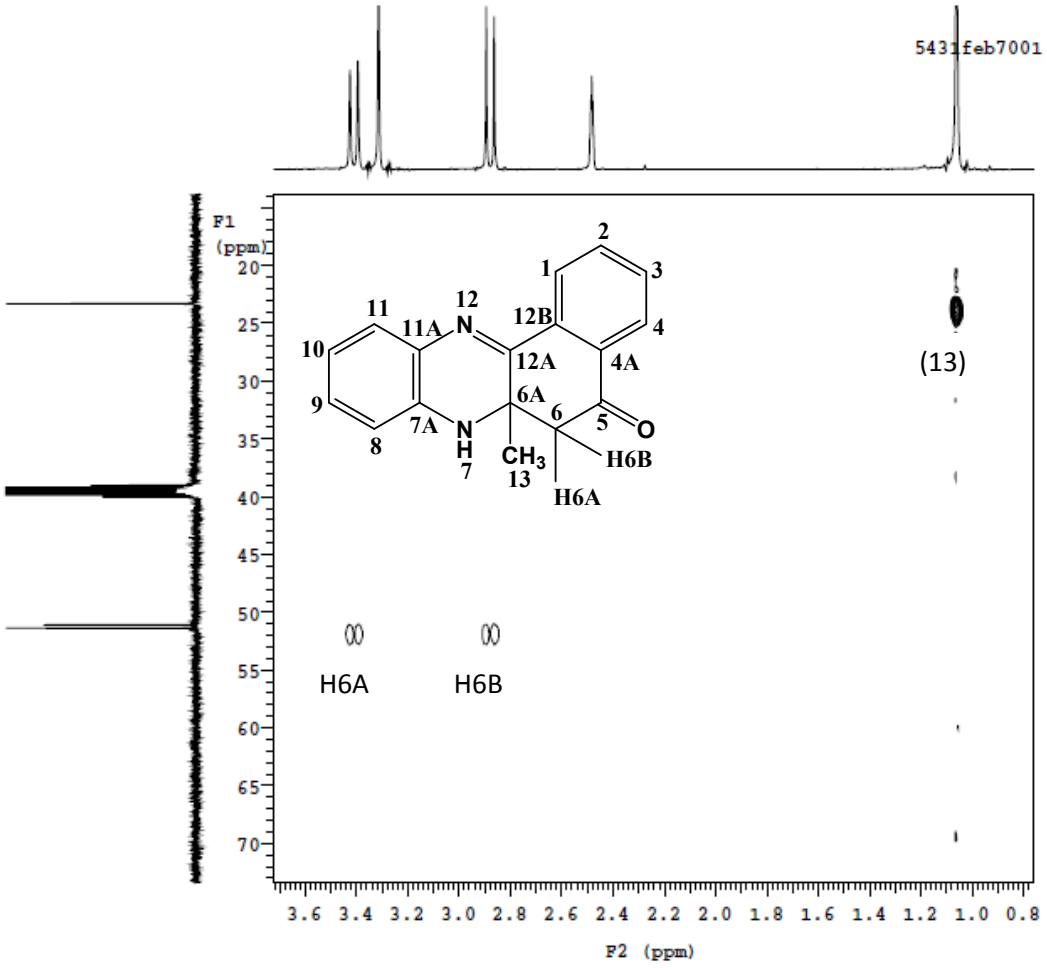


Fig.S7 2D gHSQCAD NMR spectra of **1** in saturated carban region

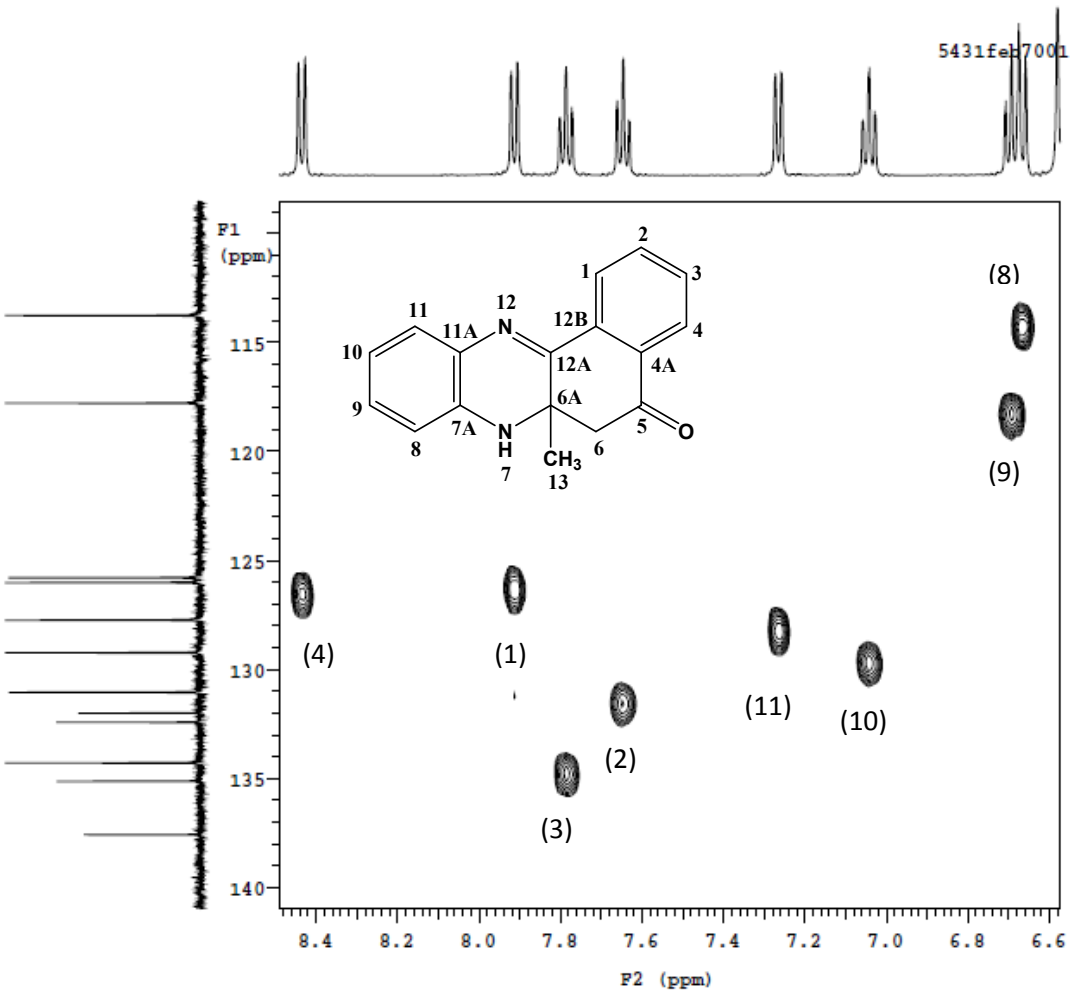


Fig.S8 2D gHSQCAD NMR spectra of **1** for aromatic carbons

Interpretation of the 2D gHSQCAD NMR of 1 that shows the correlation between the Carbon and Proton.

Spot (1) show the correlation between the proton i.e. observed at 7.90 ppm (C1-H) in proton NMR and the carbon observed at 125.79ppm in carbon NMR.

Spot (2) show the correlation between the proton i.e. observed at 7.64 ppm (C-2H) in proton NMR and the carbon observed at 131.05 ppm in carbon NMR.

Spot (3) show the correlation between the proton i.e. observed at 7.78 ppm (C-3H) in proton NMR and the carbon observed at 134.28 ppm in carbon NMR.

Spot (4) show the correlation between the proton i.e. observed at 8.43 ppm (C4-H) in proton NMR and the carbon observed at 126.01 ppm in carbon NMR.

Spot (H6A) show the correlation between the proton i.e. observed at 3.40 ppm (C-6H axi) in proton NMR and the carbon observed at 51.37 ppm in carbon NMR.

Spot (H6B) show the correlation between the proton i.e. observed at 2.84 ppm (C4-H) in proton NMR and the carbon observed at 51.37 ppm in carbon NMR

Spot (8) show the correlation between the proton i.e. observed at 6.67 ppm (C8-H) in proton NMR and the carbon observed at 115.60 ppm in carbon NMR.

Spot (9) show the correlation between the proton i.e. observed at 6.69 ppm (C9-H) in proton NMR and the carbon observed at 117.79 ppm in carbon NMR.

Spot (10) show the correlation between the proton i.e. observed at 7.04 ppm (C11-H) in proton NMR and the carbon observed at 129.26 ppm in carbon NMR.

Spot (11) show the correlation between the proton i.e. observed at 7.25 ppm (C11-H) in proton NMR and the carbon observed at 127.74 ppm in carbon NMR.

Spot (13) show the correlation between the proton i.e. observed at 1.06 ppm (C13-H) in proton NMR and the carbon observed at 23.30 ppm in carbon NMR.

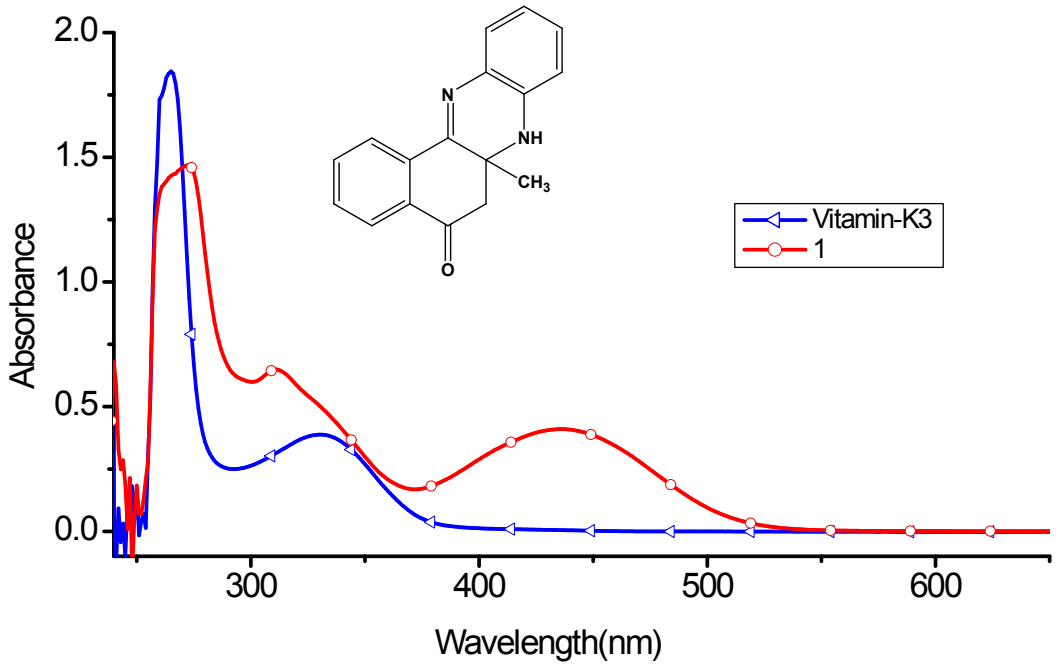
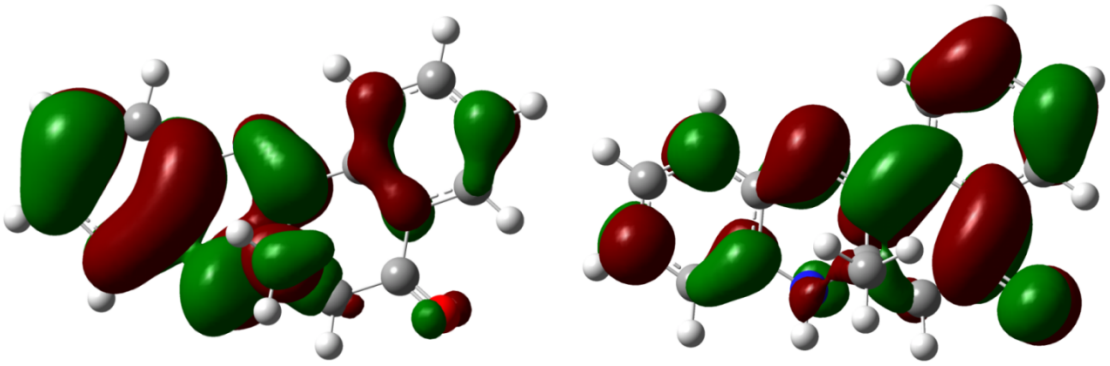


Fig.S9 UV-Visible spectra of MNQ and **1** in DMSO with concentration ~ 1×10^{-4} M



HOMO LUMO

Fig.S10 HOMO and LUMO orbital's of **1** (Isosurface value of -17.5 kJ mol^{-1})

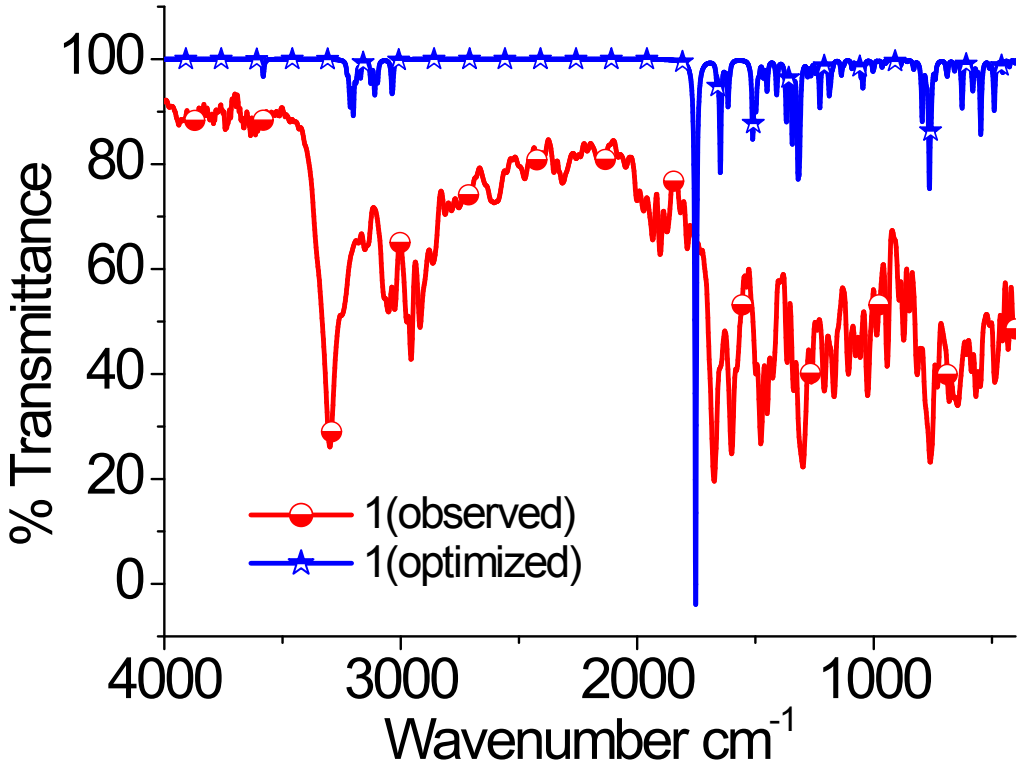


Fig.S11 Observed and optimized IR spectra of **1**

Table S1 Crystallographic data of **1**

Parameters	**1**
Formula	$C_{17}H_{14}N_2O$
Formula weight	262.30
Crystal system	Orthorhombic
Space group	*Pbca*
a /Å	7.518(5)
b /Å	14.238(5)
c /Å	25.049(5)
α (°)	90.00
β (°)	90.00
γ(°)	90.00
V(Å^3)	2681(2)
Z	8
ρ(g cm^{-3})	1.300
μ(mm^{-1})	0.082
F(000)	1104
T(K)	293
λ(Mo K_α)(Å)	0.71073
Θ_{min}(°)	2.9
Θ_{max}(°)	25.1
Total data	95214
Unique data	2381
R_{int}	0.043
Data[I>2σ(I)]	2006
$^aR_1$	0.0363
wR_2	0.1115
S	0.87

Table S2 Selected bond lengths (Å) and angles (°) for **1**

O1-C5	1.217(2)	C3-C4-C4A	120.46(14)
N7-C6A	1.453(2)	C5-C4A-C12B	120.57(13)
N7-C7A	1.375(2)	C4-C4A-C12B	120.05(12)
N12-C11A	1.405(2)	C4-C4A-C5	119.36(13)
N12-C12A	1.285(2)	O1-C5-C4A	121.79(14)
C1- C12B	1.393(2)	O1-C5-C6	121.60(14)
C1- C2	1.372(2)	C4A-C5-C6	116.53(13)
C2-C3	1.380(2)	C5-C6-C6A	114.02(12)
C3-C4	1.371(3)	N7-C6A-C13	112.32(11)
C4-C4A	1.389(2)	C6-C6A-C12A	110.76(11)
C4A-C12B	1.404(2)	C6-C6A-C13	110.36(11)
C4A-C5	1.482(2)	C12A-C6A-C13	108.39(11)
C5-C6	1.492(2)	N7-C6A-C6	107.52(11)
C6-C6A	1.519(2)	N7-C6A-C12A	107.47(11)
C6A-C12A	1.521(2)	N7-C7A-C8	123.07(12)
C6A-C13	1.536(2)	C8-C7A-C11A	119.27(13)
C7A-C11A	1.406(2)	N7-C7A-C11A	117.45(12)
C7A-C8	1.388(2)	C7A-C8-C9	120.16(14)
C8-C9	1.379(2)	C8-C9-C10	120.79(15)
C9-C10	1.381(3)	C9-C10-C11	119.55(15)

C10-C11	1.378(2)	C10-C11-C11A	120.75(15)
C11-C11A	1.388(2)	N12-C11A-C11	119.68(14)
C12A-C12B	1.473(2)	N12-C11A-C7A	120.73(13)
C6A-N7-C7A	118.16(12)	C7A-C11A-C11	119.44(13)
C11A-N12-C12A	118.49(12)	N12-C12A-C12B	119.42(12)
C7A-N7-H7N	118.1(10)	C6A-C12A-C12B	117.25(11)
C6A-N7-H7N	115.0(10)	N12-C12A-C6A	123.07(12)
C2-C1-C12B	120.68(13)	C4A-C12B-C12A	121.37(11)
C1-C2-C3	120.67(14)	C1-C12B-C4A	118.35(12)
C2- C3-C4	119.78(15)	C1-C12B-C12A	120.15(12)