Strength from weakness: Exploitation of CH...N hydrogen bond for engineering waves in crystals

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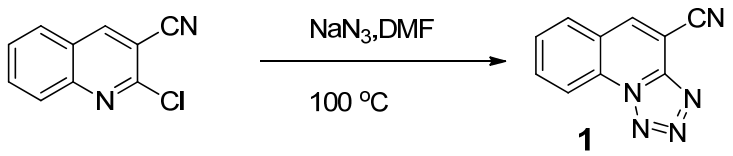
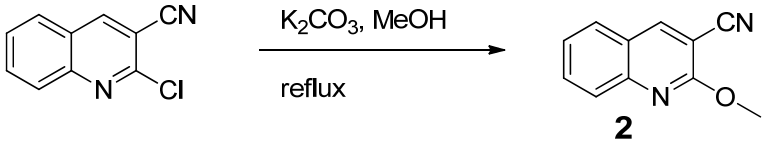
Synthesis of 2-azido-3-cyanoquinoline (1)



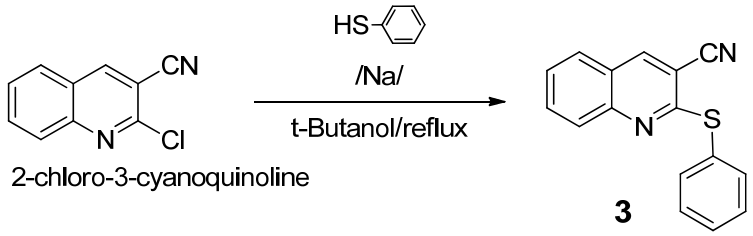
A mixture of 2-chloro-3-cyanoquinoline[i] (1.88 g, 9.973 mmol) and sodium azide (0.65 g, 10 mmol) in DMF (20 mL) was heated at 100 ^{o}C for 5 h. The mixture was then cooled to rt and poured into ice-water. The resultant solid was filtered, washed with water and dried to obtain crude **1**. The crude product thus obtained was recrystallized from chloroform / methanol to get pure **1** (1.69 g, 87%), mp 250 ^{o}C (decomp.), IR (KBr): ν_{max} /cm^{-1} 2999, 2260, 2226, 2217, 1619; ^{1}H NMR (300 MHz, DMSO): δ 9.10 (s, 1H, *H*-4), 8.60 (d, 1H, *J* = 8.1Hz, *H*-5), 8.22 (d, 1H, *J* = 8.1 Hz, *H*-8), 8.08 (m,1H, *H*-6), 7.85 (m,1H, *H*-7); ^{13}C NMR (100 MHz, $CDCl_3$): δ 102.4, 119.2(*C*-5), 121.7, 121.8, 128.0(*C*-7), 134.1(*C*-8), 136.1, 136.6(*C*-6), 140.0, 148.5(*C*-4), 148.6, 150.96 ; HRMS calculated for $(M+H)^+$ $(C_{10}H_6N_5)^+$:196.0545, Found (ES^+):196.0612

Synthesis of 3-cyano-2-methoxyquinoline (2)



A mixture of 2-chloro-3-cyanoquinoline (1.88 g, 9.973 mmol) and K_2CO_3 (1.38 g, 10 mmol) in methanol (20 mL) was refluxed for 6 h. Then half of the Methanol was distilled off and the mixture was cooled to rt, poured into ice-water, and then neutralized with few drops of acetic acid. The resultant solid was filtered, washed with water and dried to obtain crude **2**. The product was further purified by recrystallization from ethyl acetate to yield white solid (1.83g, 85%), mp 112-114 ^{o}C, IR(KBr): ν_{max}/cm^{-1} 3033, 3000, 2955, 2908, 2217, 1619 ; ^{1}H NMR (500 MHz, $CDCl_3$) : δ 8.33 (s, 1H, *H*-4), 7.81-7.71 (m, 1H, *H-5*), 7.71-7.68 (m, 2H, *H-6*, *H-8*), 7.41-7.38 (m, 1H, *H-7*), 4.09 (s, 3H, -*OCH*$_3$) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.4(-*CH*$_3$), 98.4, 115.3, 123.2, 125.5(*C-4*), 127.6(*C-5*), 128.0(*C-6* or *C-8*), 132.8(*C-6* or *C-8*), 145.3(*C-4*), 147.6, 159.7; HRMS calculated for [M+H]$^+$ $(C_{11}H_8N_2O)^+$: 185.1940, Found (ES^+): 185.1964

Synthesis of 3-cyano-2-thiophenylquinoline (3)



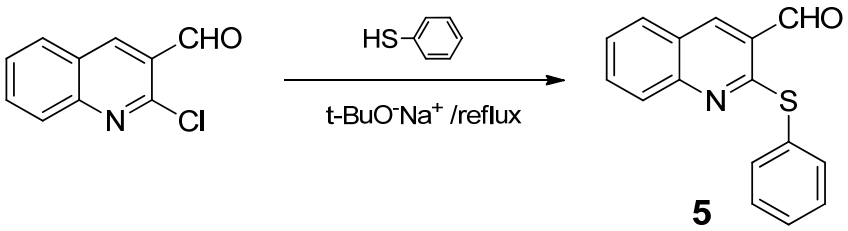
Sodium metal (0.23 g, 10 mmol) was added to t-butanol (20 mL) at rt in small portions and the mixture stirred well until a clear solution was formed. To this solution was added a mixture of 2-chloro-3-cyanoquinoline (1.88 g, 10 mmol) and thiophenol (1.03 mL, 10 mmol). The resulting mixture was refluxed for 4 h. The mixture was then cooled to room temperature. The yellow solid separated out which was filtered, washed with *t*-butanol (2×5 mL) and dried to obtain crude **3**. The product was further purified by recrystallization from ethylacetate. (2.35 g, 90%), mp 138 ^{o}C. IR (KBr): υ_{max} / cm^{-1} 3059, 2232, 1580; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (s, 1H, *H*-4), 7.78 (m, 3H, *Ar-H*), 7.69-7.62 (m, 2H, *Ar-H*), 7.53-7.45 (m, 4H, *Ar-H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ105.9, 115.7, 124.2, 127.1, 127.9, 128.5, 128.8, 129.1, 129.3, 132.8, 135.2, 143.0 (*C-4*), 148.6, 158.4; HRMS calcd. for $[M+H]^+$ $(C_{16}H_{11}N_2S)^+$: 263.0564. Found (ES^+): 263.0651

Synthesis of 3-formyl-2-p-toluyloxyquinoline (4)

A mixture of 2-chloro-3-formyl quinoline[ii] (1.91 g, 10 mmol), 4-methyl phenol (1.08 g, 10 mmol), K_2CO_3 (1.38 g, 10 mmol) and TBAB (0.3 g) in DMF (15 mL) was heated at 100 ^{o}C for 9 h. The mixture was then cooled to rt, poured into ice water and neutralized with acetic acid. The separated solid was filtered, washed with water and dried to obtain crude **4**. The product was further purified by recrystallization from ethylacetate to obtain as an yellow solid (1.49 g, 92%), mp 138 ^{o}C. IR (KBr): υ_{max} / cm^{-1} 3349, 3034, 2886, 1692; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.65 (s, 1H, -*CHO*), 8.73 (s, 1H, *H*-4), 7.90 (d, 1H, *J* = 8 Hz, *H*-5), 7.76-7.67 (m, 2H, *H*-8, *H*-7), 7.47-

7.43 (m, 1H, *H*-6), 7.27-7.20 (m, 4H, Ar-*H*), 2.41 (s, 3H, *Ar*-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9(*Ar*-CH_3), 120.2(*toulyl*), 121.5, 125.1,(*C-8*) 125.6(*C-6*), 127.8(*C-5*), 129.6, 130.0(*toulyl*), 132.6(*C-7*), 134.7, 140.4(*C-4*), 148.6, 150.7, 160.6, 189.1(-*CHO*); HRMS calcd. for $[M+H]^+$ $(C_{17}H_{14}NO_2)^+$: 264.1025. Found (ES^+): 264.1026

Synthesis of 3-formyl-2-thiophenylquinoline (5)



5

Sodium metal (0.23 g, 10 mmol) was added to t-butanol (20 mL) in small lots at rt and was stirred well until a clear solution was formed. To this solution, 2-chloro-3-formylquinoline (1.91 g, 10 mmol) and thiophenol (1.10 g, 10 mmol) were added and the mixture was refluxed for 4 h. The yellow precipitate obtained upon cooling to rt was filtered, washed with *t*-butanol (2×5 mL) and dried to obtain crude **5** . The product was further purified by recrystallization from EtOAc to get pale yellow solid.(1.48 g, 90%); mp 137-138 ^{o}C, IR (KBr): υ_{max} / cm^{-1} 3043, 2844, 1981, 1695. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.28 (s, 1H, -*CHO*), 8.55(s, 1H, *H*-4), 7.87 (d, 1H, *J* = 8 Hz, *H*-5), 7.71(m, 2H, *H*-7, *Ar-H*), 7.62-7.60(m, 2H, *Ar-H*), 7.51-7.48(m, 1H, *H*-6), 7.45-7.43(m, 3H, *H*-8, *Ar-H*) ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.2, 126.6(*C-6*), 127.2, 128.7, 128.8, 129.0(*C-5*), 129.1, 130.0, 132.9(*C-7*), 135.1, 142.3(*C-4*), 149.5, 158.8, 190.1(-*CHO*)

Determination of wavelength , amplitude and interplanar distance

A plane through the identical atoms on the crests of a wave is drawn. Similarly a plane passing through the identical atoms on the trough was also drawn. The distance between these two planes is taken as the amplitude. The linear distance between identical atoms on two consecutive crests (or troughs) in a layer is taken as the wave length. A plane passing through the quinoline ring carbons is drawn for a layer. The distance between two such adjacent planes (layers) is taken as the interplanar distance.

Table S1: Non-covalent interactions in 1

	Type	Interaction (D-H…A)	H…A (Å)	Angle D-H…A (°)	Symmetry operation
1	CH…N	C8-H8…N5	2.679(3)	133.1(2)	1+x, y, 1+z
2		C4-H4…N3	2.798(3)	164.2(2)	1-x, ½+y, ½-z
3		C4-H4…N2	2.574(3)	155.8(2)	1-x, ½+y, ½-z
4		C5-H5…N2	2.937(3)	143.0(2)	1-x, ½+y, ½-z
5		C6-H6…N4	2.772(3)	129.8(3)	2-x, ½+y, 1.5-z
6		C7-H7…N3	2.782(3)	147.7(2)	2-x, ½+y, 1.5-z
7		C4-H4…N5	2.874(4)	114.5(2)	1-x, 2-y, -z
8		C5-H5…N5	2.822(4)	133.4(2)	1-x, ½+y, ½-z
9		C7-H7…N4	2.951(3)	121.8(2)	2-x, ½+y, 1.5-z
10	π…π	$Quin_p$…$Quin_p$	3.42		1-x, 2-y, 1-z
11		$Quin_p$…$Quin_p$	3.44		2-x, 2-y, 1-z

Table S2: Non-covalent interactions in 2

	Type	Interaction (D-H…A)	H…A (Å)	Angle D-H…A (°)	Symmetry operation
1	CH…O	C12-H12B…O1	2.606(3)	152.9(3)	2-x, -y, 2-z
2	CH…N	C6-H6…N1	2.743(4)	170.9(4)	-1+x, ½-y, -½+z
3		C12-H12A-N1	2.838(4)	135.5(3)	1+x, y, z
4		C5-H5…N2	3.021(6)	149.1(3)	-x, -y, 1-z
5		C4-H4…N2	3.009(6)	122.7(3)	1-x, -y, 1-z
6	CH…π	C8-H8…C5 (CH…π)	2.994(5)	130.9(3)	x, ½ -y, ½ +z
7		C12-H12A…C6 (CH…π)	3.051(6)	126.9(3)	1+x, ½-y, ½+z
8	π…π	$Quin_p$...$Quin_p$ (π…π)	3.514		1+x,y,z

9		$Quin_p$...$Quin_p$ (π…π)	3.514		-1+x, y, z

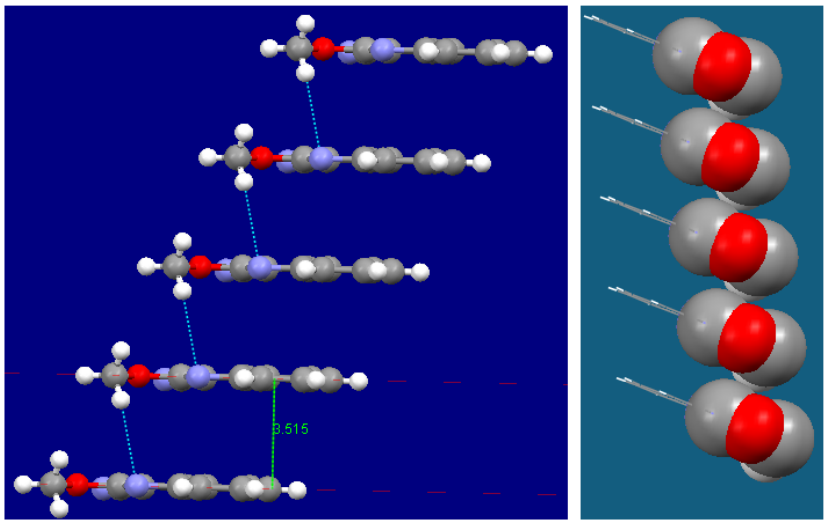


Figure S1: Slipped parallel stacking of individual molecules of **2** in the direction "a". This arrangement is further reinforced by the C12-H12A…N1 interaction (shown as blue dotted lines). This interaction makes a spiral/helical arrangement of N1-C2-O1-C12-H12A unit along the direction "a" (shown as space fill model in the right panel).

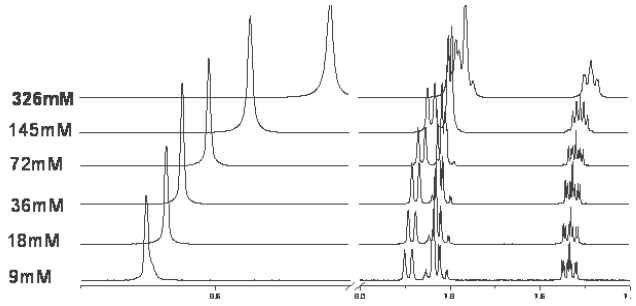


Figure S2: Concentration dependent ^{1}H NMR of **2** in CD_3CN suggested self assembly in the solution state also. As the concentration increased, the proton signals shifted up-field probably due to the anisotropic shielding effect suggesting aggregation through π-π stacking similar to the solid state arrangement.

Table S3: Non-covalent interactions in 3

	Type	Interaction (D-H…A)	H…A (Å)	Angle D-H…A (°)	Symmetry operation
1	C-H…N	C17-H17…N1	2.84(3)	147.0(3)	1+x,y,z
2		C4-H4…N2	2.94(3)	115.2(2)	2-x, 1-y, 2-z
3		C4-H4…N2	2.58(3)	146.3(2)	3-x, 1-y, 2-z
4		C14-H14…N2	2.64(3)	143.8(3)	-1+x, ½-y, -½+z
5	C-H…π	C5-H5…C14	2.95(3)	163.3(3)	2-x, ½+y, 1.5-z
6		C8-H8…C8	2.87(3)	120.6(3)	1-x, 1-y, 1-z
7		C7-H7…C16	3.02(3)	132.4(2)	1-x, 1-y, 1-z
8		C16-H16…C6	3.05(3)	162.4(3)	2-x, 1-y, 1-z
9	π…π	$Quin_p$…$Quin_p$	3.45		-1+x, y, z
10		$Thioph_p$…$Thioph_p$	3.37		-1+x, y, z
11	C-H…S	C15-H15…S1	3.16(3)	145.2(2)	x, ½-y, -½+z

Table S4: Non-covalent interactions in 4

	Type	Interaction (D-H…A)	H…A (Å)	Angle D-H…A (°)	Symmetry operation
1	C-H…O	C5-H5…O2	2.648(2)	141.5(1)	2-x,-y,-z
2		C17-H17…O2	3.041(2)	146.0(2)	2-x, 1-y, -z
3		C11-H11…O2	2.647(2)	144.3(2)	3-x, 1-y, -z
4	C-H…N	C18-H18A…N1	3.042(2)	146.9(2)	2-x, 1-y, 1-z
5	C-H…π	C5-H5…C5	3.032(3)	120.9(1)	1-x, -y, -z
6		C17-H17…C6	3.018(3)	133.4(2)	x, 1+y, z
7		C16-H16…C7	3.060(3)	148.2(2)	x, 1+y, z
8		C18-H18A…C13	3.055(3)	149.0(2)	2-x, 1-y, 1-z
9		C7-H7…C16	2.917(3)	155.3(2)	-1+x, -1+y, z

10		C6-H6…C17	3.136(3)	126.8(2)	-1+x, -1+y, z
11	π…π	$Quin_p$…$Quin_p$	3.44		-1+x, y, z
12		Tol_p…Tol_p	3.58		-1+x, y, z

Table S5: Non-covalent interactions in 5

	Type	Interaction (D-H…A)	H…A (Å)	Angle D-H…A (°)	Symmetry operation
1	C-H…O	C16-H16…O1	2.941(2)	133.8(2)	-½+x, -½+y,-1+z
2		C6-H6…O1	2.545(2)	144.0(2)	-½+x, ½+y,-1+z
3		C17-H17…O1	2.895(2)	119.9(2)	-½+x, 1.5-y, -½+z
4	C-H…S	C16-H16…S1	3.256(2)	131.9(2)	-½+x, 1.5-y, -½+z
5	CH…π	C15-H15…C17	2.994(2)	168.3(3)	x, 1-y, -1/2+z
6		C14-H14…C8	3.118(2)	150.9(3)	½+x, -½+y, z
7		C8-H8…C13	2.815(2)	143.2(2)	-½+x, 1.5-y, -½+z
8		C5-H5…C15	3.027(2)	151.1(2)	x, 2-y, ½+z
9		C4-H4…C13	2.862(2)	160.3(2)	x, 2-y, ½+z
10		C4-H4…C14	2.904(2)	169.5(2)	x, 2-y, ½+z
11		C4-H4…$C_{g(Thioph)}$	2.89	149.9	x, 2-y, ½+z
12		C11-H11…C13	3.00(4)	151.3(3)	x, 2-y, ½+z

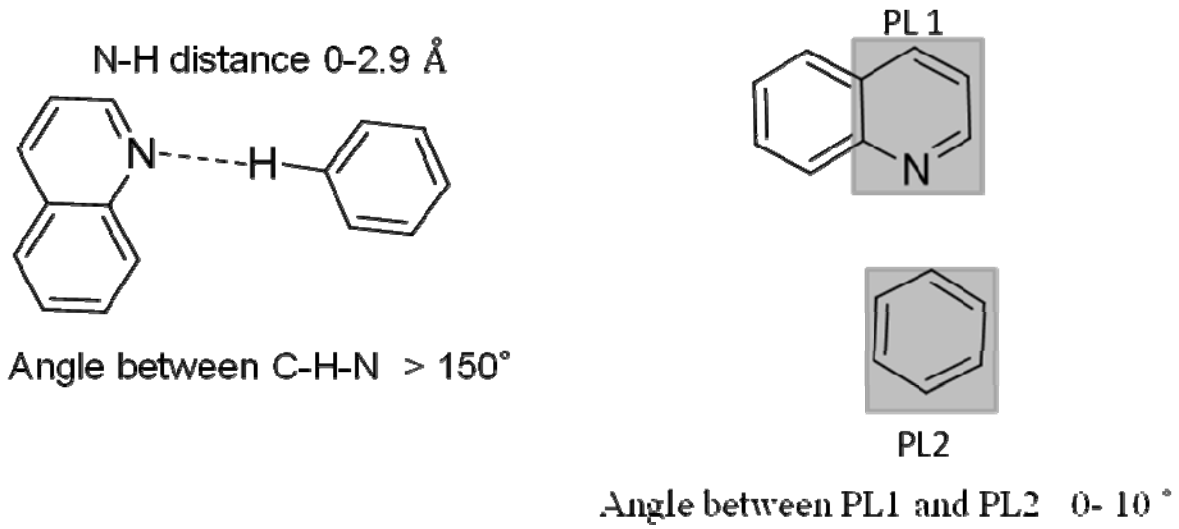


Figure S3: Geometric parameters used for CSD search

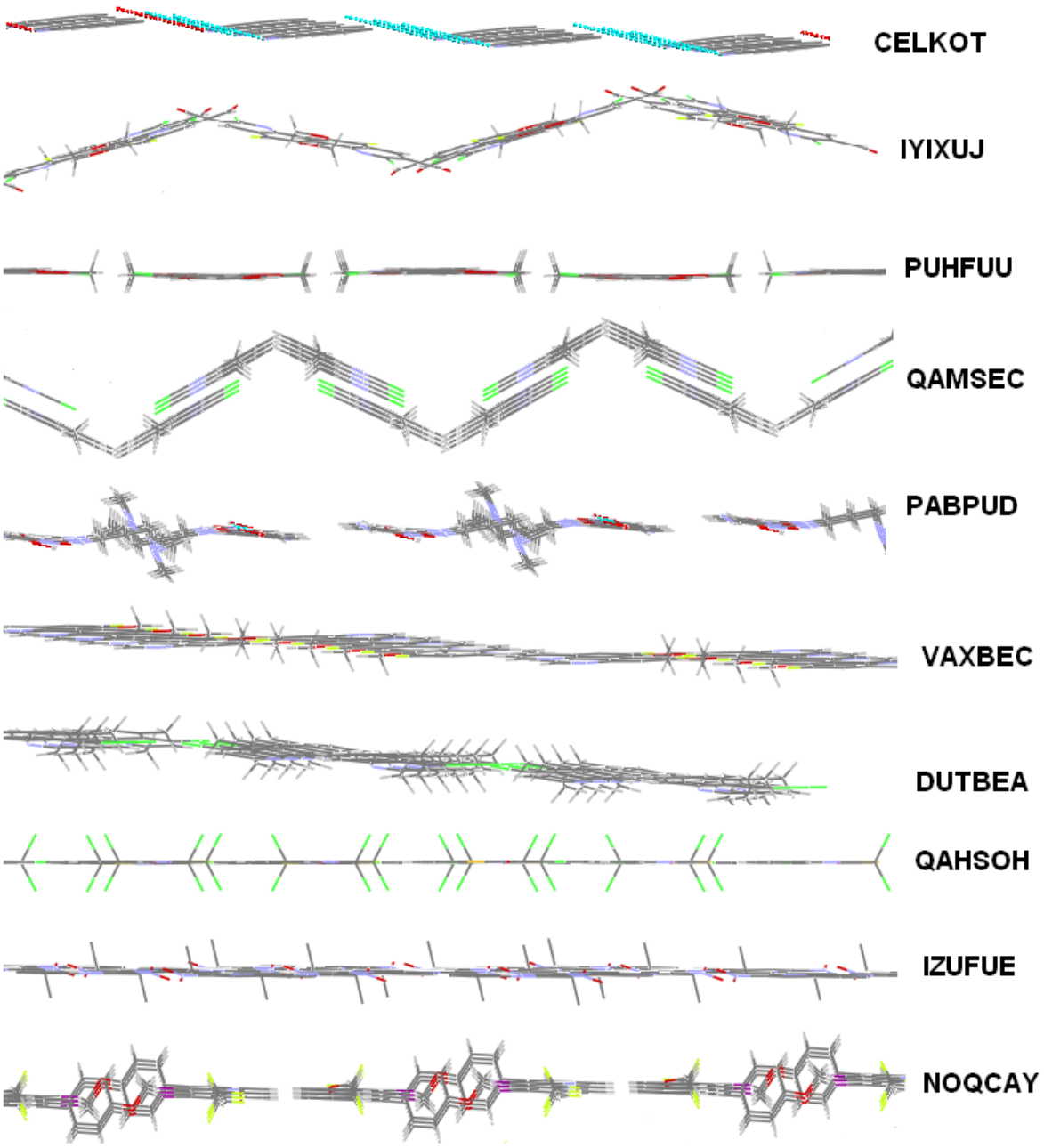
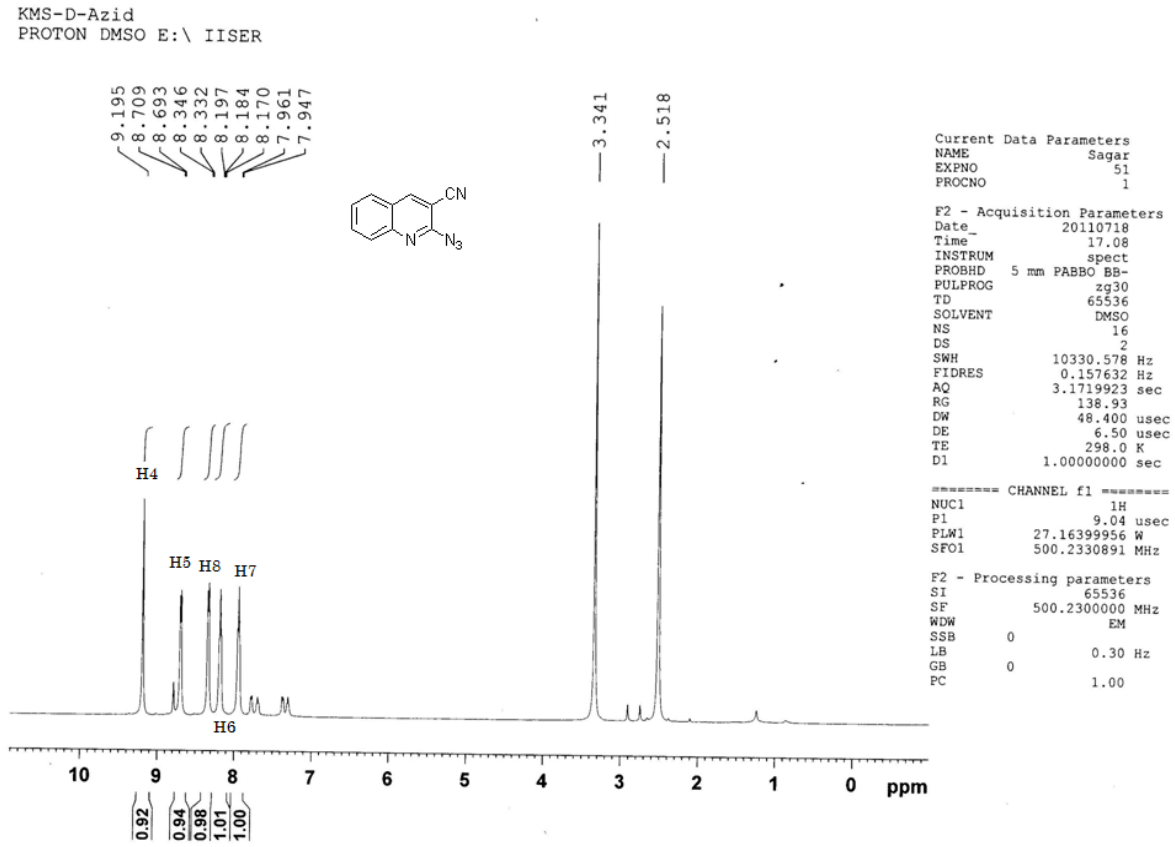
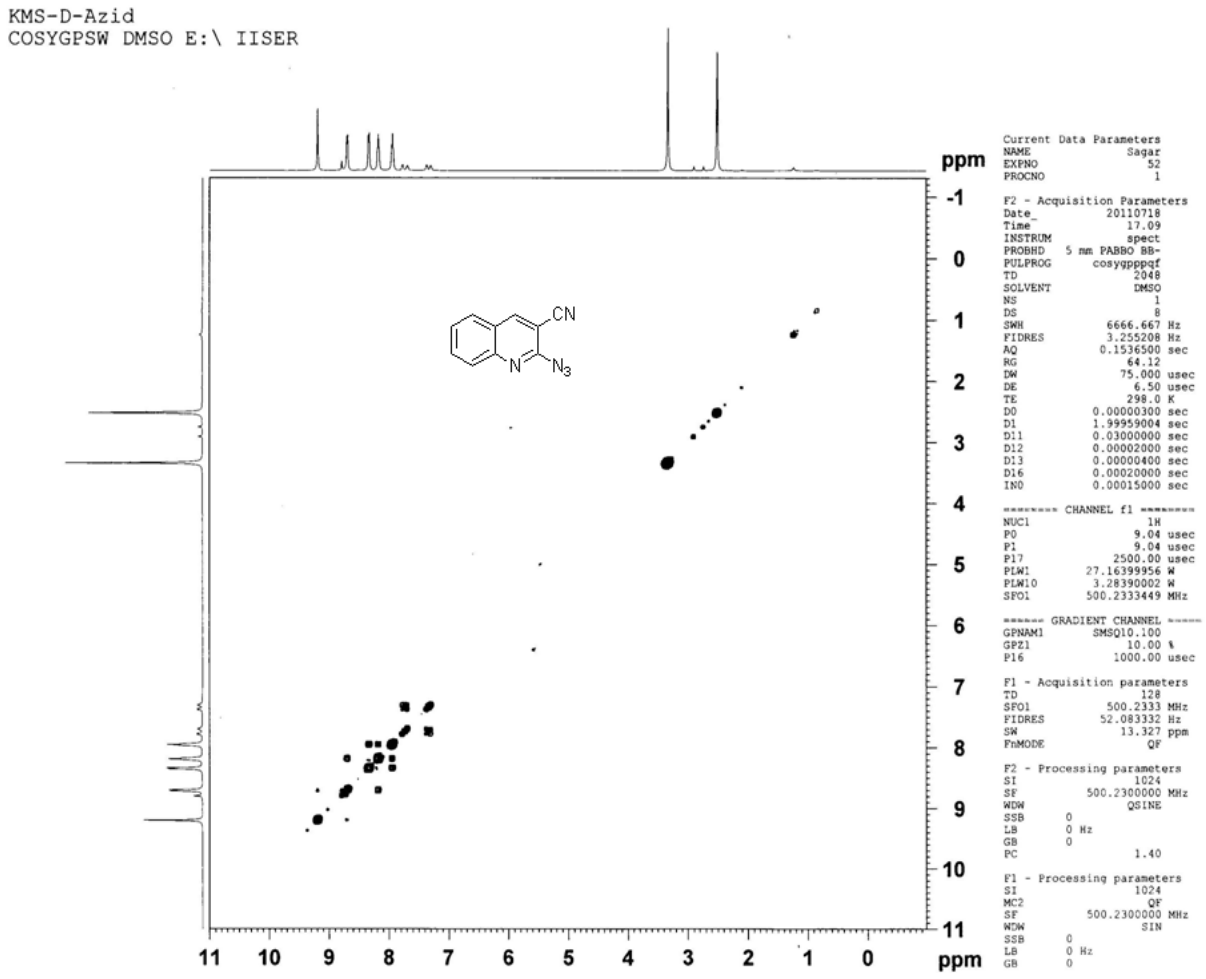


Figure S4: Layer packing in the quinolines obtained through CSD search

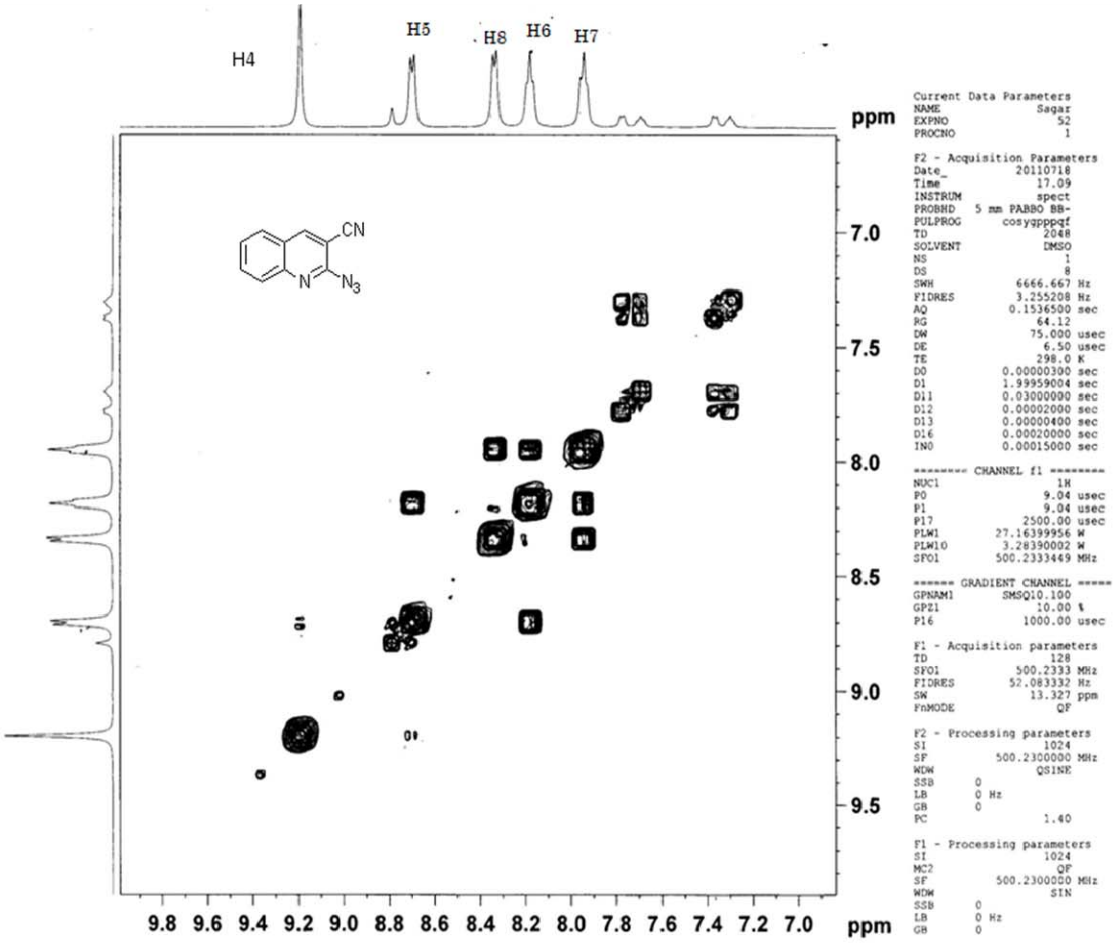
^{1}H NMR of compound **1**



COSY of compound **1**



COSY of compound **1** (zoom)

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PLW10           3.28390002 W
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====== GRADIENT CHANNEL =====
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SSB          0
LB           0 Hz
GB           0
PC                       1.40

F1 - Processing parameters
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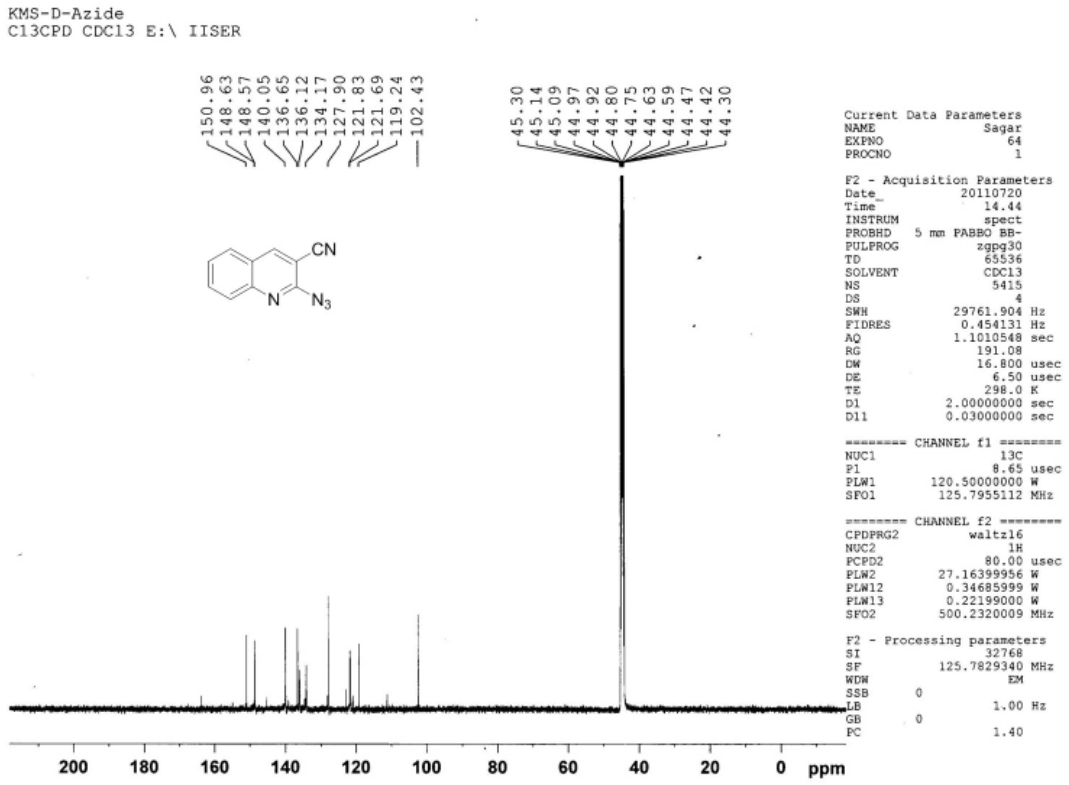
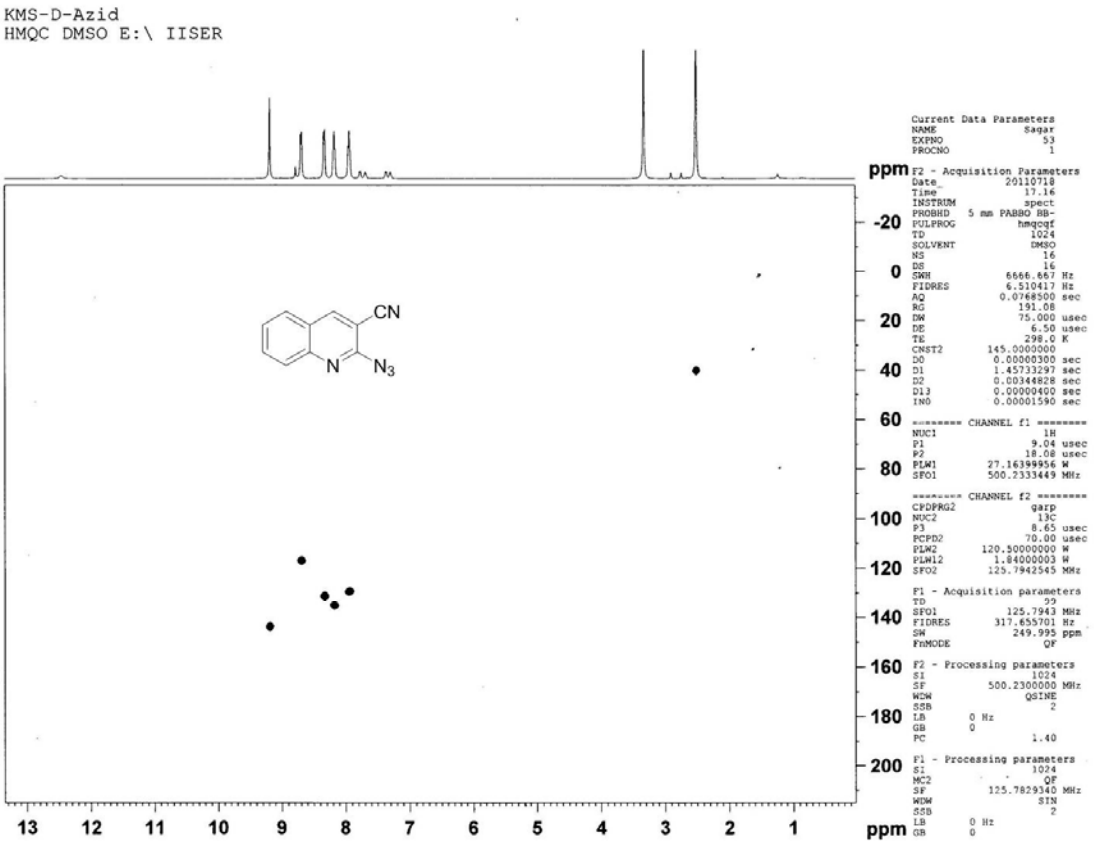
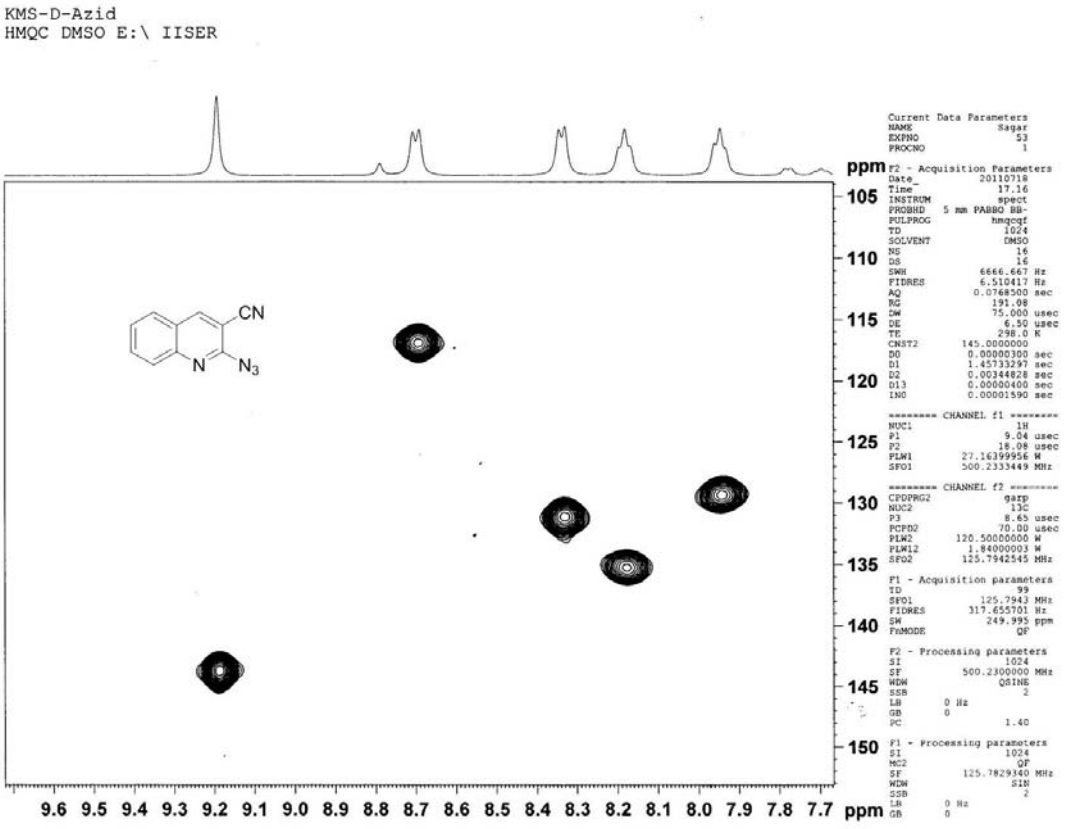
^{13}C NMR of compound **1**



HMQC of compound **1**

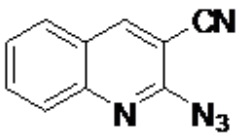


HMQC of compound **1** (zoom)



HRMS of compound **1**

Elemental Composition Report



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Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
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Elements Used:
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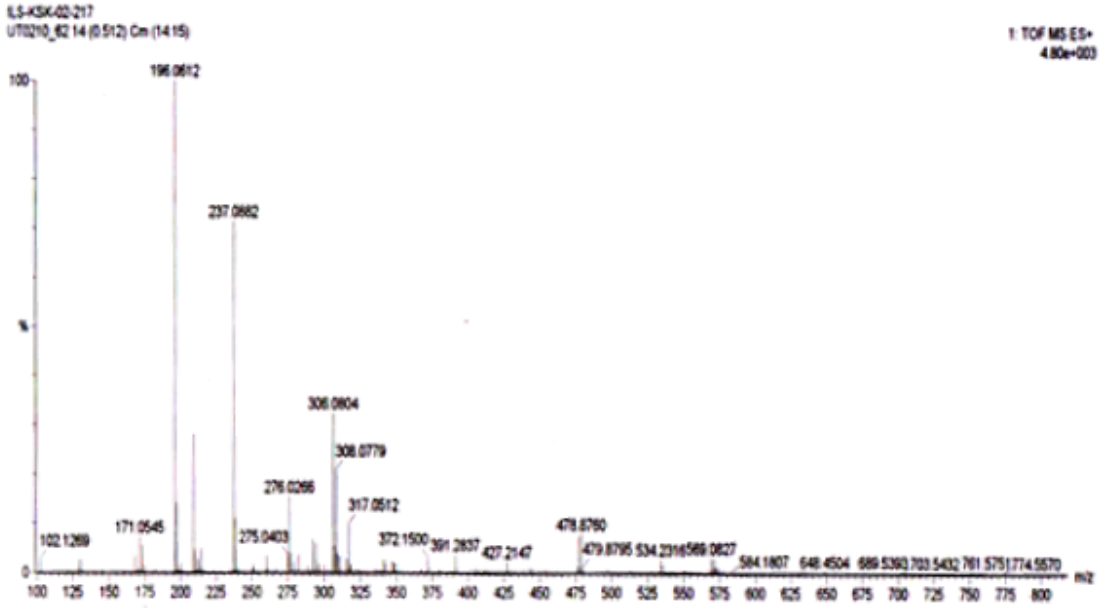

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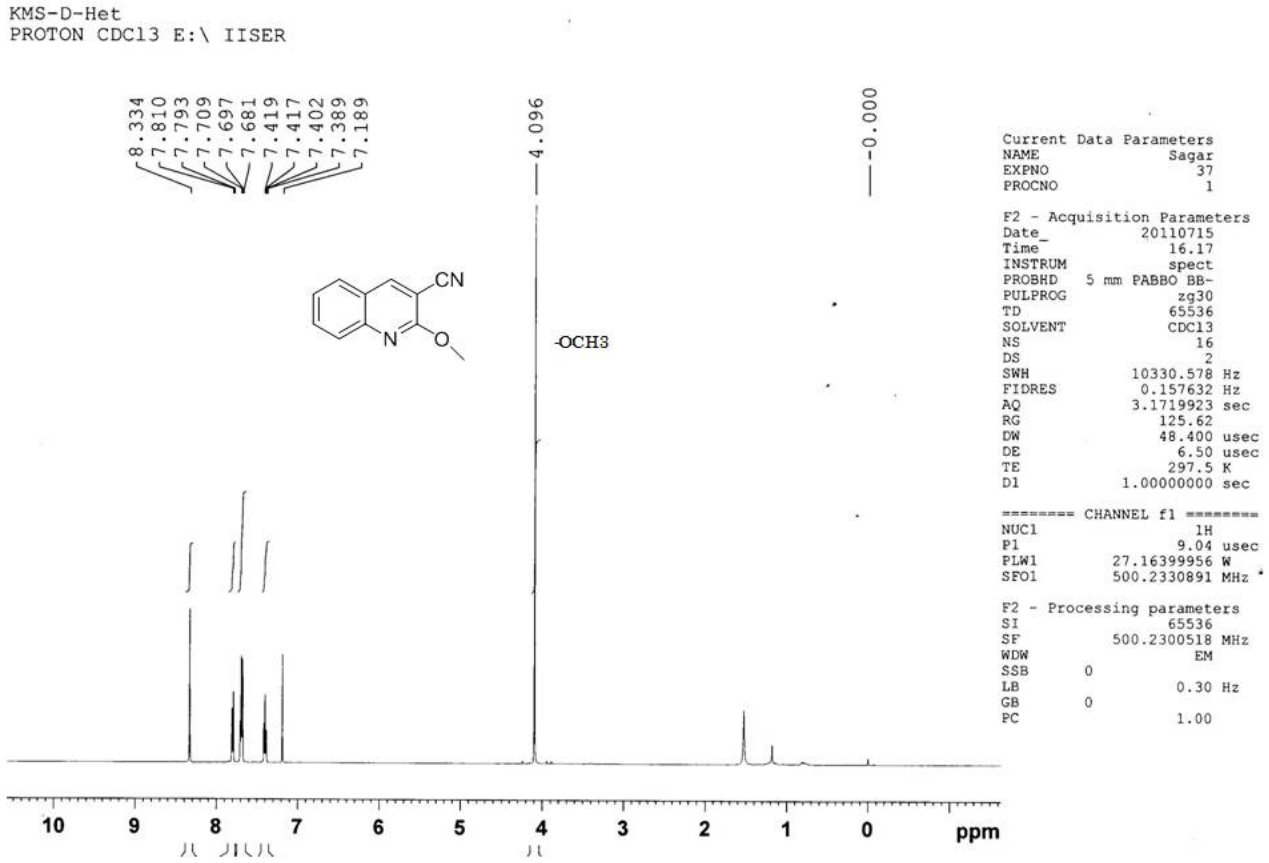
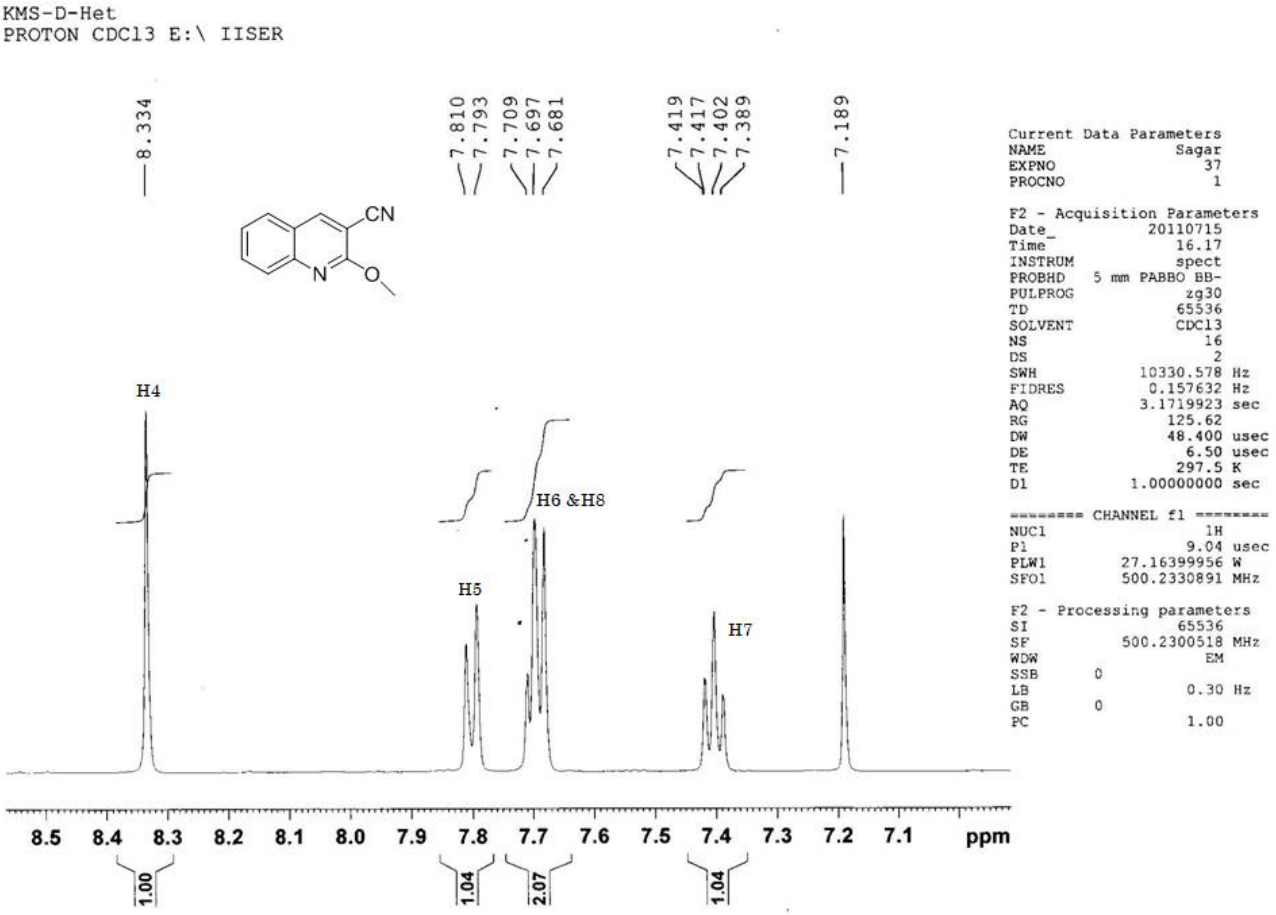
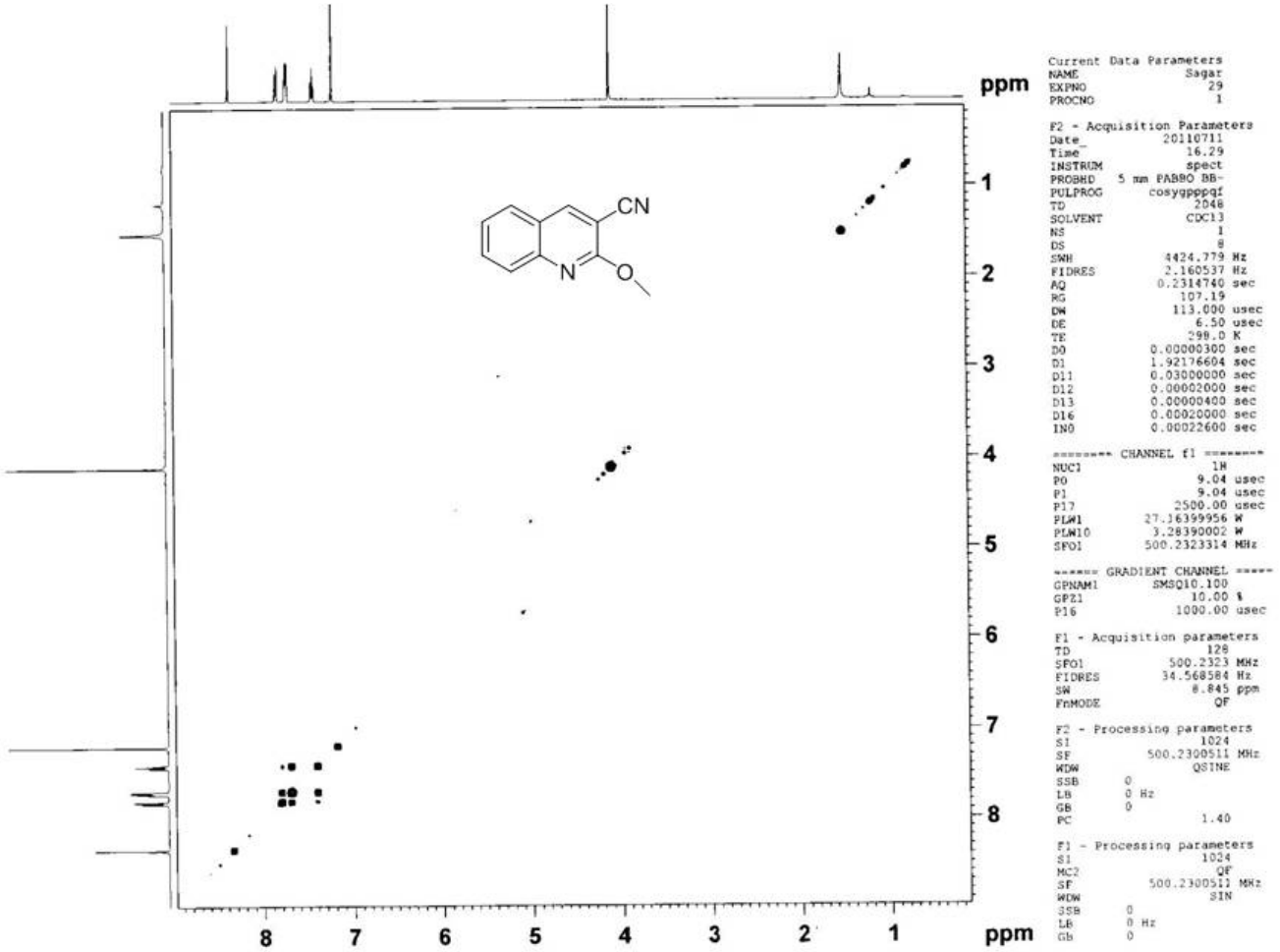
^{1}H NMR of compound **2**



^{1}H NMR of compound **2** (zoom)

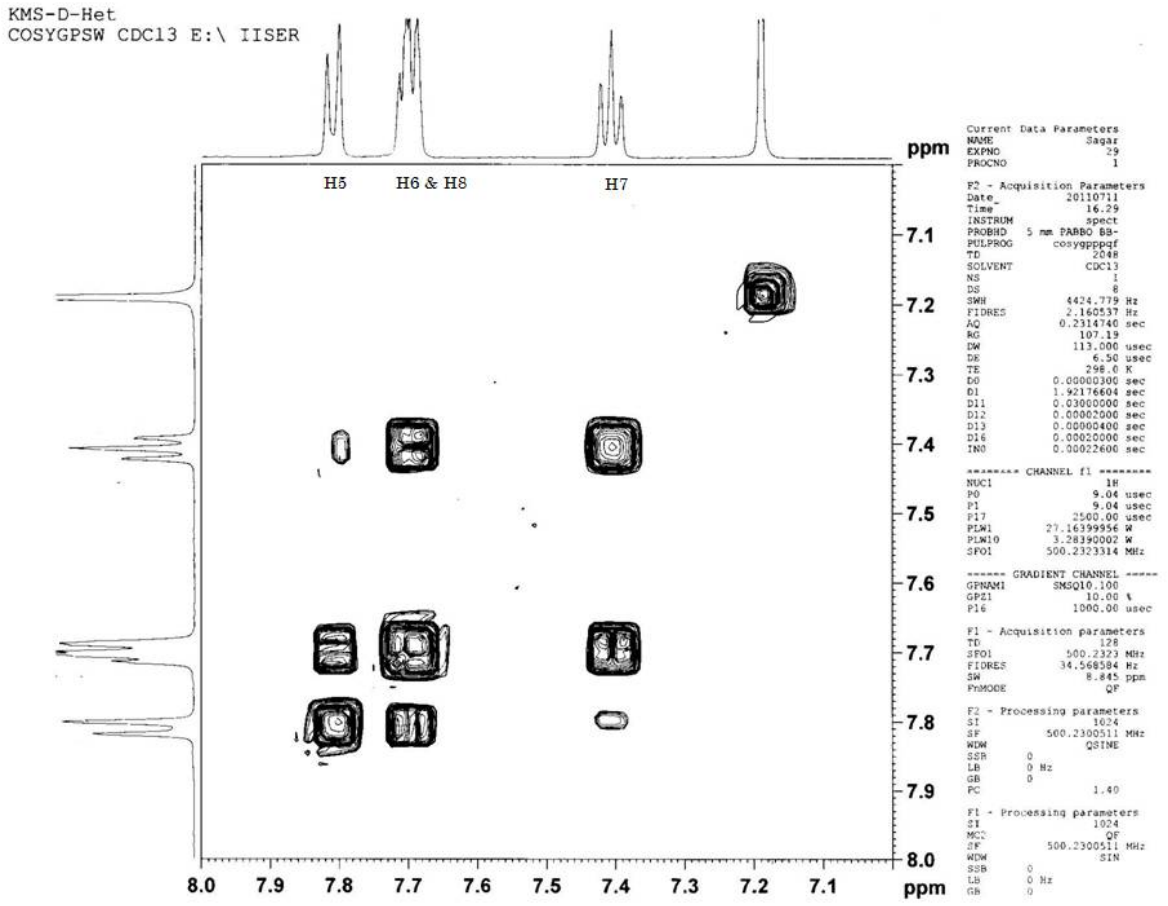


COSY of compound **2:**

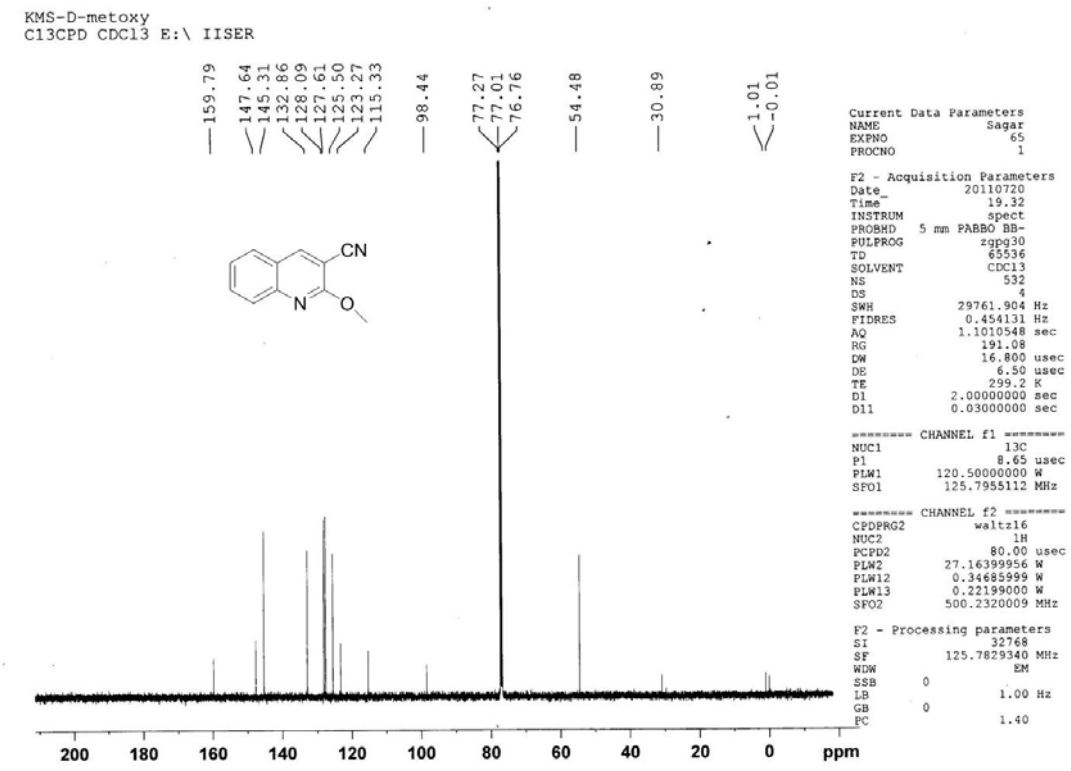



```
Current Data Parameters
NAME                  Sagar
EXPNO                    29
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110711
Time                  16.29
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG          cosygpppqf
TD                     2048
SOLVENT                CDCl3
NS                        1
DS                        8
SWH               4424.779 Hz
FIDRES            2.160537 Hz
AQ                0.2314740 sec
RG                   107.19
DW                 113.000 usec
DE                   6.50 usec
TE                  298.0 K
D0                0.00000300 sec
D1                1.92176604 sec
D11               0.03000000 sec
D12               0.00002000 sec
D13               0.00000400 sec
D16               0.00020000 sec
IN0               0.00022600 sec

======== CHANNEL f1 ========
NUC1                      1H
P0                      9.04 usec
P1                      9.04 usec
P17                  2500.00 usec
PLW1              27.16399956 W
PLW10              3.28390002 W
SFO1             500.2323314 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SMSQ10.100
GPZ1                  10.00 %
P16                 1000.00 usec

F1 - Acquisition parameters
TD                       128
SFO1             500.2323 MHz
FIDRES           34.568584 Hz
SW                   8.845 ppm
FnMODE                   QF

F2 - Processing parameters
SI                       1024
SF               500.2300511 MHz
WDW                    QSINE
SSB                      0
LB                       0 Hz
GB                       0
PC                    1.40

F1 - Processing parameters
SI                       1024
MC2                      QF
SF               500.2300511 MHz
WDW                      SIN
SSB                      0
LB                       0 Hz
GB                       0
```

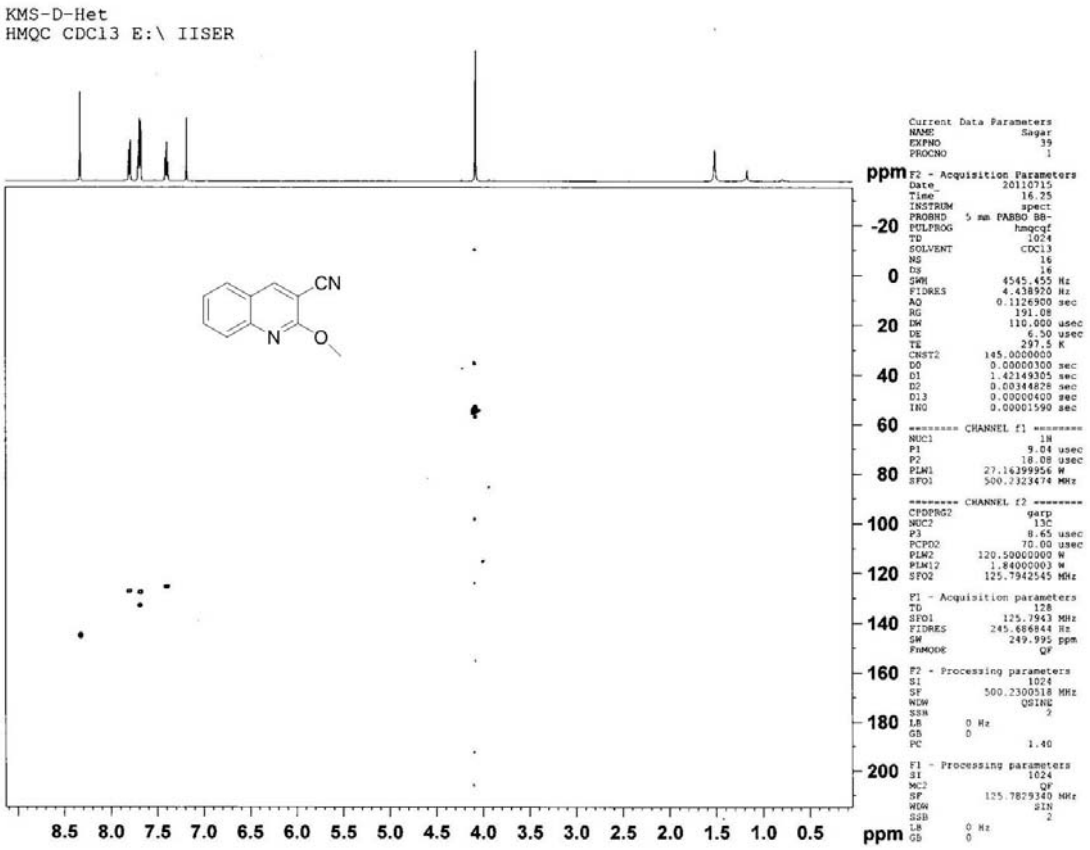
COSY of compound **2** (zoom)



^{13}C NMR of compound **2**



HMQC of compound **2**



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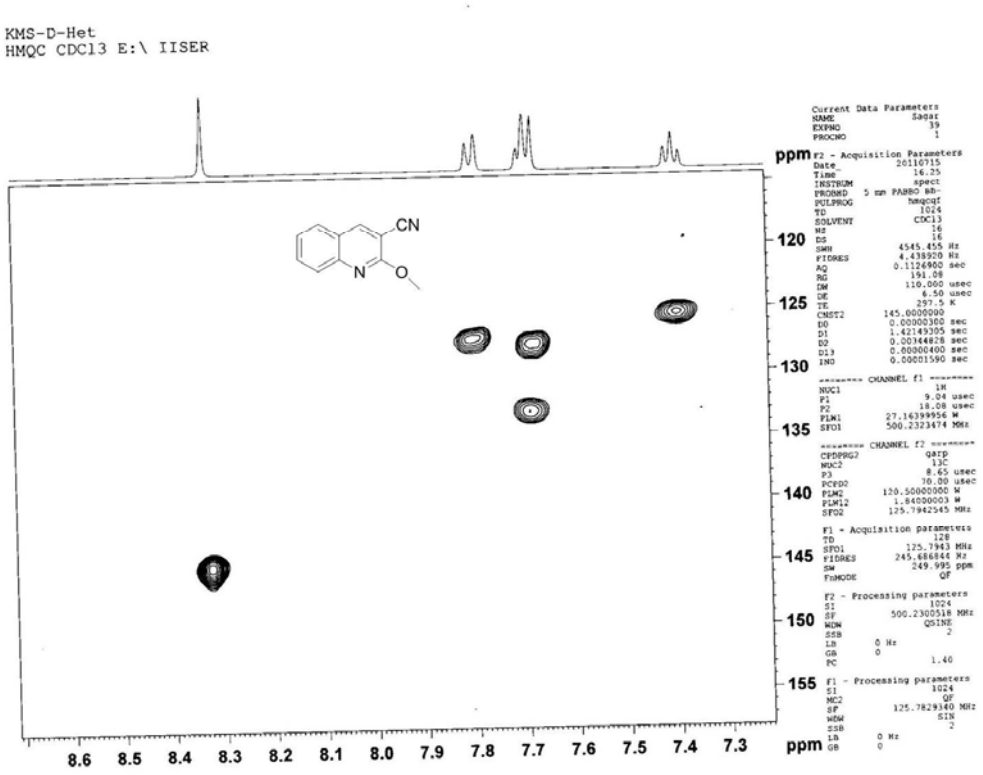
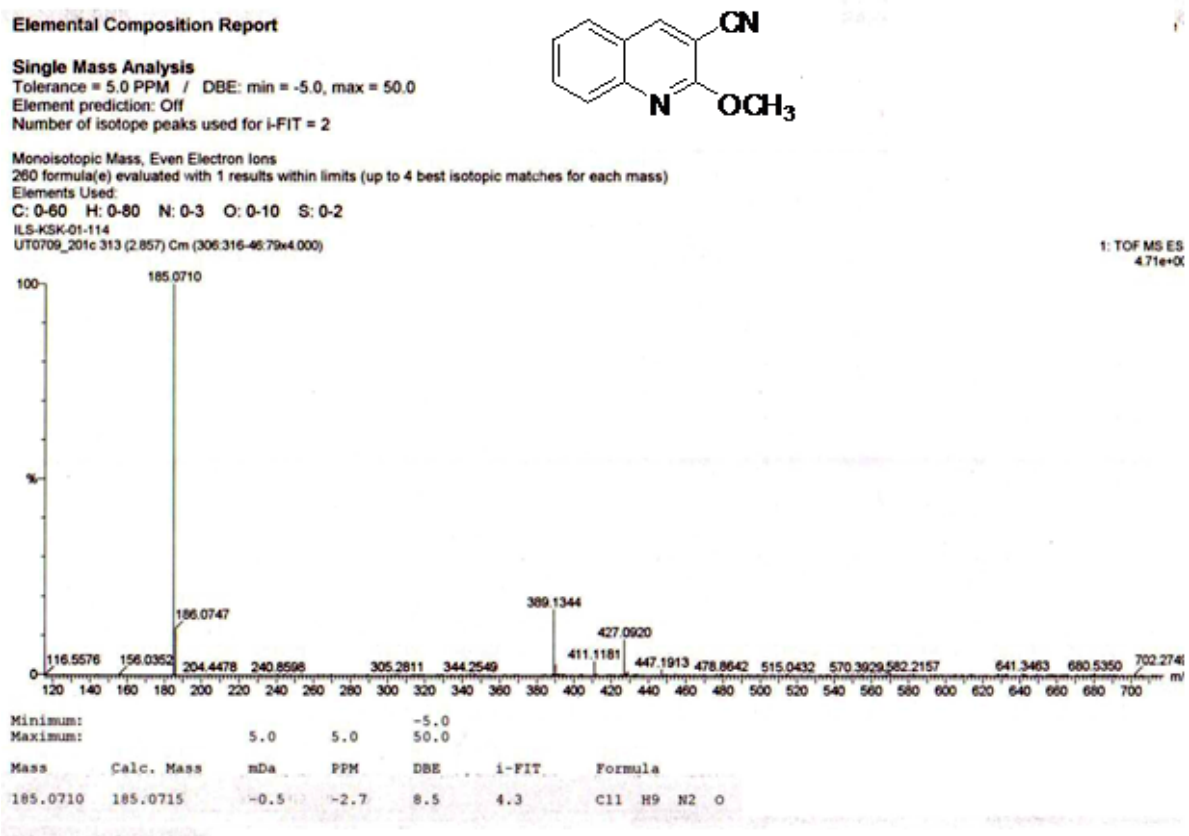
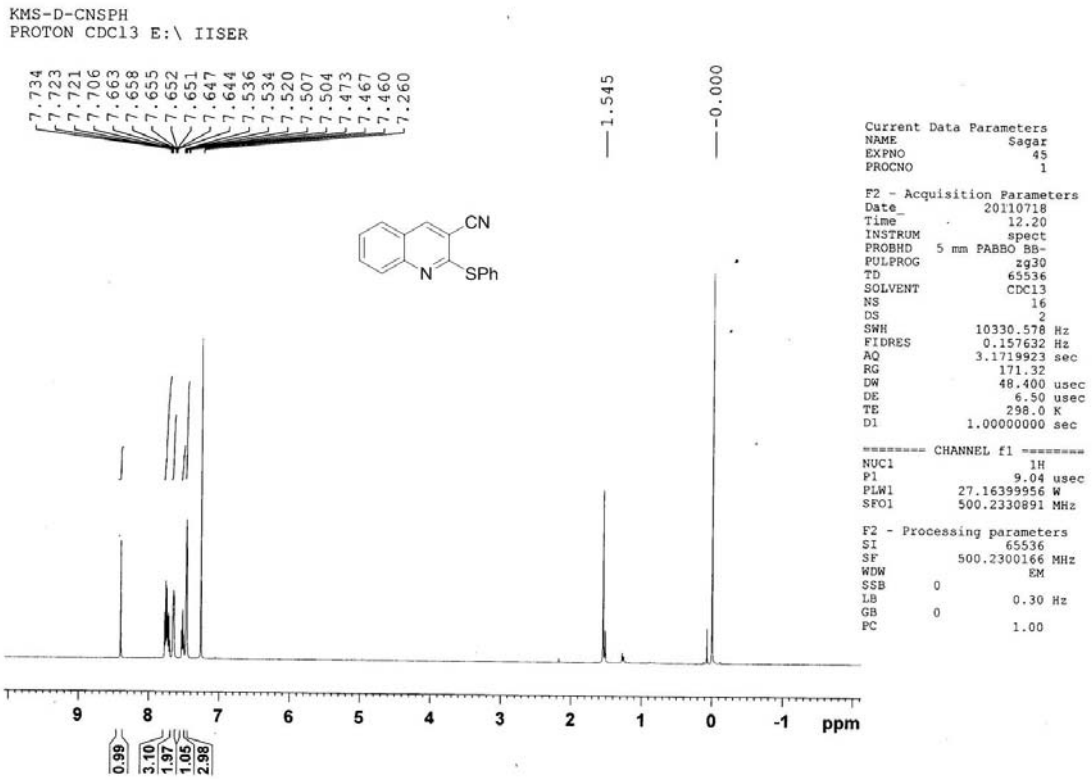
HMQC of compound **2** (zoom)



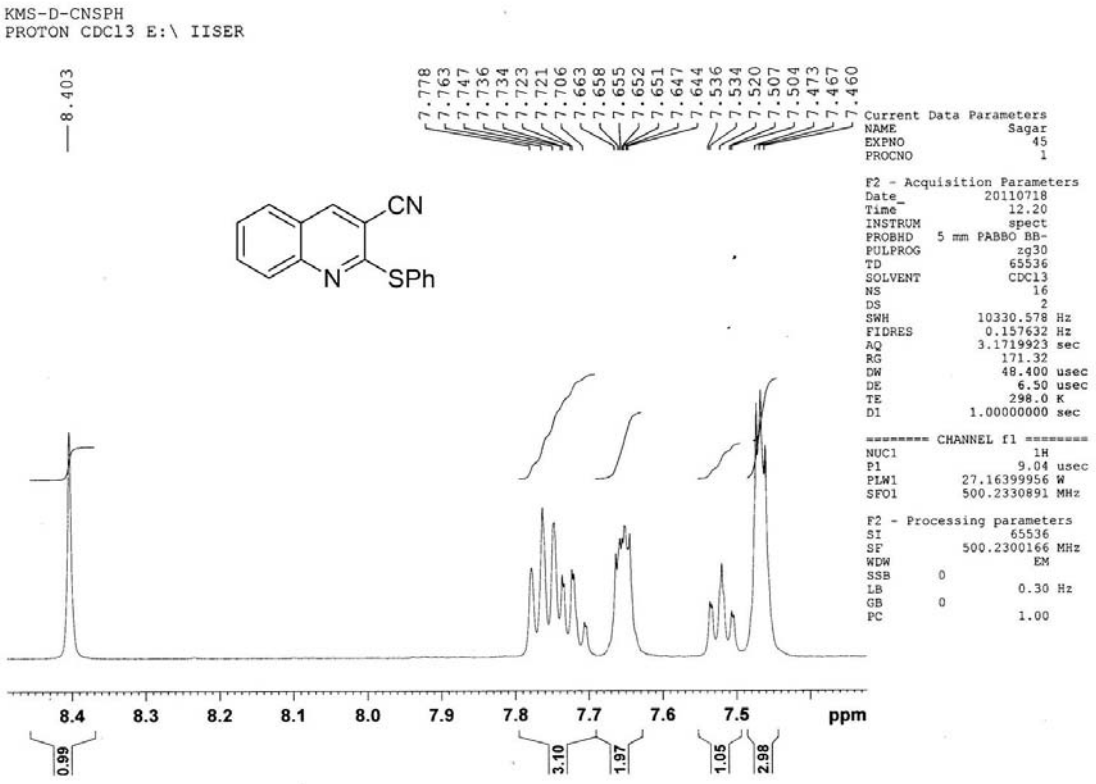
HRMS of compound **2**



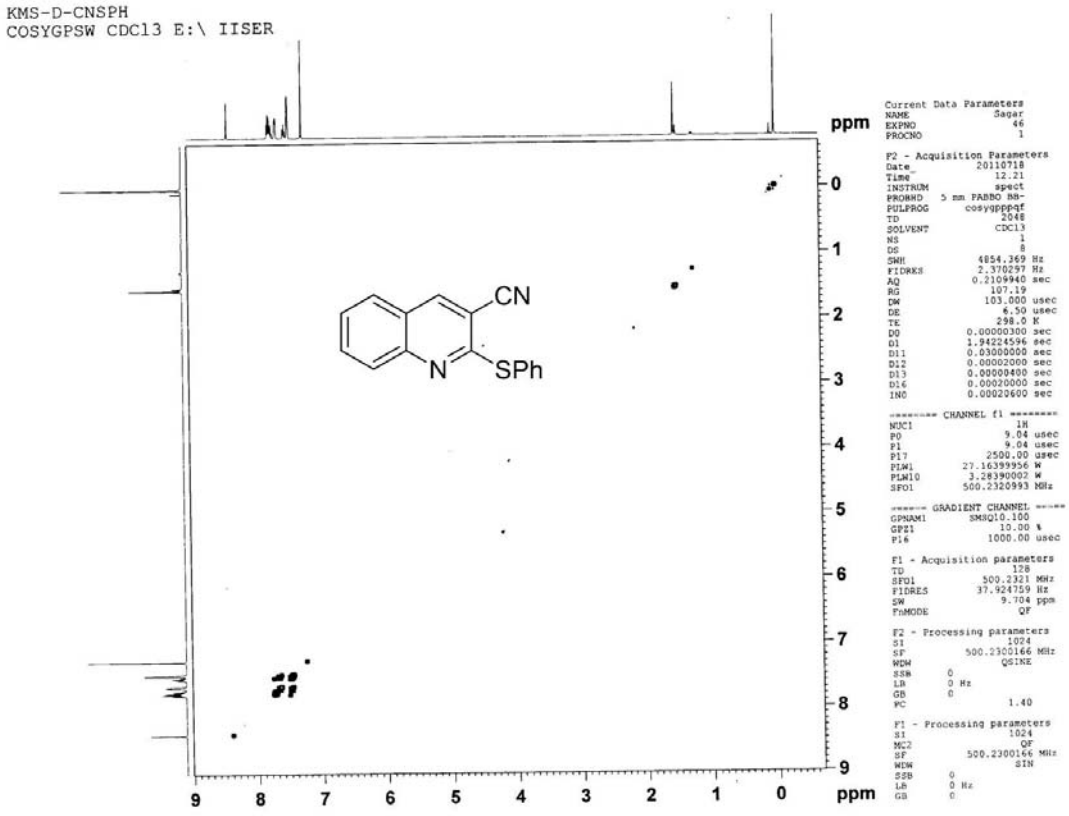
^{1}H NMR of compound **3**



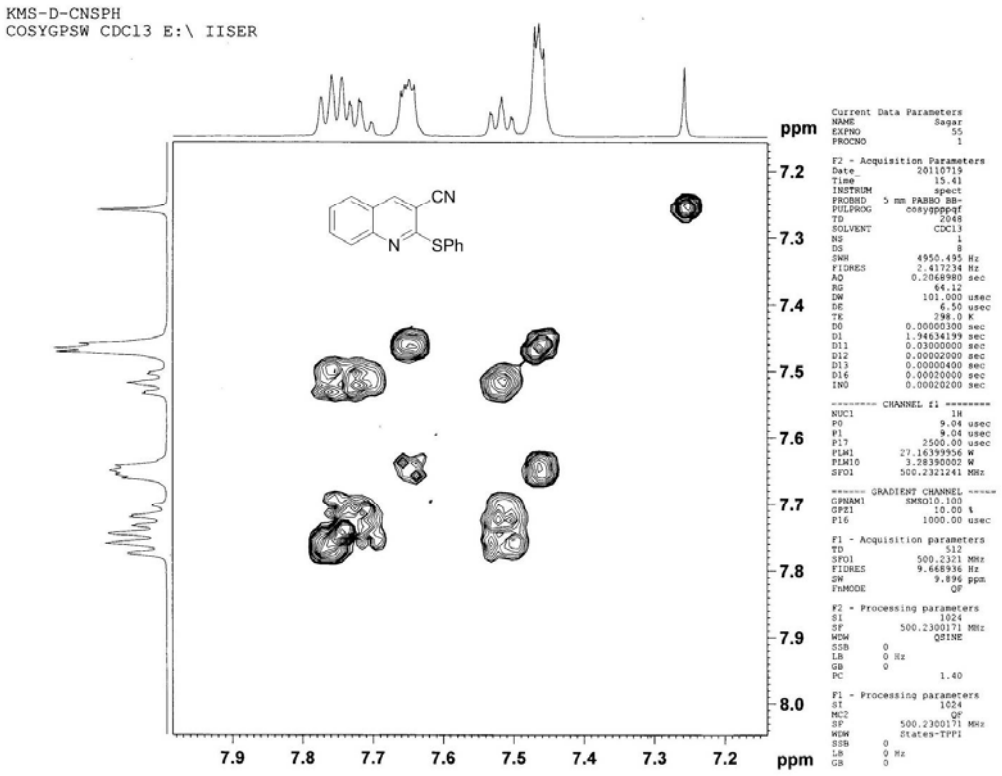
^{1}H NMR of compound **3** (zoom)



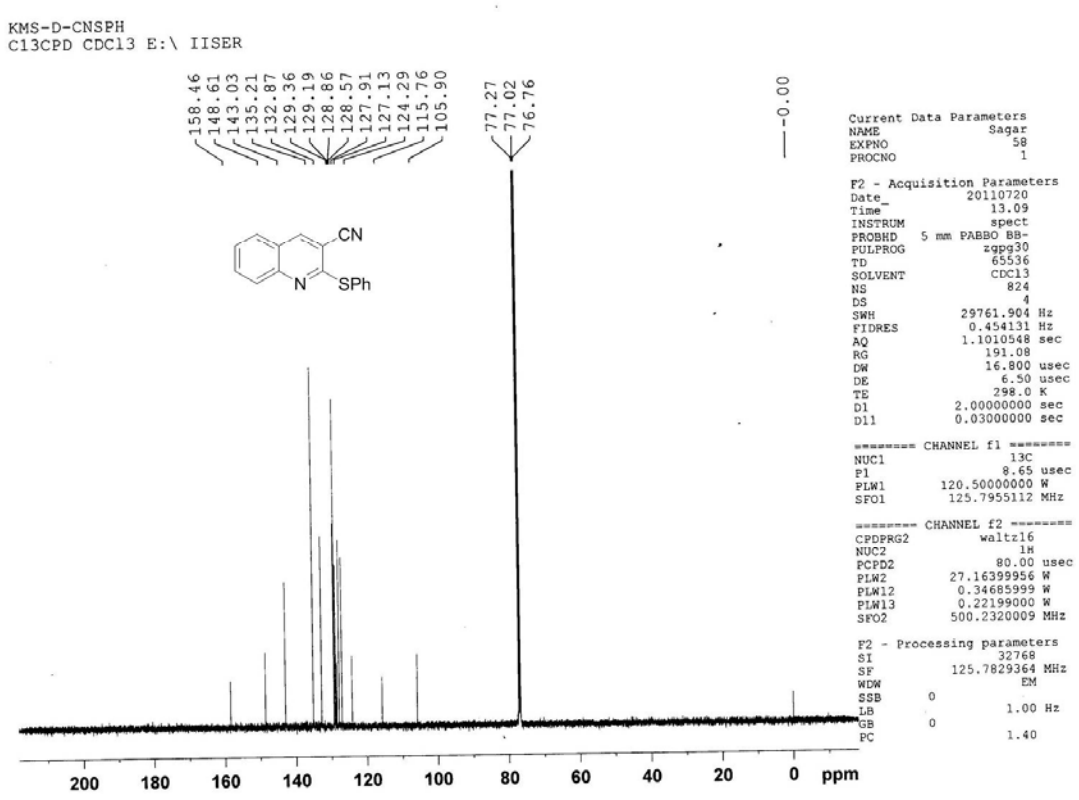
COSY of compound **3**



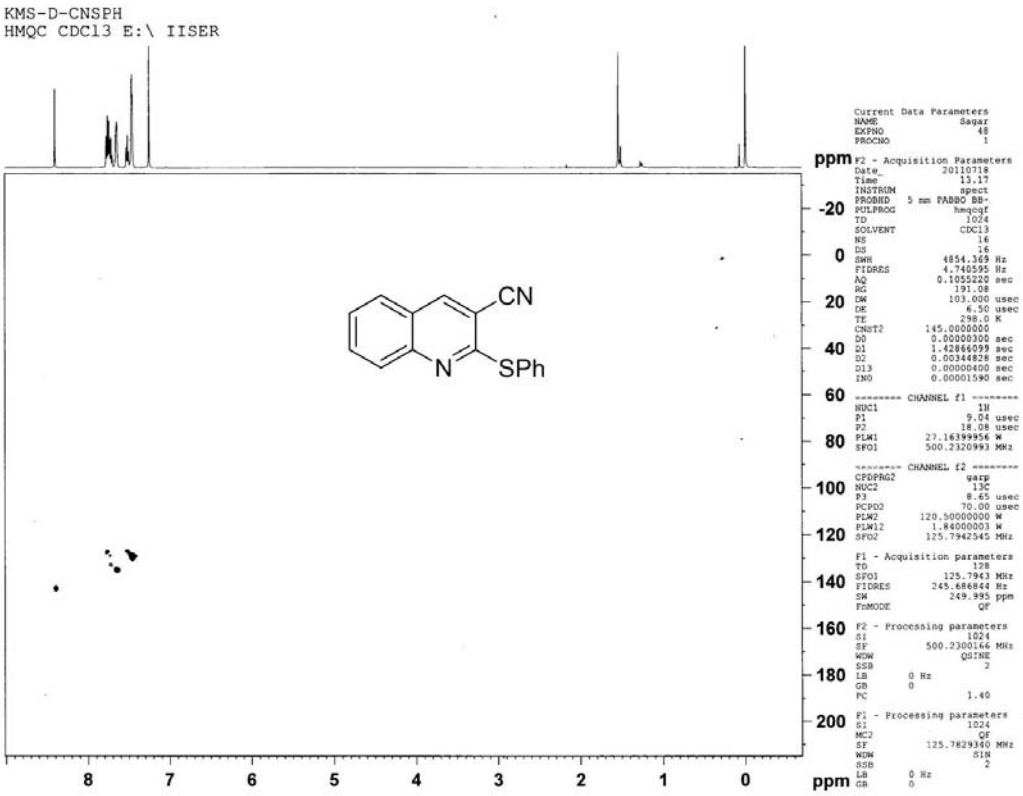
COSY of compound **3** (zoom)



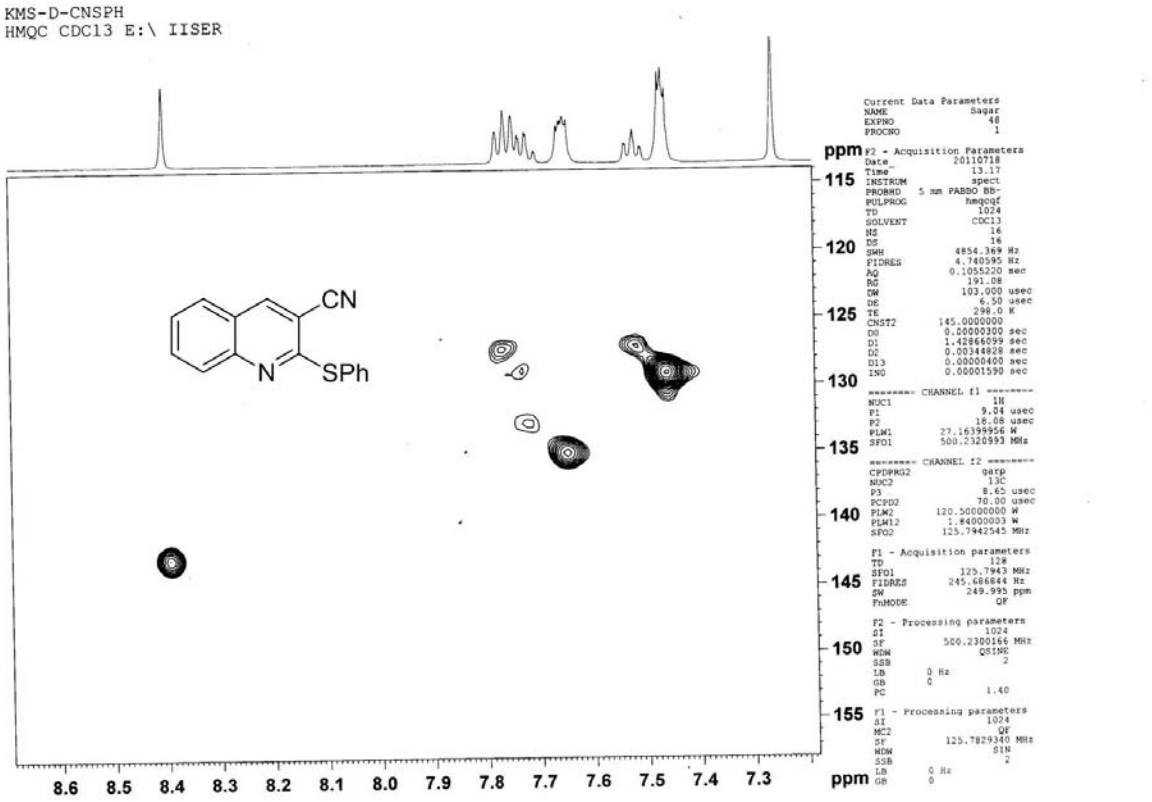
^{13}C NMR of compound **3**



HMQC of compound **3**



HMQC of compound **3** (zoom)



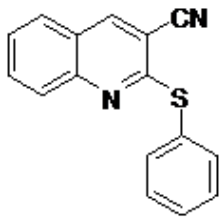
HRMS of compound **3**

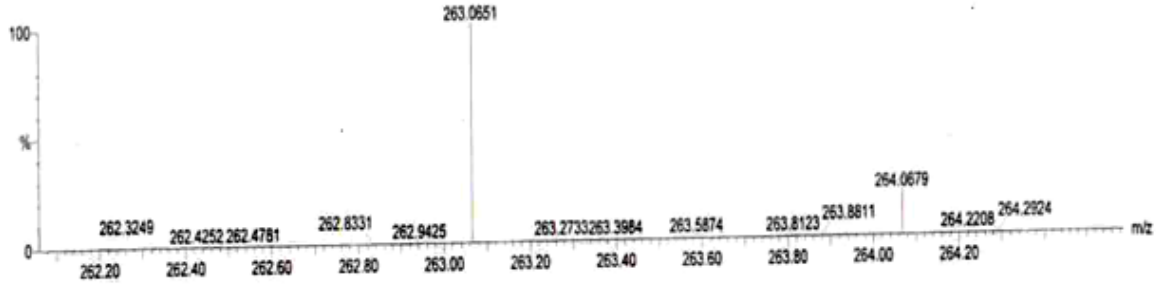
Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -5.0, max = 80.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
26 formula(e) evaluated with 1 results within limits (up to 4 closest results for each mass)
Elements Used:
C: 0-20 H: 0-20 N: 0-4 S: 0-2

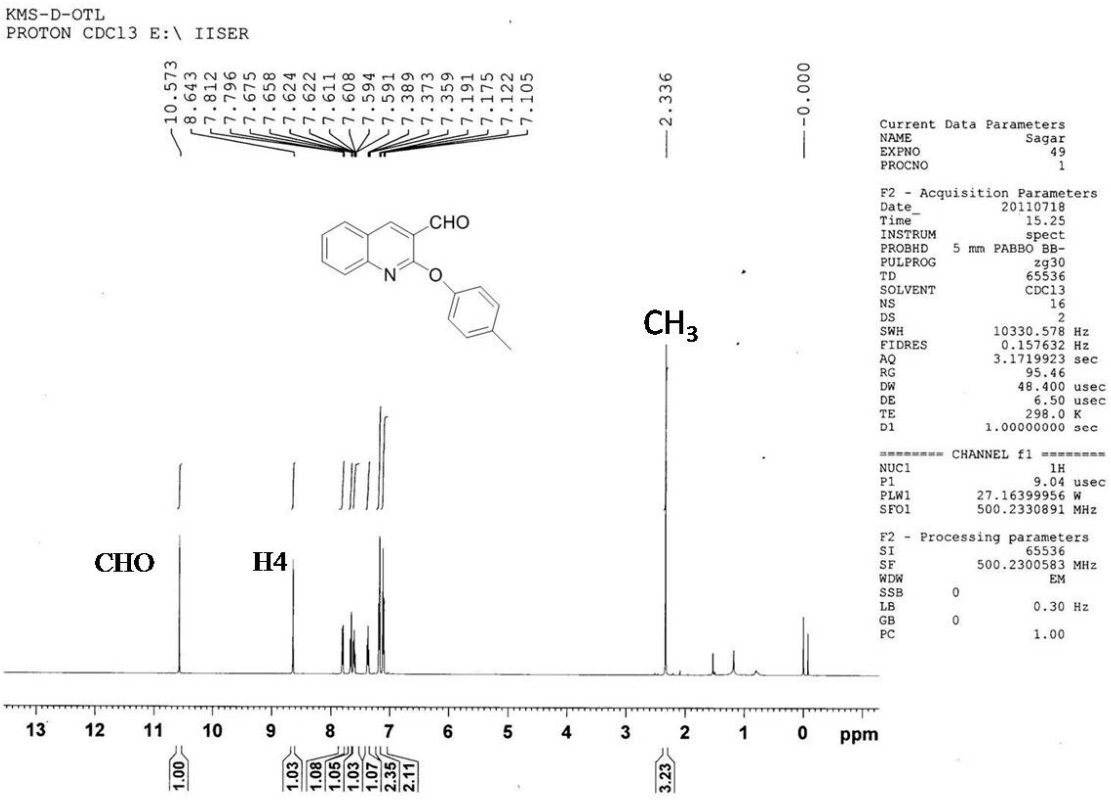
ILS-KSK-01-151-2
UT0710_04 42 (0.605) Cm (41:43-95:97)



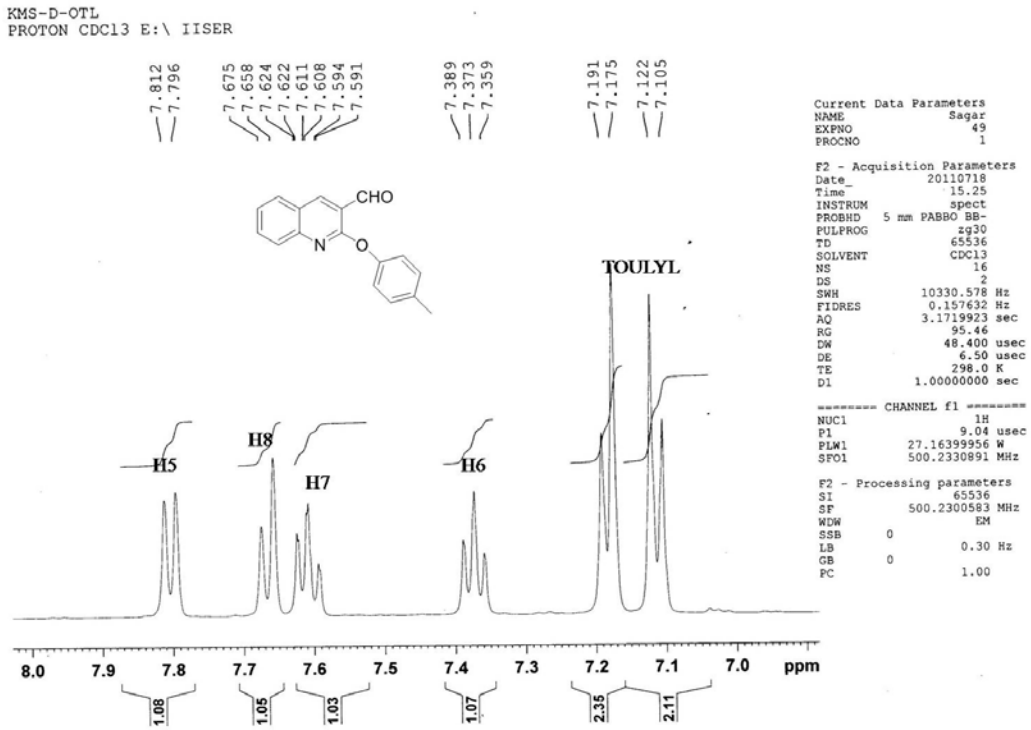


Minimum:				-5.0		
Maximum:		5.0	5.0	80.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
263.0651	263.0643	0.8	3.0	12.5	n/a	C16 H11 N2 S

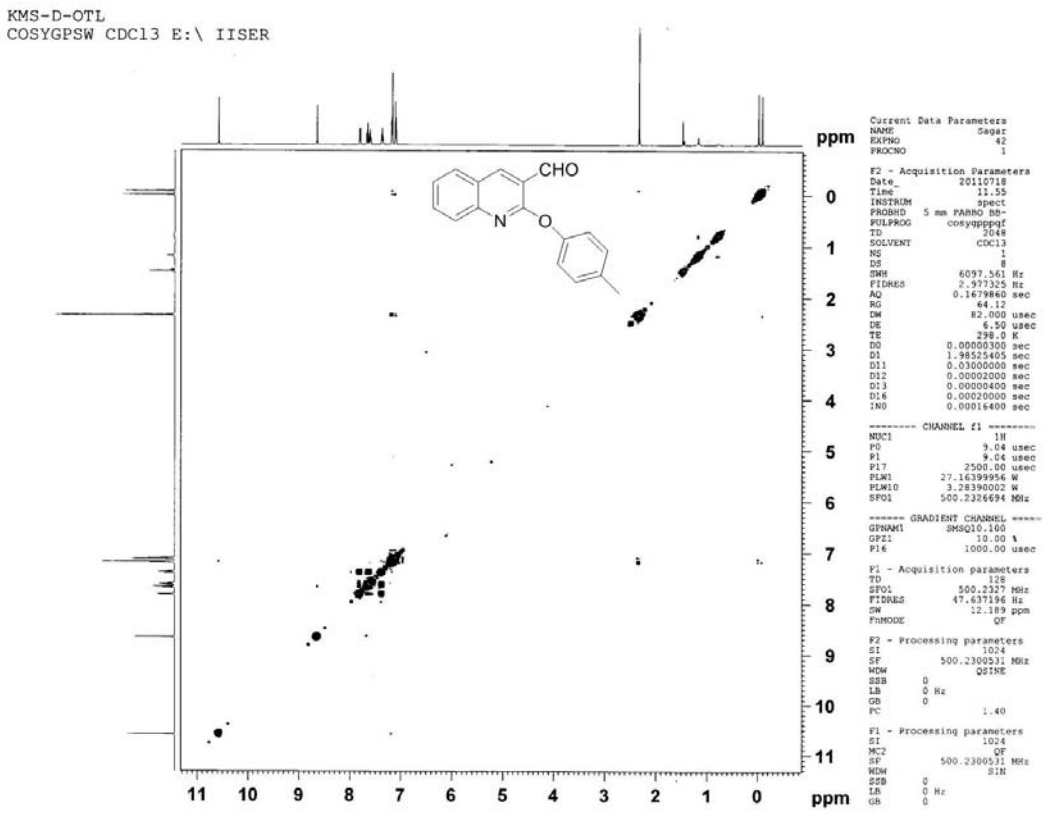
^{1}H NMR of compound **4**



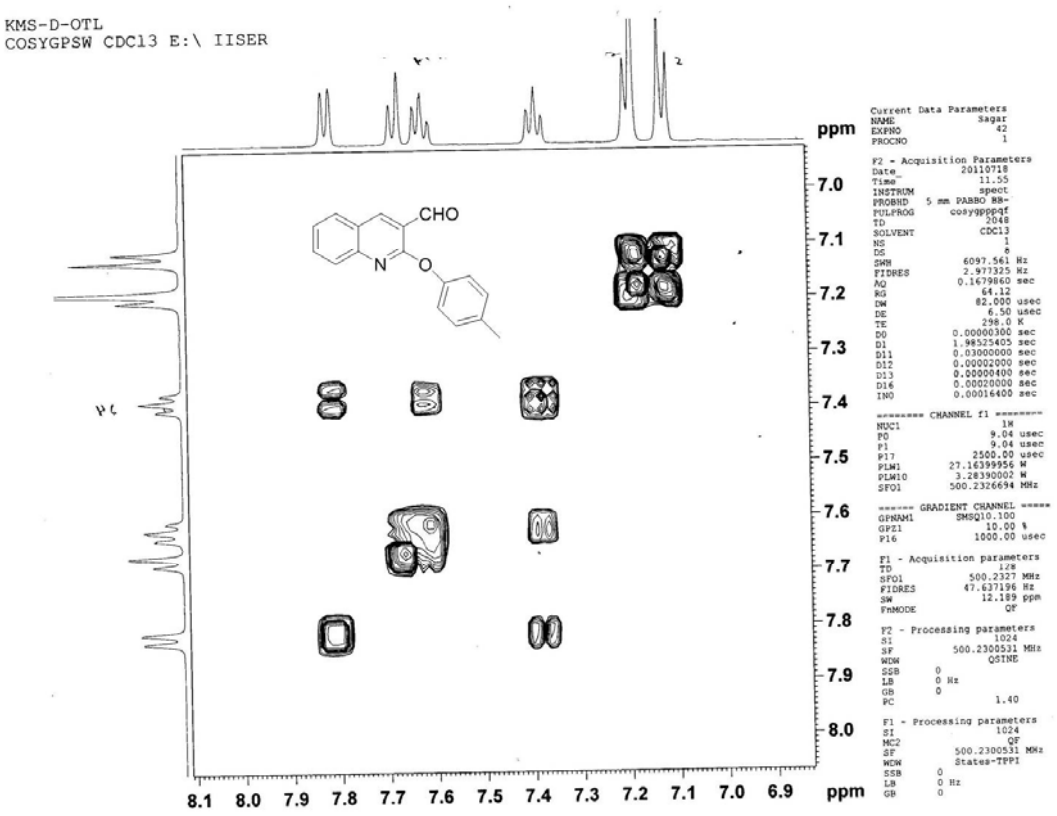
^{1}H NMR of compound **4** (zoom)



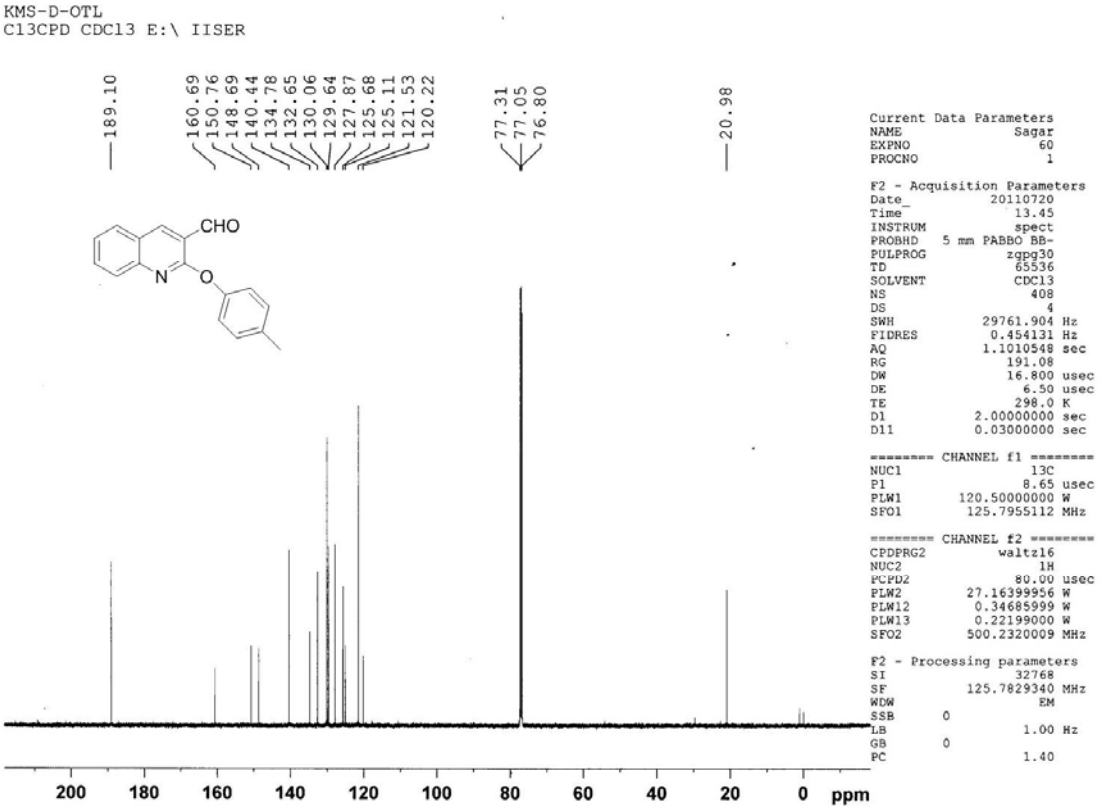
COSY of compound **4**



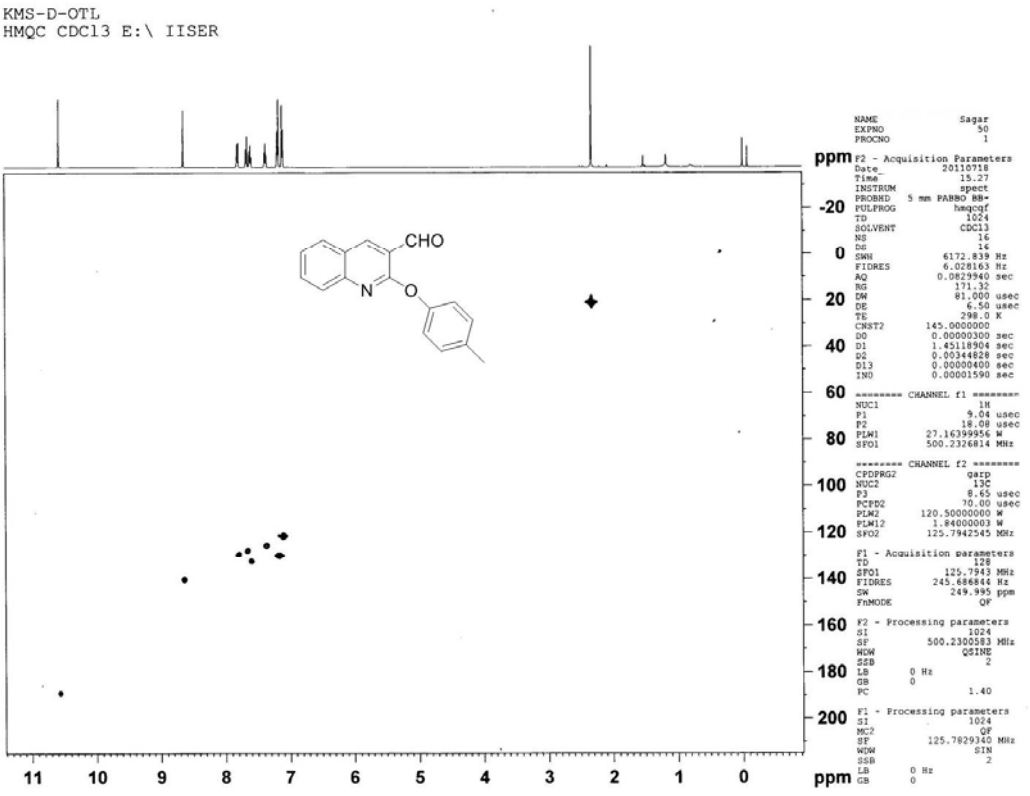
COSY of compound **4** (zoom)



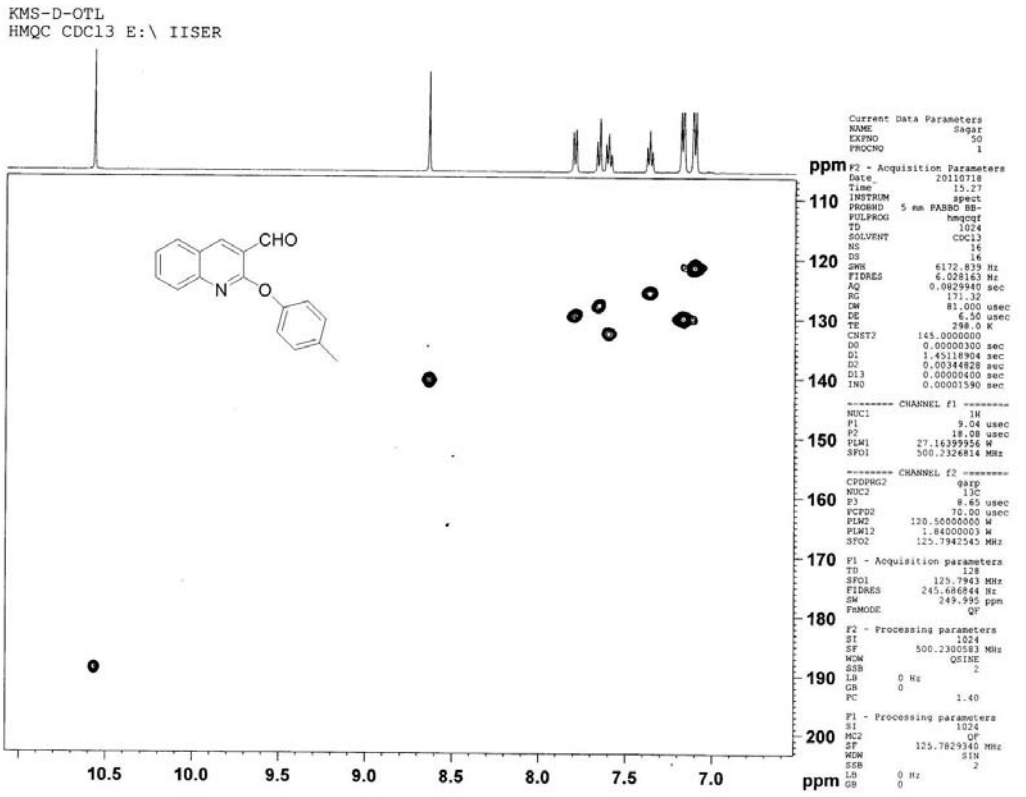
^{13}C NMR of compound **4**



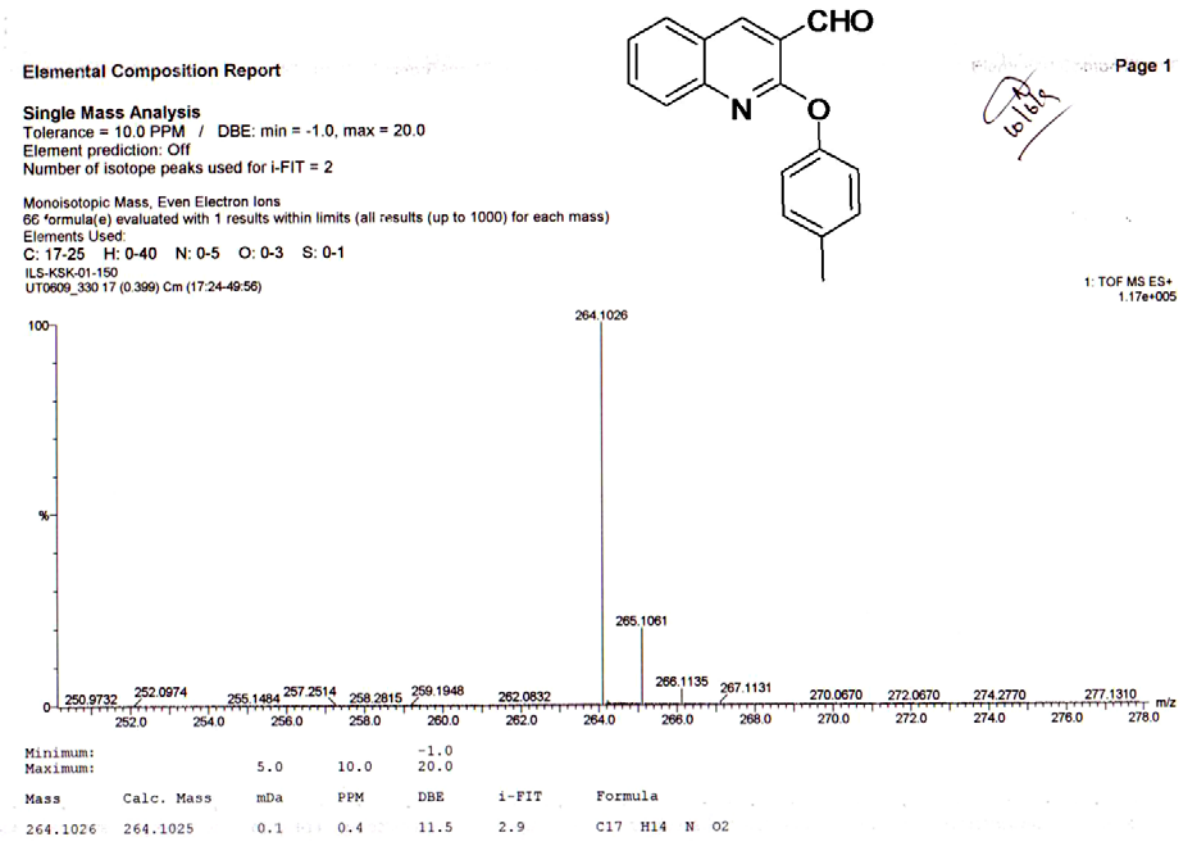
HMQC of compound **4**



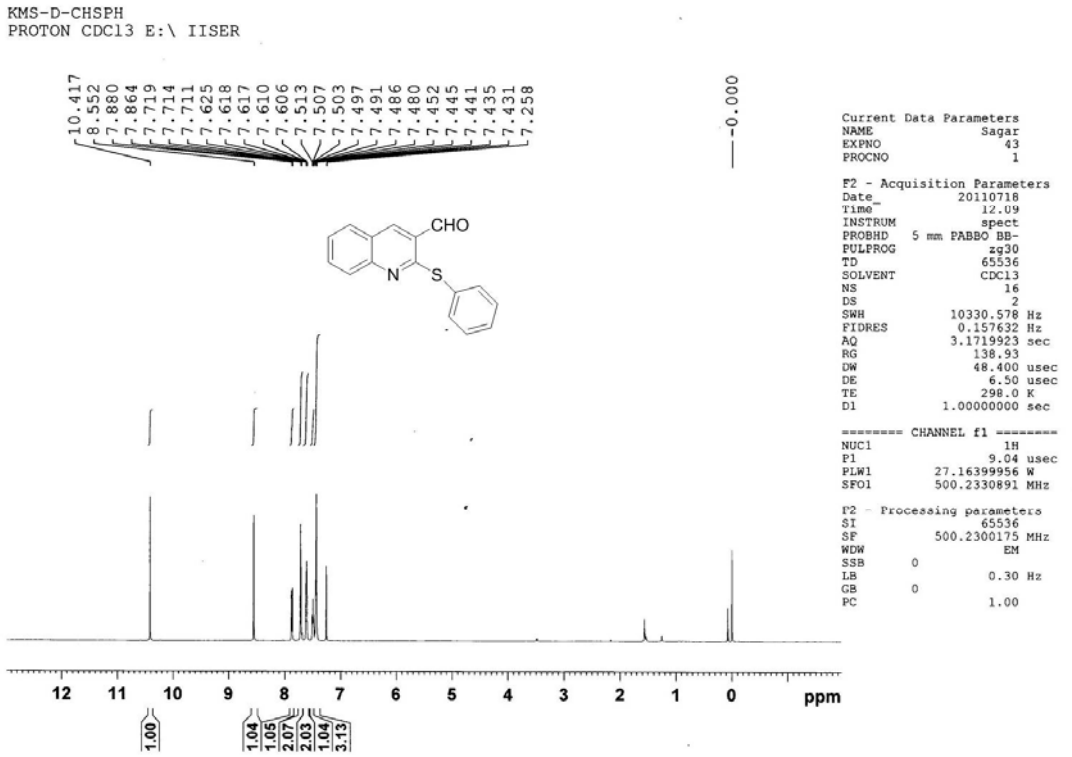
HMQC of compound **4**



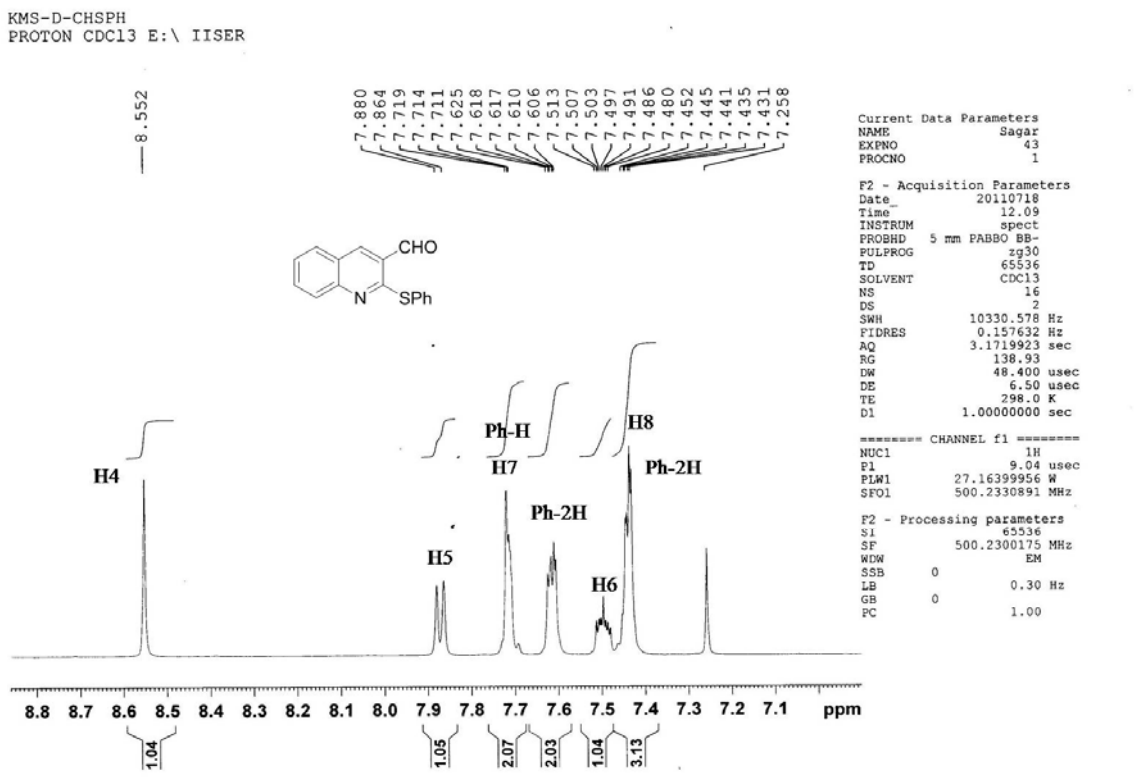
HRMS of compound **4**



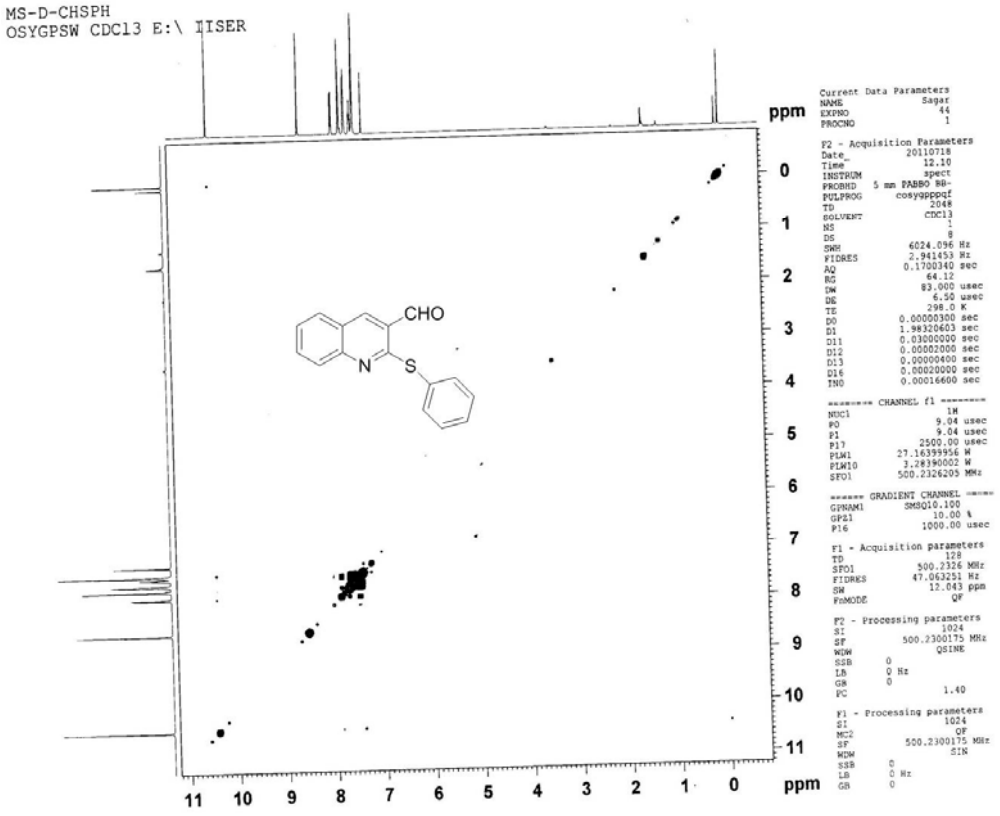
^{1}H NMR OF COMPOUND **5**



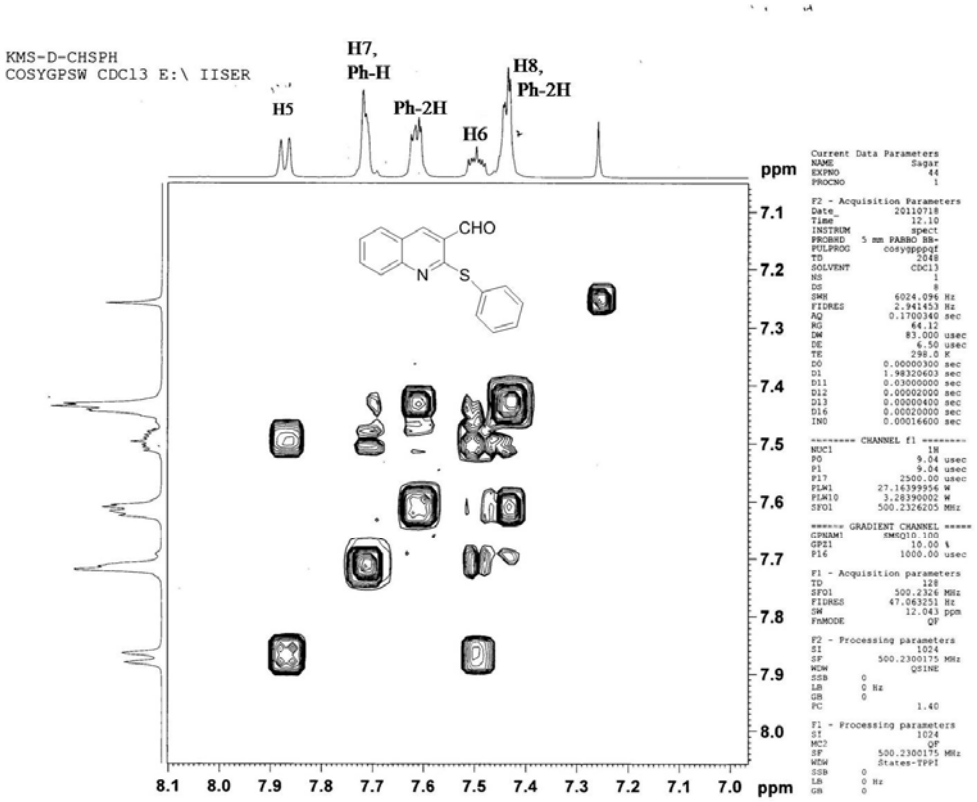
^{1}H NMR OF COMPOUND **5** (zoom)



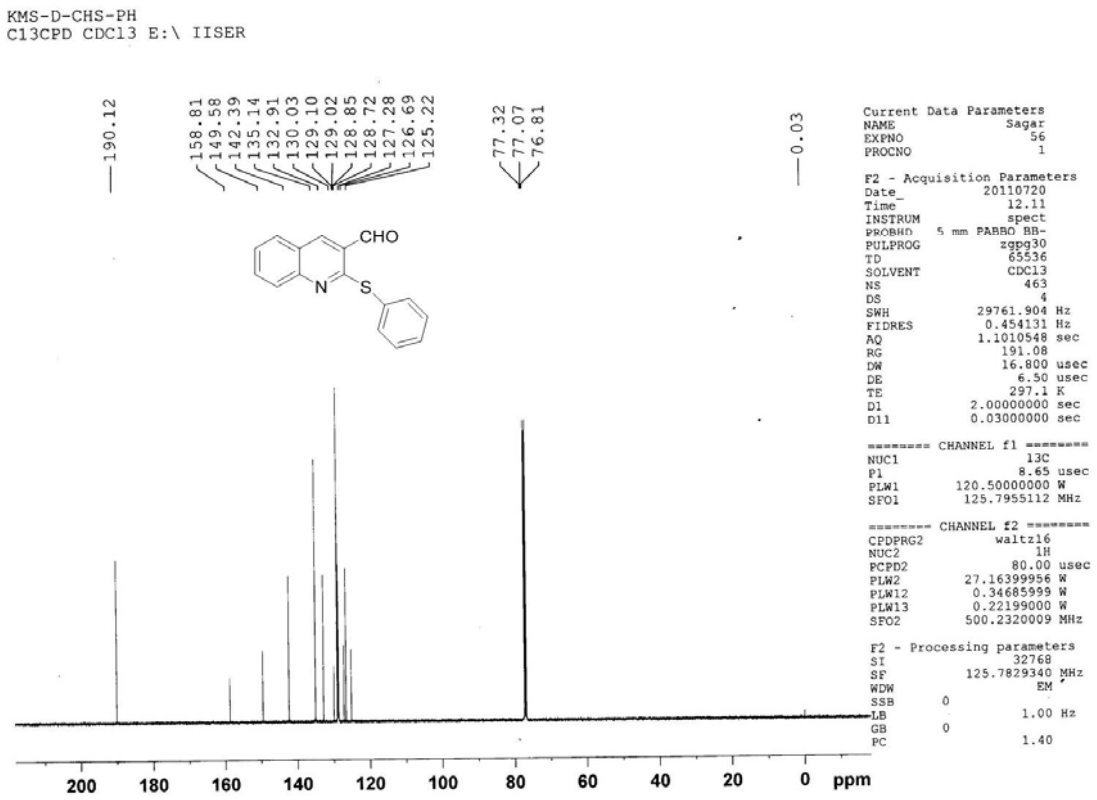
COSY of compound **5**



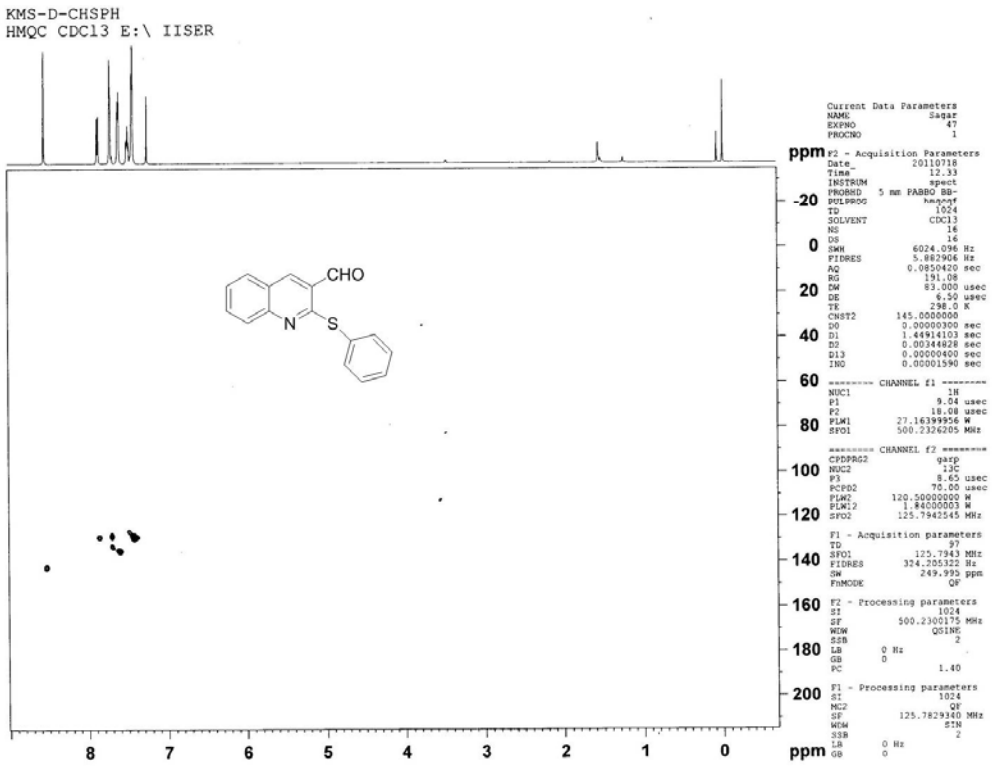
COSY of compound **5** (zoom)



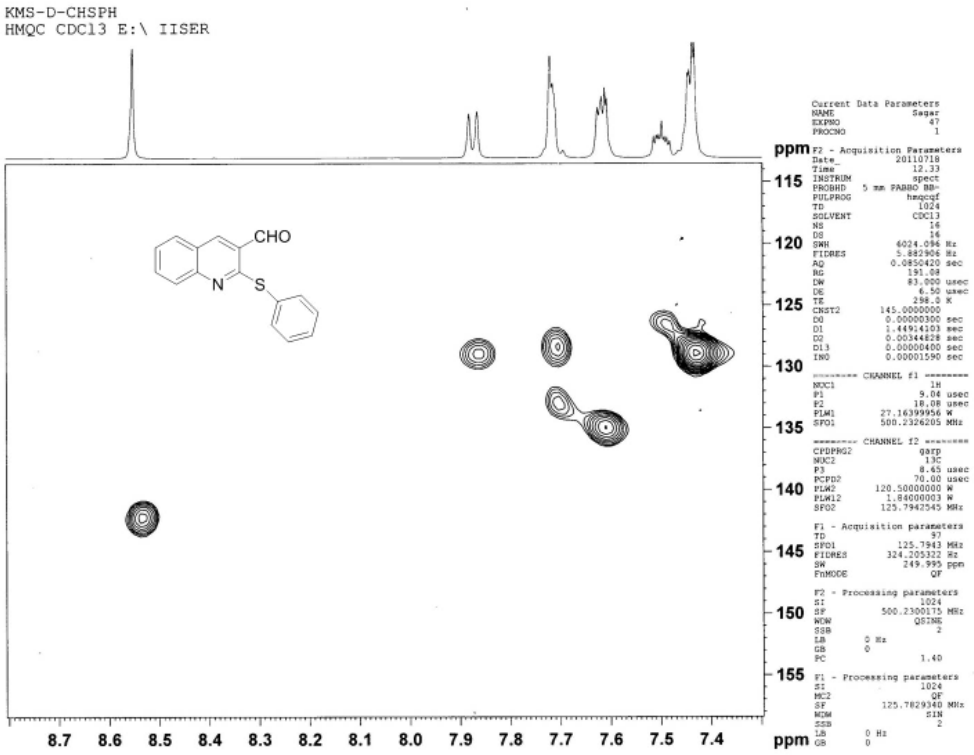
^{13}C NMR OF COMPOUND **5**



HMQC of compound **5**



HMQC of compound **5** (zoom)



References:

i. S. Upadhyay, A. Chandar, R. M. Sing, *Indian J. Chem*., **2009**, *48B*, 152.
ii. O. Meth-Chon, B. Narine, B. Tarnowski, *J. Chem. Soc*., *Perkin Trans*. I, **1981**,1520.