

## **Heterogeneous Cu(II)/L-His@Fe<sub>3</sub>O<sub>4</sub> nanocatalyst: a novel, efficient and magnetically-recoverable catalysts for organic transformations in green solvents**

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## General Methods

Chemicals were purchased from Sigma-Aldrich, Fisher, and Merck. The products were characterized by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra ( $^1\text{H}$  NMR, 400 MHz;  $^{13}\text{C}$  NMR, 100 MHz) and IR.

### *General synthesis for the preparation of 2,3-dihydroquinazolin-4(1H)-ones*

A mixture of aldehyde (1 mmol), 2-aminobenzamide (1mmol), Cu(II)/L-His@Fe<sub>3</sub>O<sub>4</sub> (4 mg) and ethanol (4 mL) was stirred at 80 °C. Upon completion, the progress of the reaction was monitored by TLC. After the TLC indicates the disappearance of starting materials, the reaction was cooled to room temperature. The catalyst was separated by an external magnet and reused as such for the next experiment. The filtrate was evaporated to remove solvent, the resultant solid was then washed with ethanol to obtain pure 2,3-dihydroquinazolin-4(1H)-ones in 89-99% yields.

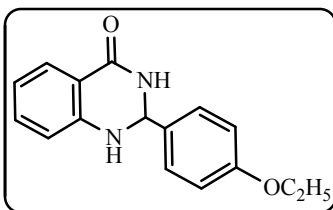
### *General synthesis for the preparation of polyhydroquinolines*

The 4 mg of Cu(II)/L-His@Fe<sub>3</sub>O<sub>4</sub> catalyst was ultrasonically dispersed in freshly distilled ethanol (5 mL). Then, aldehydes (1 mmol), dione (1 mmol), ethyl acetoacetate (1 mmol) and ammonium acetate (1.2 mmol) was added. The mixture was stirred in ethanol (5ml) at 50°C for the appropriate time, as shown in Table 3. The mixture was cooled, and the catalyst was separated from the reaction mixture using an external magnet. Subsequently, the solvent was evaporated and the residue was purified by further recrystallisation in ethanol. The products were obtained with various yields (91–98%).

### *General synthesis for the preparation of 2-amino-3,5-dicarbonitrile-6-thio-pyridines*

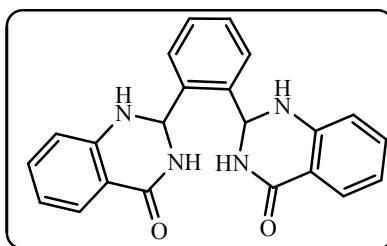
To a stirred solution of aldehyde (1 mmol), malononitrile (2 mmol) and Thiols (1 mmol) in water (4 mL) was added Cu(II)/L-His@Fe<sub>3</sub>O<sub>4</sub> (5 mg) and the reaction mixture was stirred at 80 °C for 1 h. After reaction completion, the catalyst was separated by an external magnet and reused as such for the next experiment. The mixture was diluted with ethyl acetate and water solution and the extracted organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> (1.5 g) and the solvent was evaporated. The crude product was recrystallized from ethanol to obtain pure product.

**2-(4-ethoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one:**



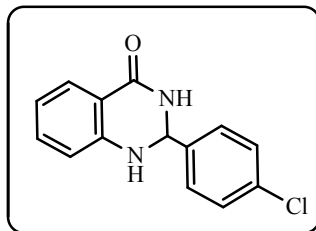
White solid, m.p. 167–168 °C, <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.98 (brs, 1H), 7.6 (d, J = 6 Hz, 2H) 7.34 (s, 1H), 7.26 (d, J = 2 Hz, 1H), 6.87–7.03 (m, 3H), 6.65 (d, J = 5.6 Hz, 1H), 5.87 (s, 1H), 5.75 (s, 1H), 4.12 (t, J= 4 Hz, 2H) 1.45 (q, J= 6.4 Hz, 3H). <sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>): δ 161.4, 148.9, 147.5, 131.52, 129.89, 120.7, 116.79, 116.01, 115.68, 69.82, 64.78, 15.9; IR (KBr): mmax 3300, 3060, 3000, 2930, 1666, 1650, 1610, 1487, 1387, 70

**2,2'-(1,2-phenylene)bis(2,3-dihydroquinazolin-4(1H)-one) :**



White solid, m.p. 272-273 °C, <sup>1</sup>H NMR (400 MHz, DMSO): δ 7.87 (d, J = 8.4 Hz, 4H), 7.64 (s, 2H), 7.46 (s, 2H), 7.32 (d, J = 6 Hz, 2H), 7.15 (s, 2H), 6.69 (s, 3H), 6.63 (s, 2H), 5.75 (s, 2H). IR (KBr): mmax 3299, 3248, 3181, 2961, 2831, 1698, 1639, 1808, 1515, 1481, 1297, 1151, 742.

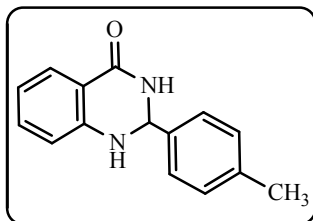
**2-(4-chlorophenyl)-2,3-dihydroquinazolin-4(1H)-one:**



Isolated Yield = 66%. Mp: 202-203 °C. <sup>1</sup>H NMR (250 MHz, DMSO-*d*<sub>6</sub>): δ 8.29 (s, 1H), 7.61-7.41 (m, 5H), 7.26-7.2 (t, 1H), 6.75-6.63 (m, 2H), 7.12 (s, 1H), 6.75-6.63 (m, 2H), 5.75 (s, 1H)

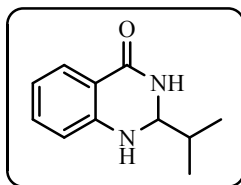
ppm.  $^{13}\text{C}$  NMR (62 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  163.9, 148.1, 141.1, 133.8, 133.4, 129.2, 128.7, 127.8, 117.7, 115.4, 114.9, 66.2 ppm.

**2-(4-methylphenyl)-2,3-dihydroquinazolin-4(1H)-one:**



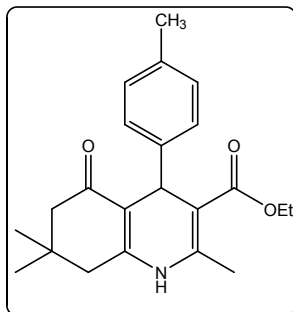
Isolated Yield = 62 %. Mp: 225-226 °C.  $^1\text{H}$  NMR (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  8.21 (s, 1H), 7.62-7.59 (d, 1H), 7.38-7.35 (d, 2H), 7.26-7.16 (m, 3H), 7.03 (s, 1H), 6.75-6.63 (m, 2H), 5.71 (s, 1H), 2.49-2.42 (s, 3H) ppm.  $^{13}\text{C}$  NMR (62 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  164.1, 148.4, 139.1, 138.2, 133.7, 129.3, 127.8, 127.2, 117.5, 115.4, 114.9, 66.8, 21.2 ppm.

**2-isopropyl-2,3-dihydroquinazolin-4(1H)-one:**



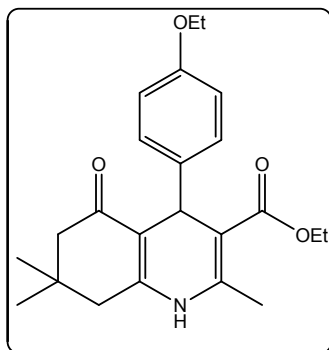
White solid, m.p. 160–164°C,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.88 (d,  $J$  = 7.6 Hz, 1H), 7.31 (t,  $J$  = 7.2 Hz, 1H), 6.84 (t,  $J$  = 7.2 Hz, 1H), 6.74 (s, 1), 6.69 (d,  $J$  = 8 Hz, 1H), 4.72 (d,  $J$  = 4.4, 1H), 2.00 (m, 6H), 1.05 (d,  $J$  = 6.8 Hz, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  =, 165.52, 147.55, 133.87, 128.46, 118.97, 115.52, 114.51, 70.16, 32.82, 148.9, 16.94.

**Ethyl 2,7,7-trimethyl-5-oxo-4-(p-tolyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate:**



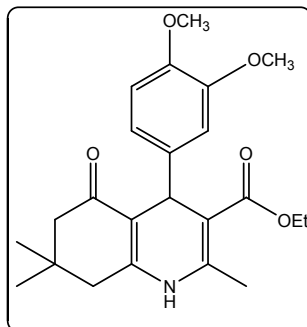
White solid, M.p. 252-254°C,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 9.05 (s, 1H, NH), 7.01-7.29 (m, 4H), 5.03 (s, 1H), 4.04 (q,  $j=8.2\text{Hz}$ , 2H), 2.21 (m, 3H), 2.28 (s, 3H), 1.96 (s, 1H), 1.25 (t,  $J=7.2\text{Hz}$ , 3H), 1.11 (s, 3H), 0.98 (s, 3H) ppm. IR (KBr,  $\text{cm}^{-1}$ ): 3274, 2956, 1699, 1603, 1488, 1378, 1233, 1139, 1030, 748, 743.

**Ethyl 4-(4-ethoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate**



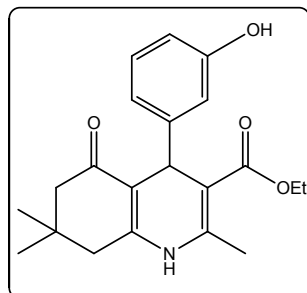
White solid, M.p. 176-178 °C,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta=$  7.19 (d,  $J = 6.4\text{Hz}$ , 2H) , 6.73 (d,  $J = 6.4\text{Hz}$ , 2H), 5.80 (s, 1H), 4.99 (s, 1H), 4.06 (t, 2H), 3.96 (t, 2H), 2.15-2.38 (m, 7H), 1.37-1.38 (m, 3H), 1.20-1.21 (m, 3H), 1.07 (s, 3H), 0.95 (s, 3H) ppm.  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta=$  198, 169, 158.3, 150.2, 144.7, 140.7, 130.1, 114.9, 113.1107.3, 64.3, 60.9, 51.9, 41.8, 36.8, 33.7, 30.6, 28.2, 20.3, 16.05, 15.4 ppm.

**Ethyl 4-(3-hydroxy-4-methoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate:**

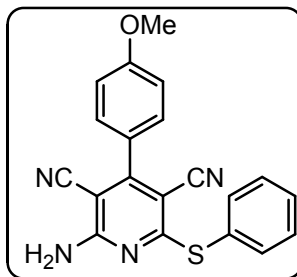


White solid, M.p. 201-202°C, IR (kbr,  $\text{cm}^{-1}$ ): 3203, 2958, 1692, 1601, 1485, 1378, 1216, 1139, 1029, 758, 730.  $^1\text{H}$  NMR (400 mhz,  $\text{DMSO-d}_6$ )  $\delta$ : 9.06 (s, NH) 6.74 (d,  $J=16$  Hz, 2H), 6.65 (d,  $J=8$  Hz, 1H), 4.80 (s, 1H), 4.02 (d,  $J=8$  Hz, 2H), 3.67 (s, 6H), 2.42 (d,  $J=8$  Hz, 1H), 2.28-2.32 (m, 4H), 2.21 (d,  $J=16$  Hz, 1H), 2.02 (d,  $J=14$  Hz, 1H), 1.17 (s, 3H), 1.03 (s, 3H), 0.90 (s, 3H) ppm.  $^{13}\text{C}$  NMR (100 mhz,  $\text{DMSO-d}_6$ )  $\delta$ : 194.8, 161.4, 149.9, 148.3, 147.4, 145.1, 144.9, 140.9, 119.6, 112.1, 111.9, 110.5, 104.3, 59.5, 55.8, 50.7, 35.6, 32.6, 29.7, 26.9, 18.7, 18.6, 14.7 ppm

**Ethyl 4-(3-hydroxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate:**

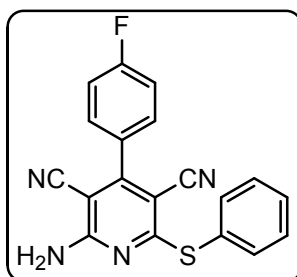


White solid, M.p. 217-219°C, IR (KBr,  $\text{cm}^{-1}$ ): 3274, 2950, 1690, 1600, 1497, 1377, 1214, 1144, 1033, 782, 722.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-d}_6$ )  $\delta$ : , 9.10 (s, OH ), 9.04 (s, NH), 6.46-6.98 (m, 4H) , 4.80 (s, 1H), 3.98 (q,  $J=4$  Hz, 2H), 2.44 (d,  $J=16$  Hz, 1H), 2.28 (q,  $J=12$  Hz, 3H), 2.17 (d,  $J=16$  Hz, 1H) , 2.00 (d,  $J=16$  Hz, 1H), 1.61 (t,  $J=7.2$  Hz, 3H) , 1.02 (s, 3H), 0.88 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-d}_6$ )  $\delta$ : , 193.9, 166.0, 194.7, 167.4, 157.3, 149.9, 149.4, 145.2, 129.0, 118.6, 115.0, 113.0, 110.2, 104.1, 59.5, 55.7, 50.7, 36.0, 32.6, 29.6, 27.0, 18.06, 18.7, 14.6. **2-Amino-4-(4-methoxy-phenyl)-6-phenylsulfanyl-pyridine-3,5-dicarbonitrile:**



Yellow solid, Mp 223-225°C. <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ: 7.81 (d, *J* = 8.1 Hz, 2H), 7.60–7.59 (m, 2H), 7.55–7.51 (m, 5H), 5.51 (s, 2H).

**2-amino-4-(4-fluorophenyl)-6-(phenylthio)pyridine-3,5-dicarbonitrile:**



Yellow solid, Mp 240-242°C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 7.43–7.59 (m, 7H), 7.08 (d, *J* = 8.8 Hz, 2H), 5.46 (s, 2H), 3.91 (3H, s).



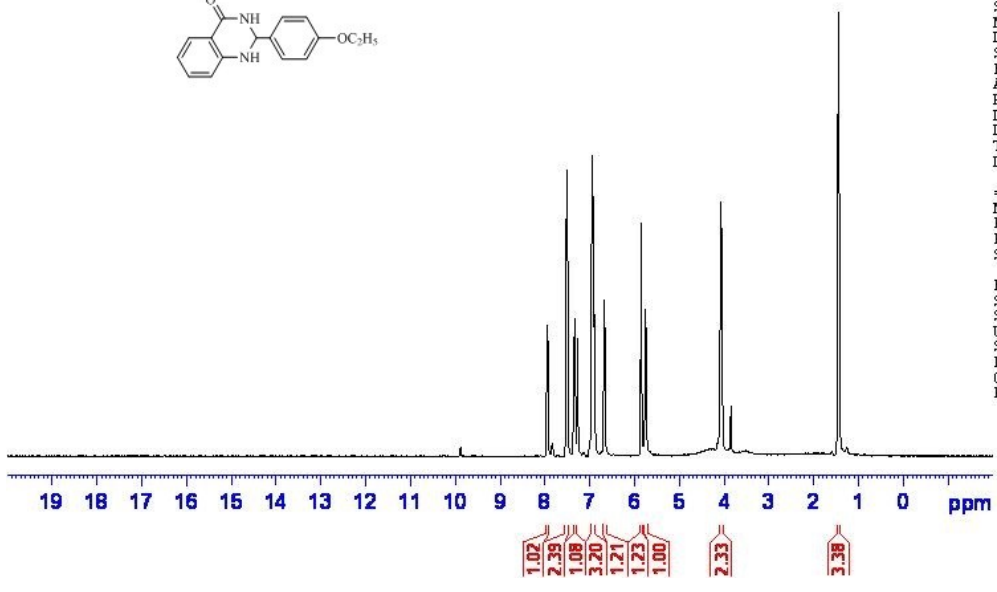
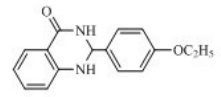
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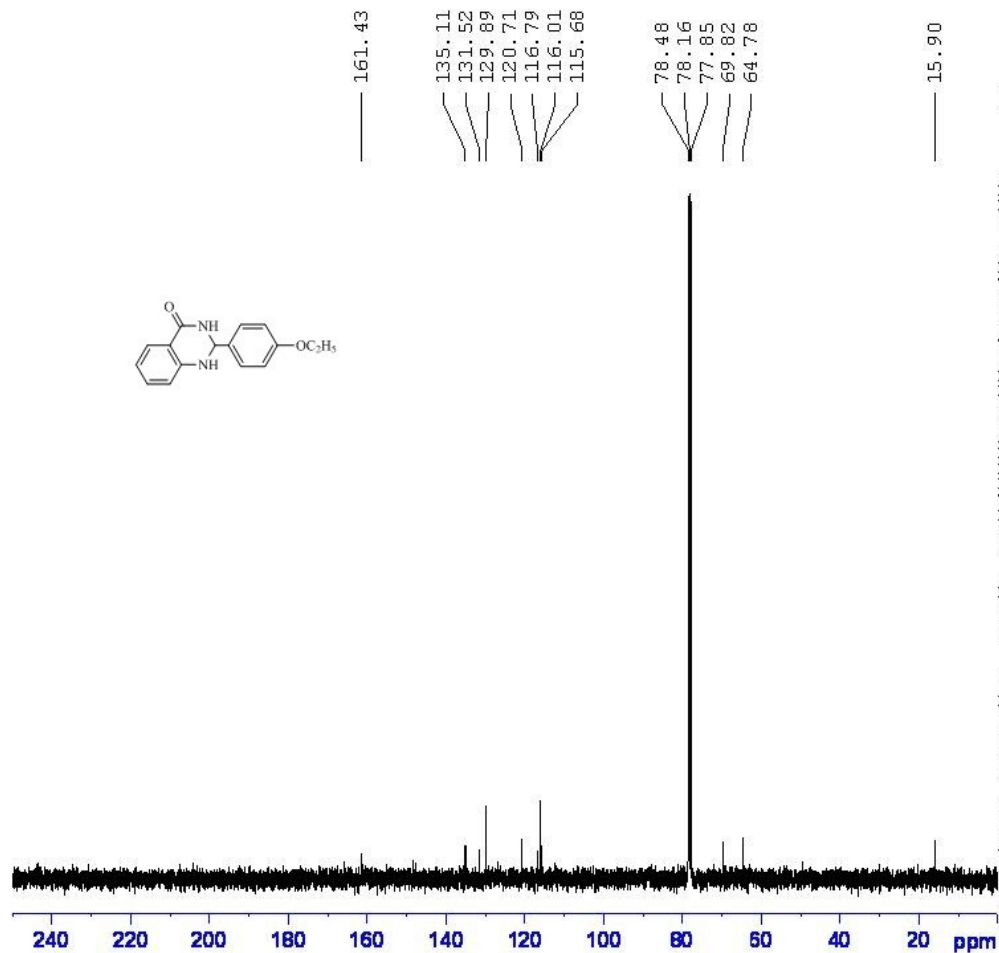
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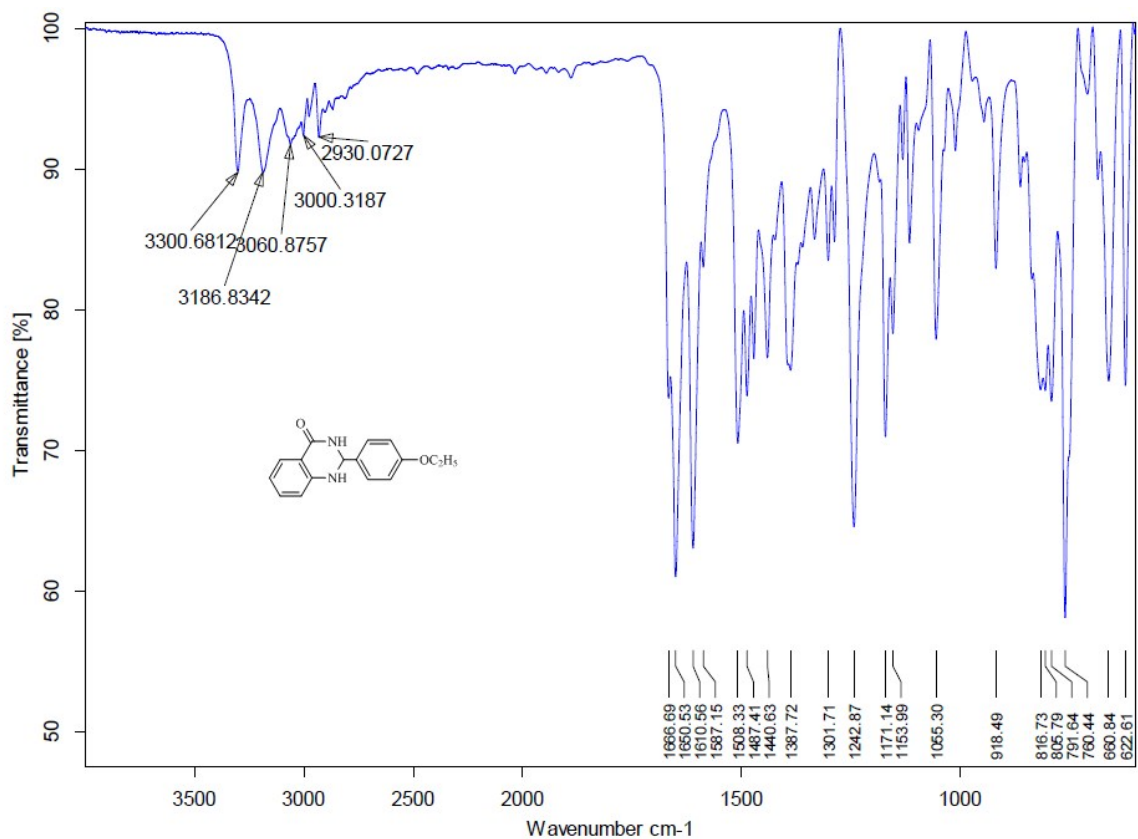
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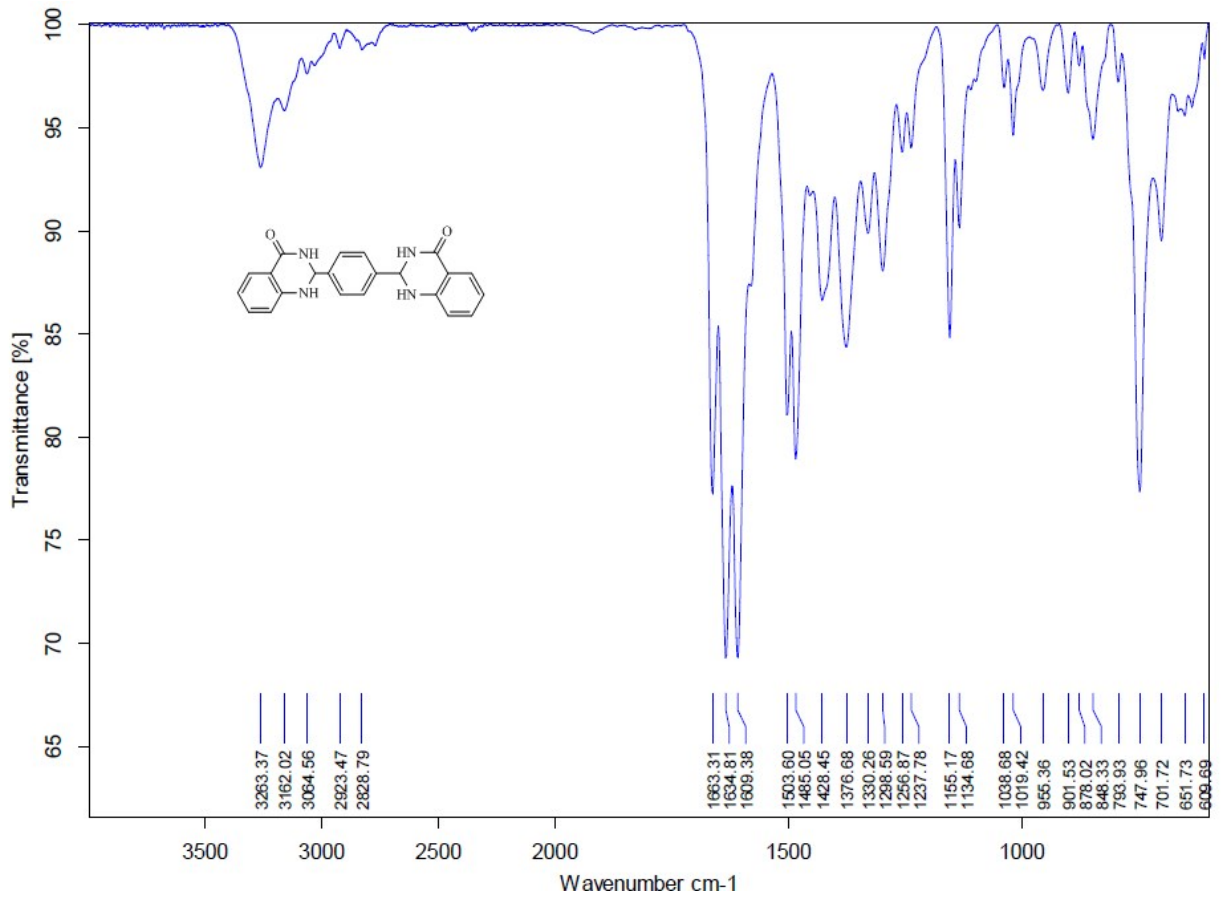
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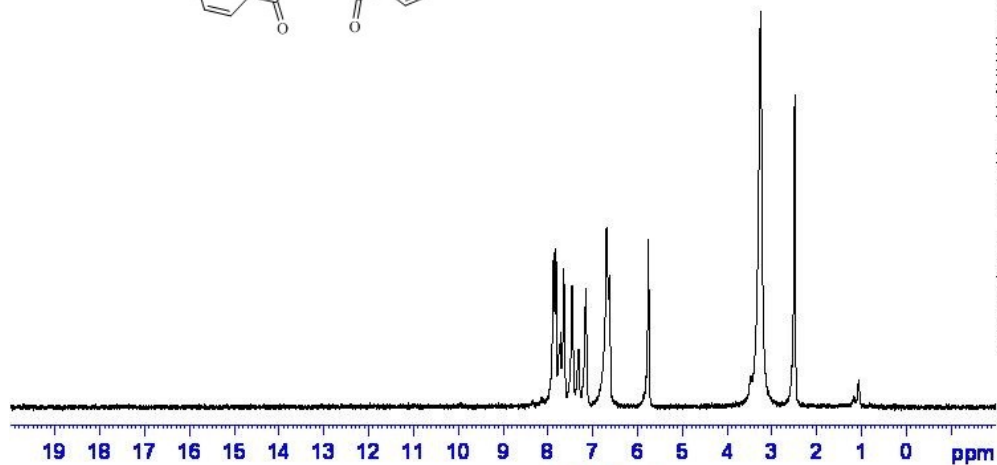
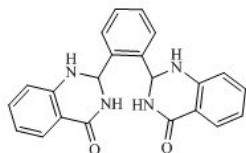


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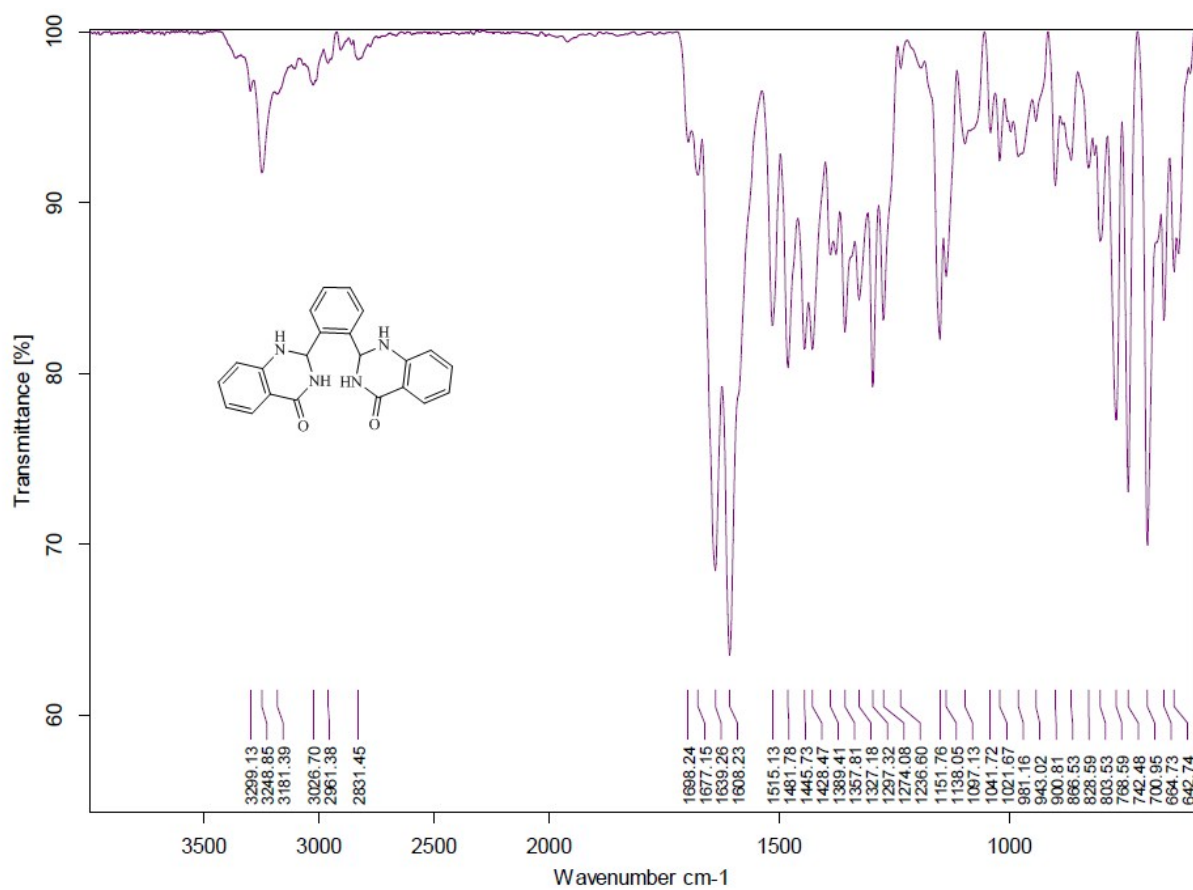
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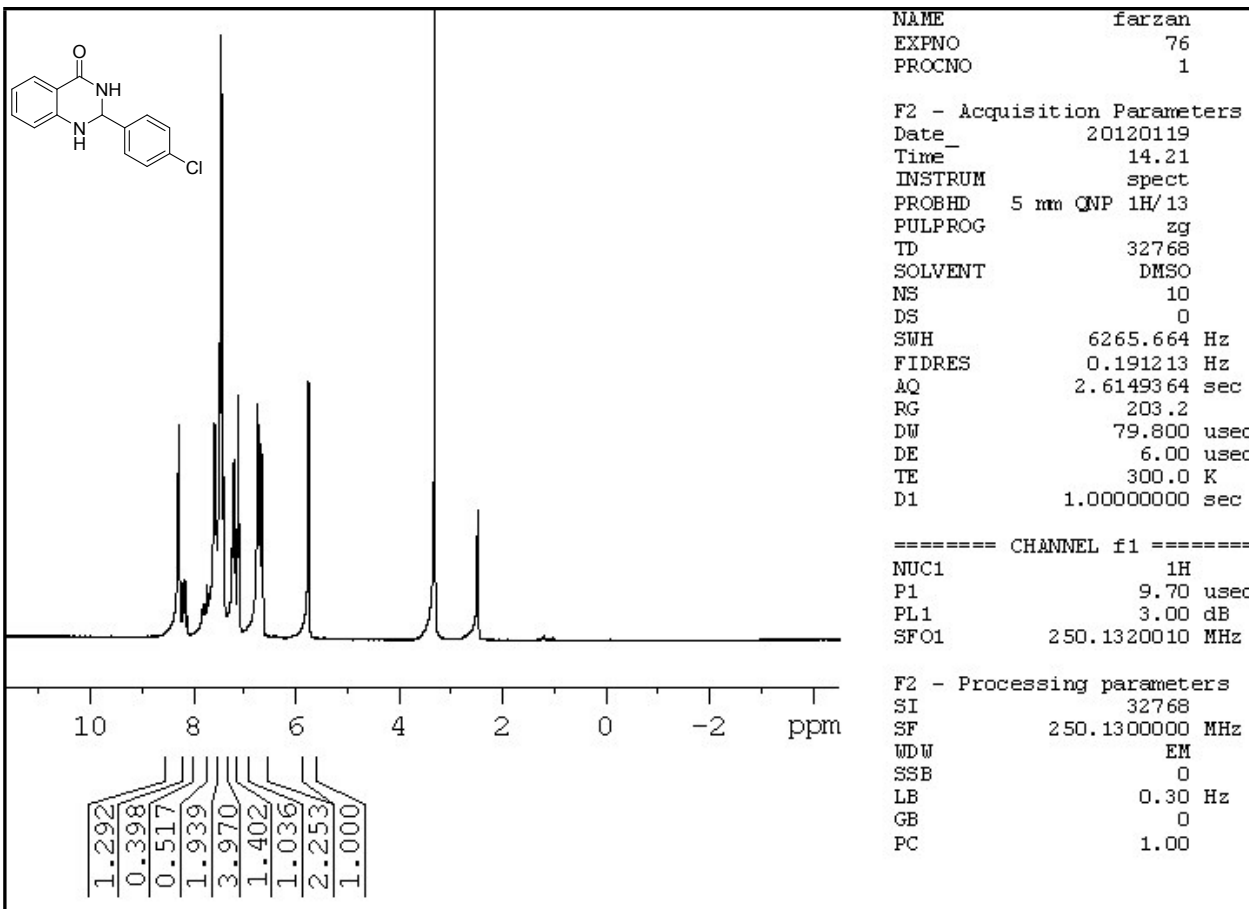
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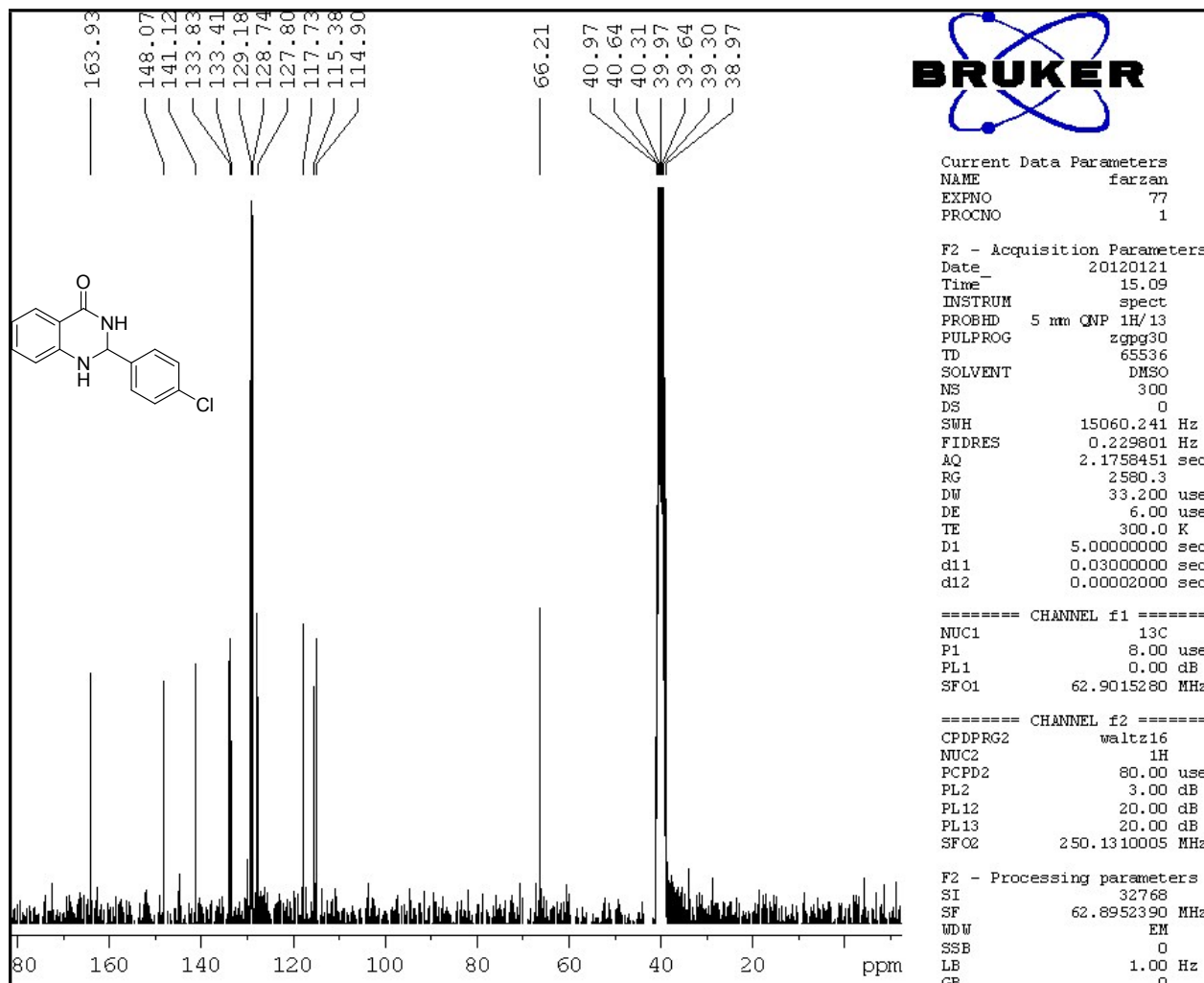


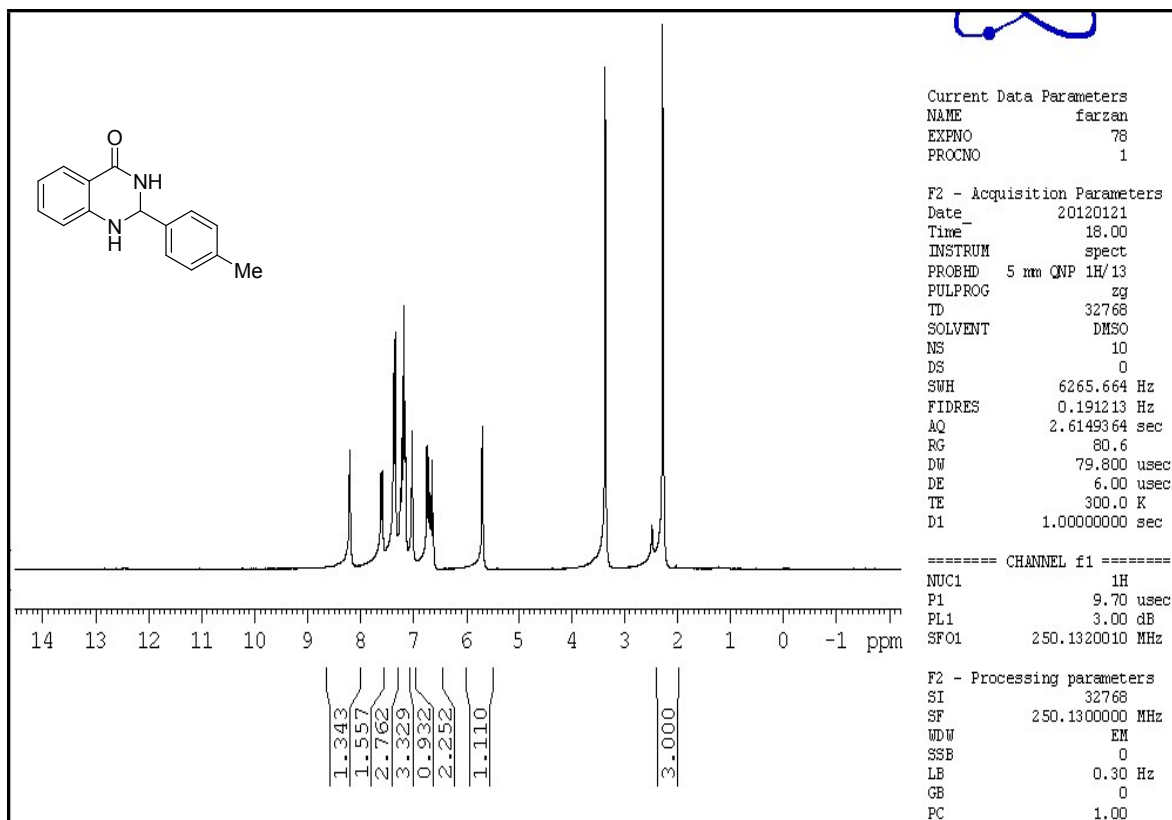
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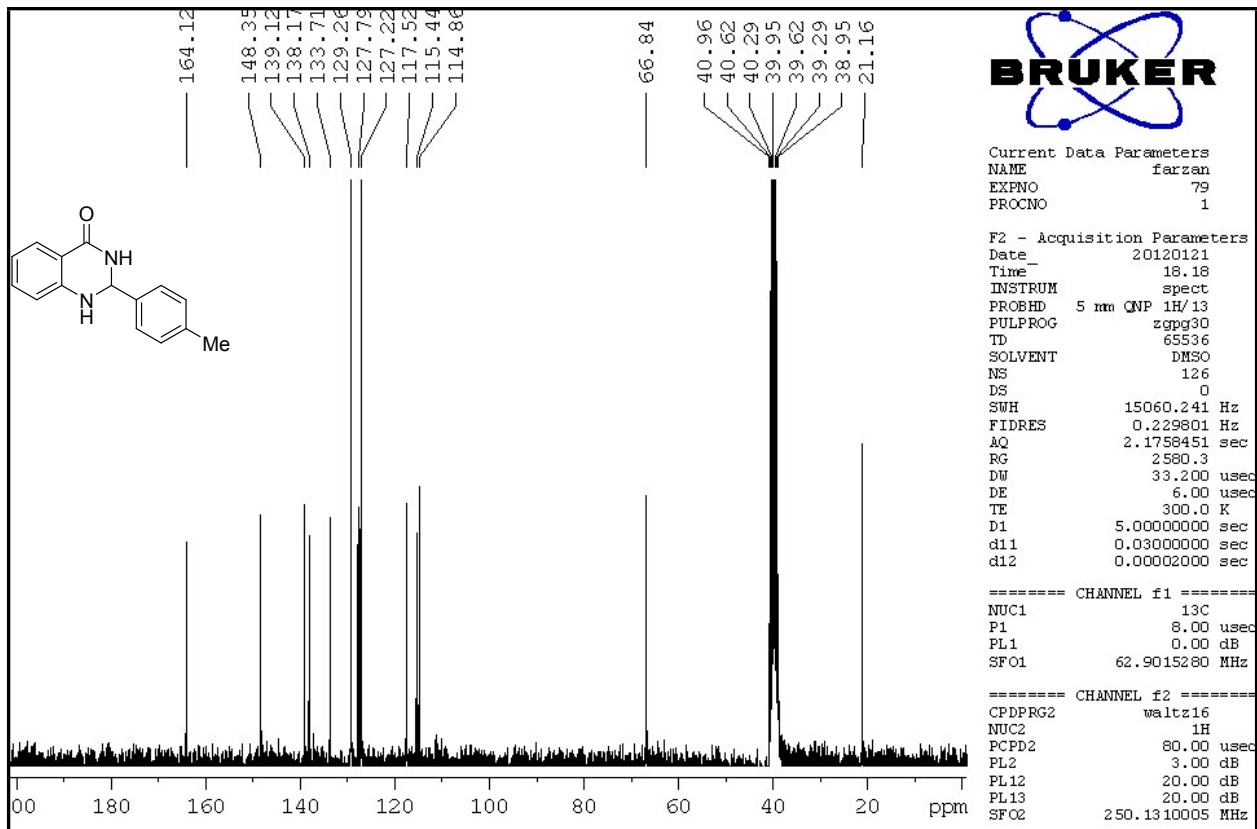


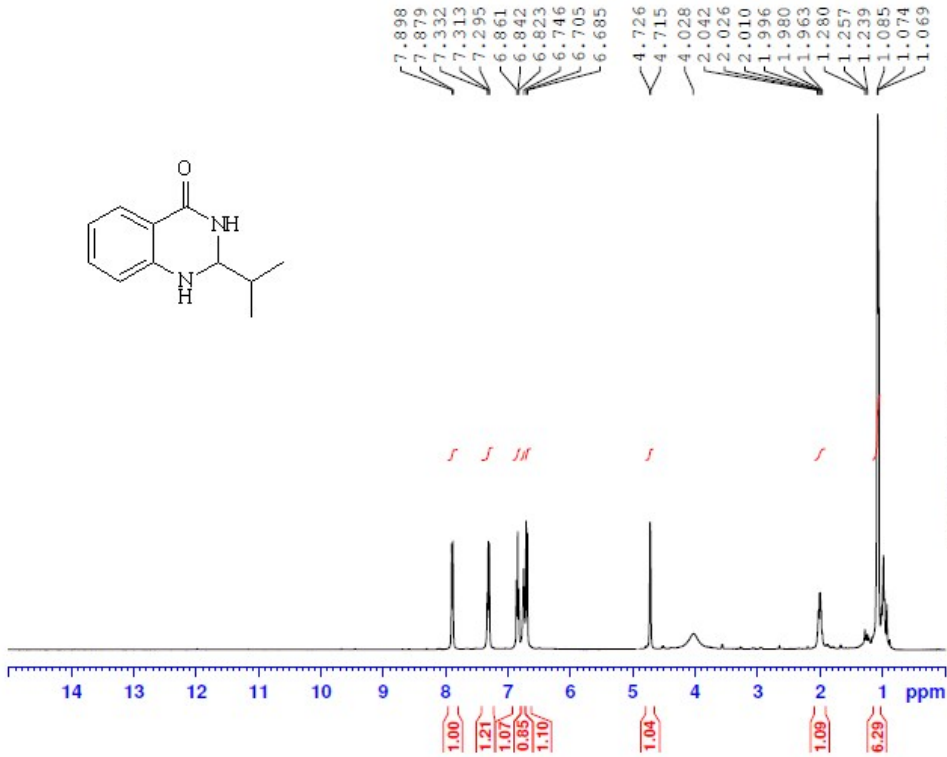
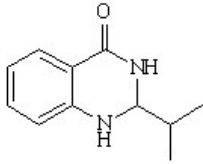
2- <sup>13</sup>C NMR









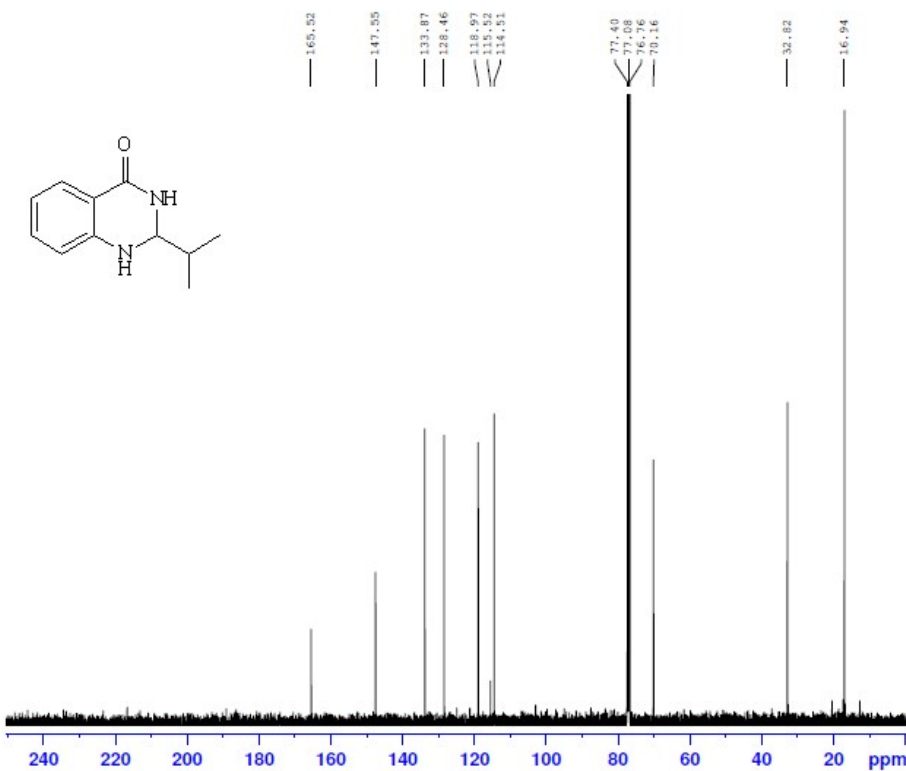


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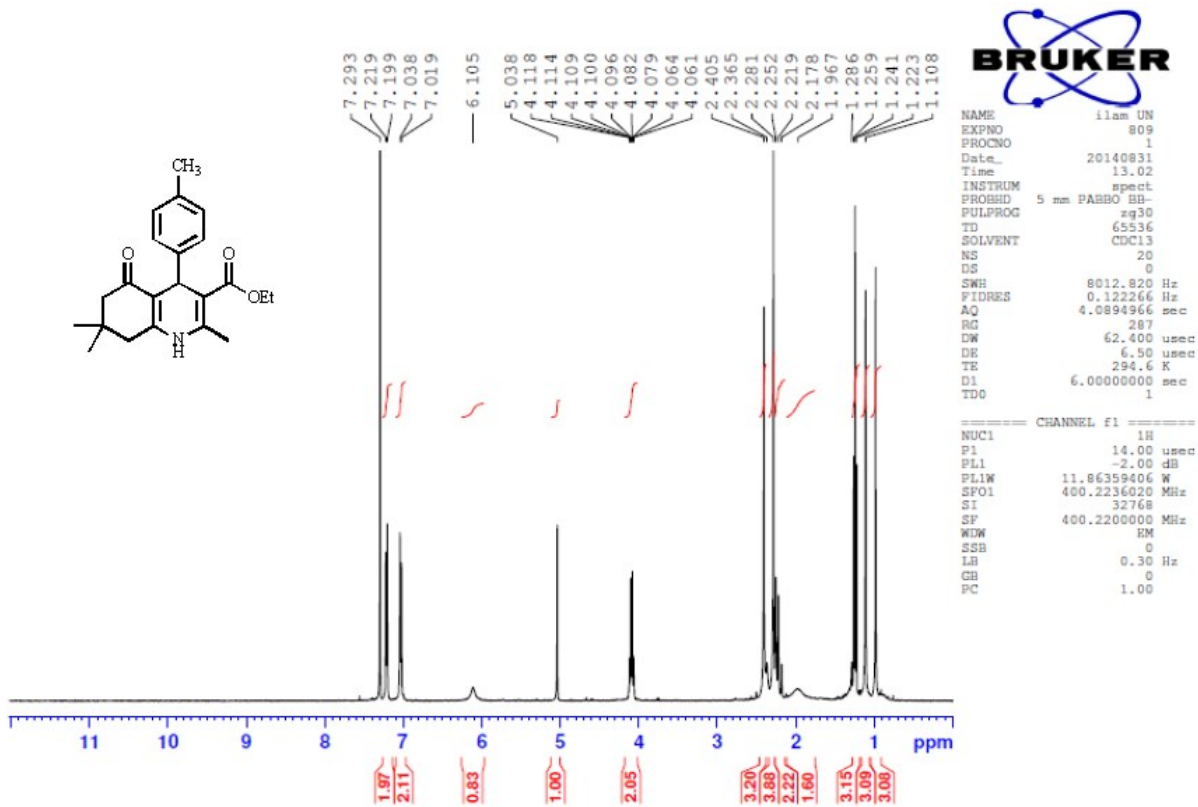
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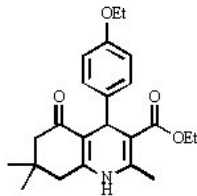
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5.803  
4.995  
4.072  
4.062  
4.055  
3.973  
3.964  
3.958  
2.387  
2.329  
2.263  
2.230  
2.194  
2.153  
1.688  
1.376  
1.371  
1.212

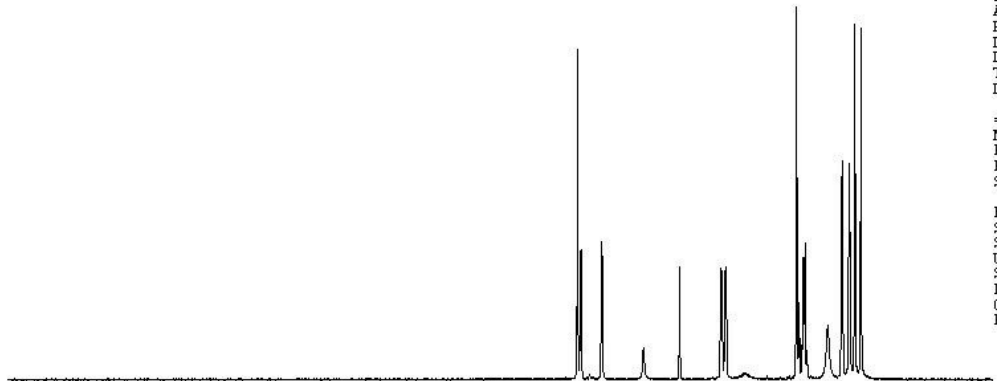


Current Data Parameters  
NAME 3H-1  
EXPNO 1188  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20140424  
Time\_ 11.09  
INSTRUM spect  
PROBHD 5 mm Multinucl  
PULPROG zg  
TD 32768  
SOLVENT CDC13  
NS 16  
DS 0  
SWH 11574.074 Hz  
FIDRES 0.353213 Hz  
AQ 1.4156276 sec  
RG 645.1  
DW 43.200 usec  
DE 6.00 usec  
TE 300.0 K  
D1 5.00000000 sec

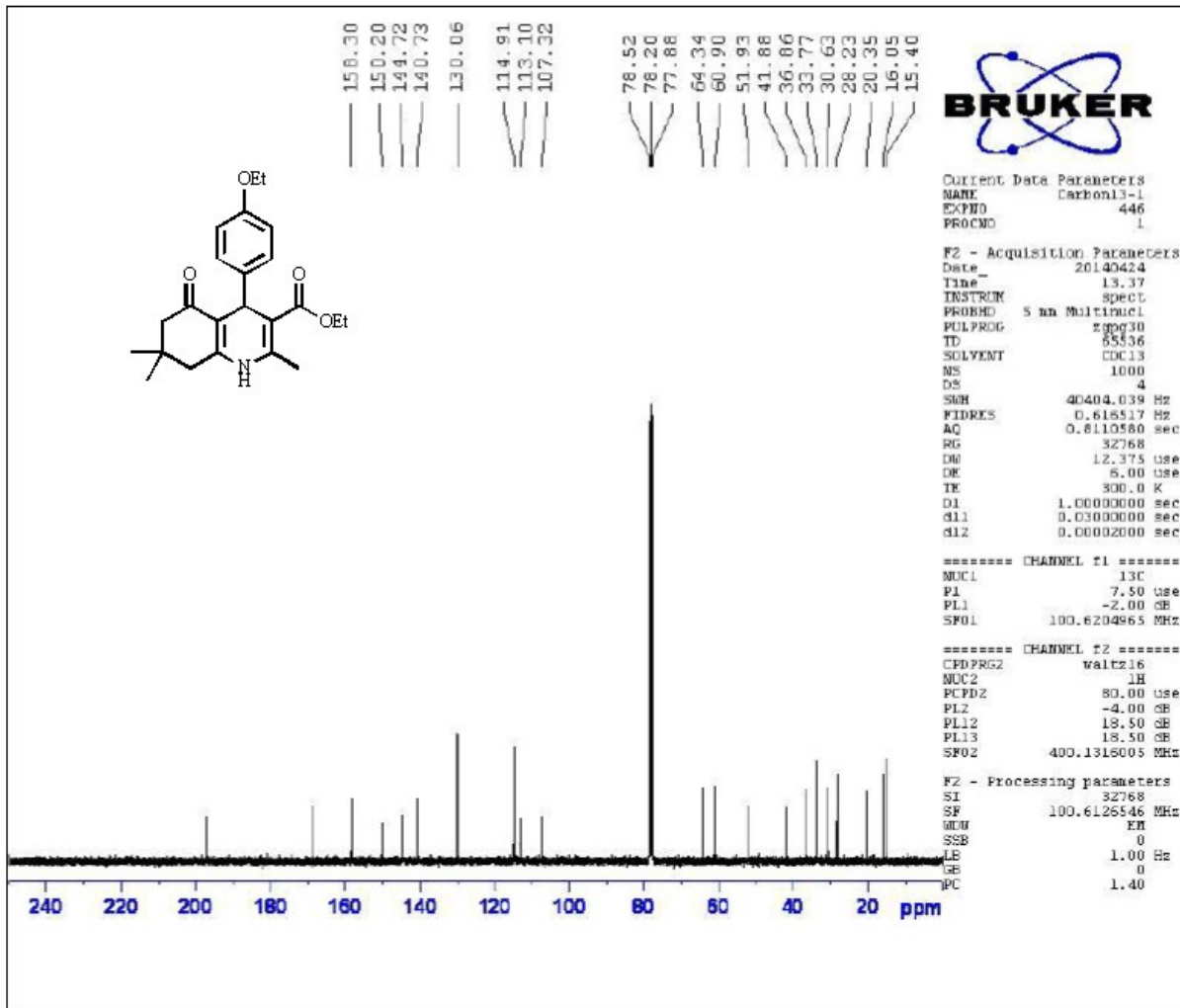
----- CHANNEL f1 -----  
NUC1 1H  
P1 9.00 usec  
PL1 -6.00 dB  
SF01 400.1324710 MHz

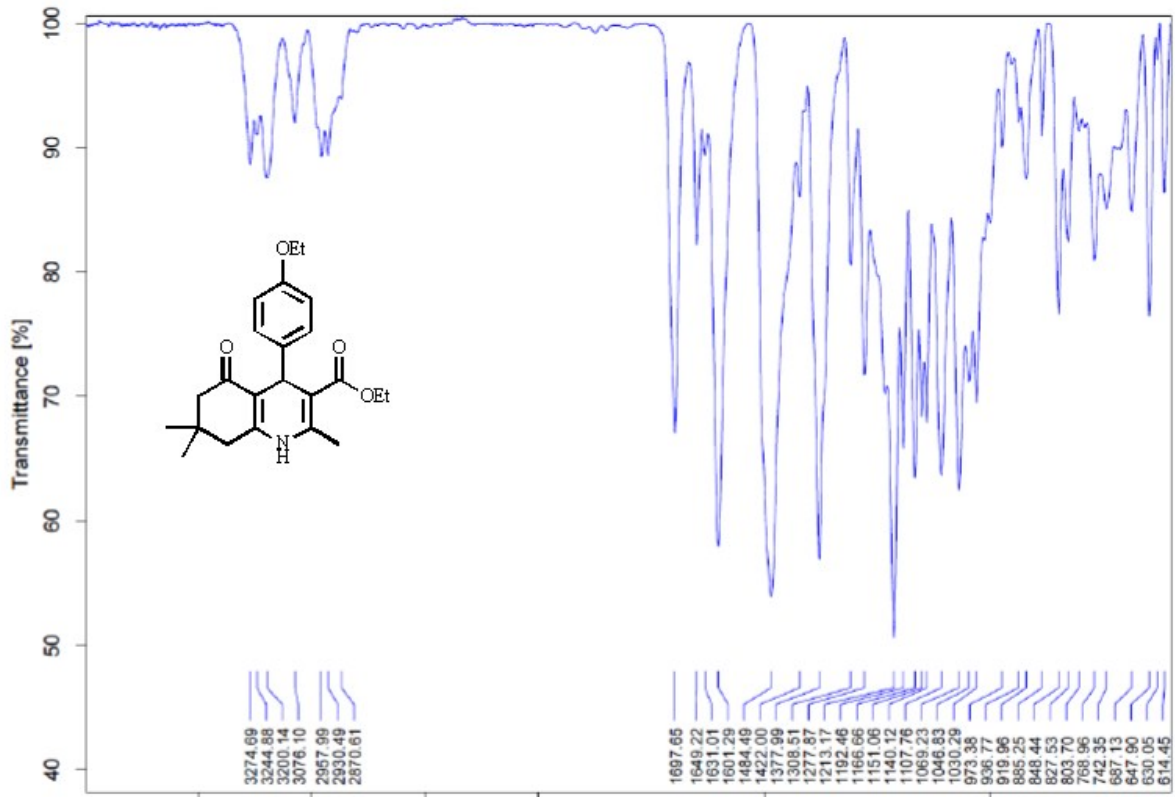
F2 - Processing parameters  
SI 32768  
SF 400.1300045 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

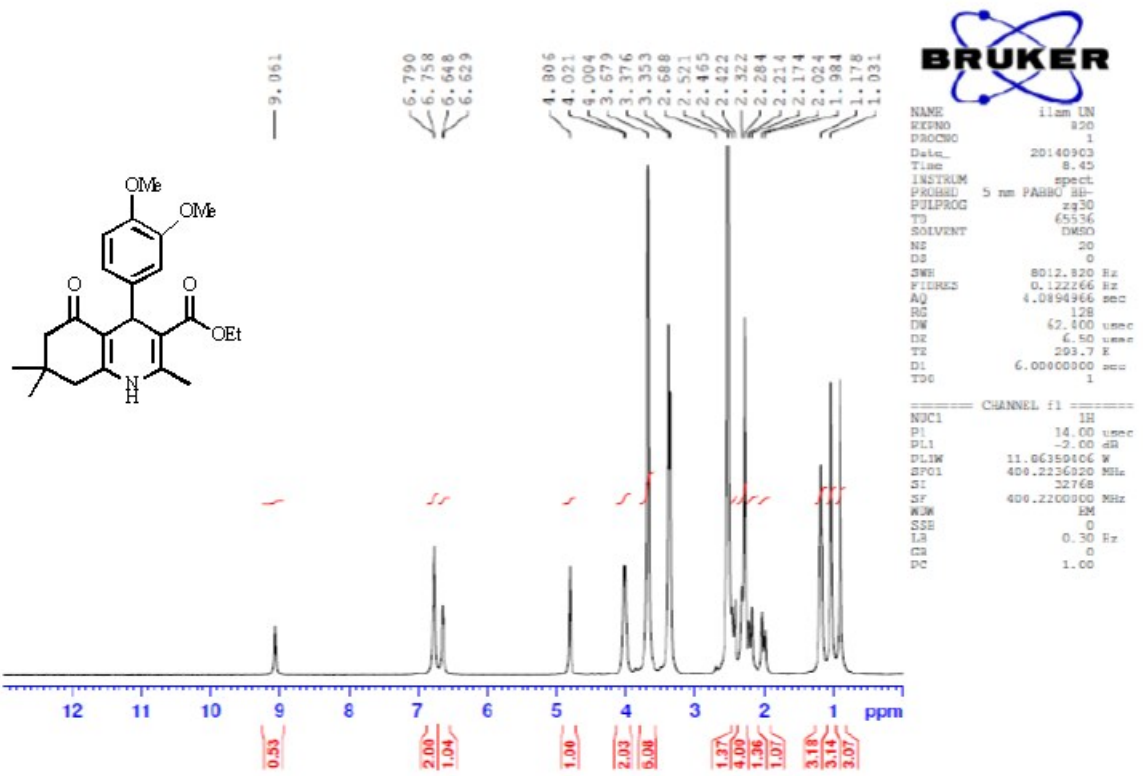


19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm

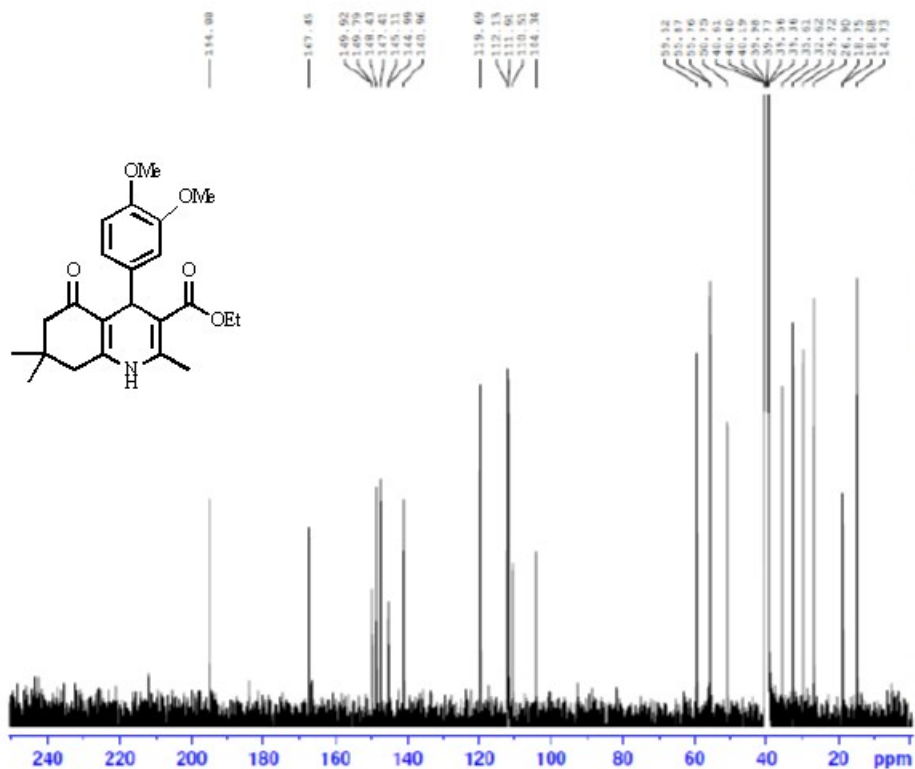
2.13 2.12 1.00 2.16 2.26 3.03 1.17 1.17 3.27 3.28 3.23 3.16











```

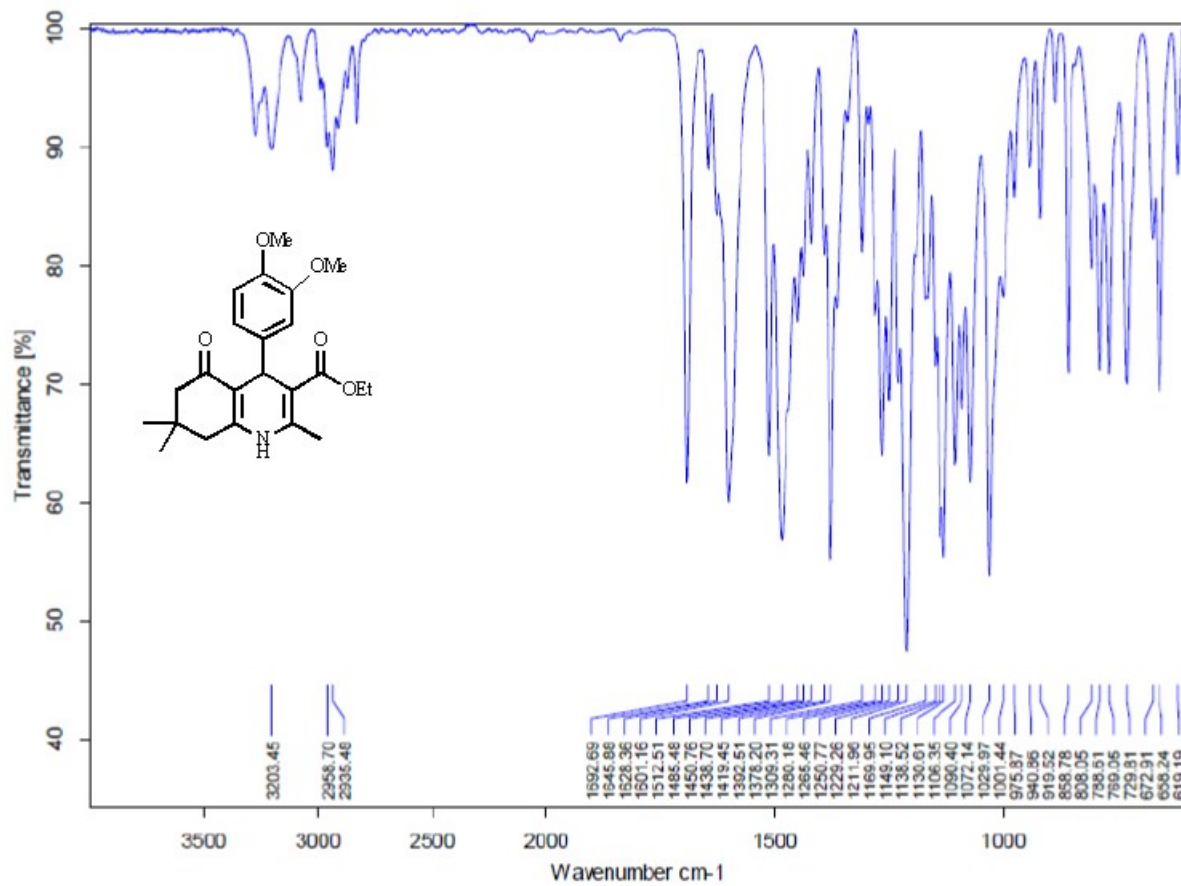
NAME      11cm UN
EXPNO     821
PROCNO    1
Date_     20100903
Time      10 50
INSTRUM   spect
PROBHD    5 mm PABBO DD-
PULPROG   zgpg30
TD         65536
SOLVENT   DMSO
NS         1000
DS         0
SWH        25252.525 Hz
FIDRES     0.385323 Hz
AQ         1.2976429 sec
RG         2050
DM         15.800 usec
DE         6.50 usec
TE         295.1 K
D1         2.0000000 sec
D11        0.0300000 sec
TD0        1
  
```

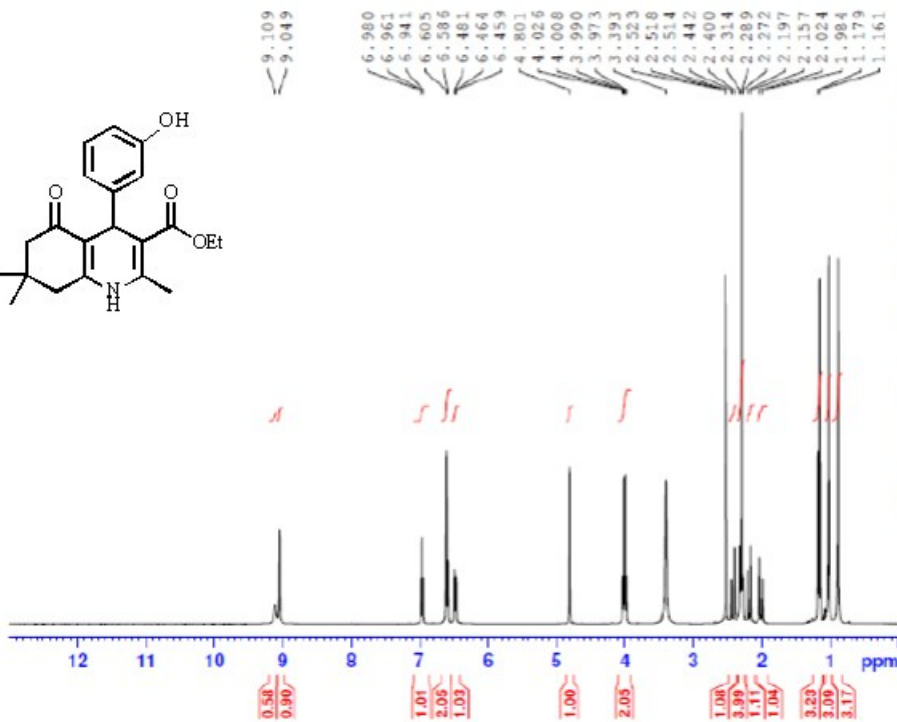
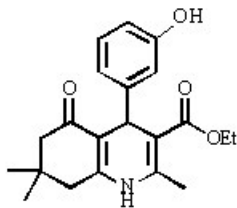
```

===== CHANNEL f1 =====
NUC1      13C
P1         9.00 usec
PL1        -0.90 dB
PL1W       42.02901890 W
SFO1      100.6261804 MHz
  
```

```

===== CHANNEL f2 =====
CFDPHSG2  waltz16
NUC2       1H
PCPD2      90.00 usec
PL2         -2.00 dB
PL12       14.16 dB
PL13       17.90 dB
PL2W       11.86350406 W
PL12W      0.58722104 W
PL13W      0.12139934 W
SFO2      400.2514009 MHz
P1         32768
SF         100.6261804 MHz
NUC3       13C
SFB        0
LB         1.00 Hz
GB         0
PC         1.40
  
```

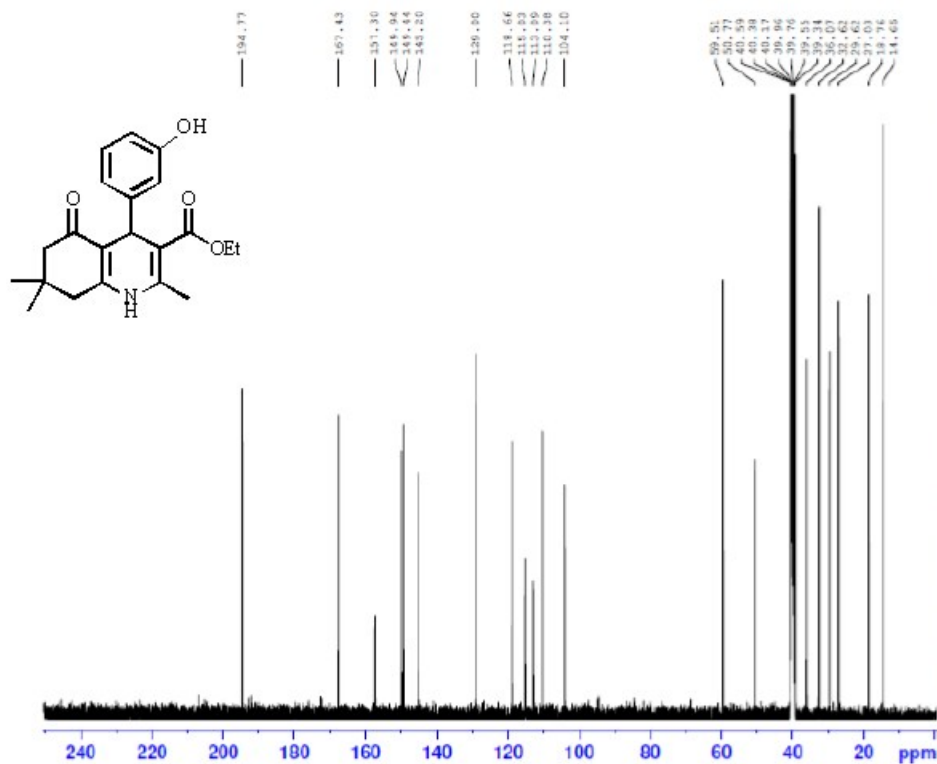




```

NAME      ilian OH
EXPNO     1
PROCNO    1
Date_     20140902
Time      16.16
INSTRUM   spect
PROBHD    5 mm PABBO BBI-
PULPROG   zg30
TD         65536
SOLVENT    DMSO
NS         20
DS         0
SWH        6012.026 Hz
FIDRES     0.122264 Hz
AQ          4.0894966 sec
RG          301
DN          0.400 usec
DE          6.56 usec
TE          294.9 K
D1          6.0000000 sec
TD0         1

===== CHANNEL f1 =====
NUC1       1H
P1         14.00 usec
PL1        -2.00 dB
PL1W       11.86359604 W
SFO1       400.2236020 MHz
SI         32768
SF         400.2200000 MHz
WDW         EM
SSB         0
LA          0.30 Hz
GB          0
PC          1.00
  
```



```

NAME      1.0m UN
EXPNO    816
PROCNO    1
Date_    20140902
Time     16.15
INSTRUM   spect
PROBHD    5 mm FARBIO BB-
PULPROG   zgpg30
TD        65536
SOLVENT   DMSO
NS        500
DS        0
SWH       25252.525 Hz
FIDRES    0.385323 Hz
AQ        1.2376629 sec
RG        2050
TW        15.800 usec
DE        6.50 usec
TR        295.1 K
D1        2.00000000 sec
D11       0.03900000 sec
TD0       1

===== CHANNEL f1 =====
NUC1      13C
P1        9.00 usec
PL1       -0.90 dB
PL1W     42.02401895 W
SFO1     100.64799784 MHz

===== CHANNEL f2 =====
CPDPRG2   waltz16
NUC2      1H
PCPD2     90.00 usec
PL2       -2.00 dB
PL12     14.16 dB
PL13     17.50 dB
PL2W     11.86139406 W
PL12W    0.28722104 W
PL13W    0.12139934 W
SFO2     400.2216009 MHz
SI        32768
SF       100.6353990 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40

```

