Discovery of novel coumarin-Schiff base hybrids as potential acetylcholinesterase inhibitors: Design, synthesis, enzyme inhibition, and computational studies

Aso Hameed Hasan [1,2], Faruq Azeez Abdulrahman [3], Ahmad J. Obaidullah [4], Hadil Faris Alotaibi [5], Mohammed M. Alanazi [4], Mahmoud A. Noamaan [6], Sankaranarayanan Murugesan [7], Syazwani Itri Amran [8], Ajmal R. Bhat [9] and Joazaizulfazli Jamalis [1,*]

[1]Department of Chemistry, Faculty of Science, University Teknologi Malaysia, Johor Bahru 81310, Johor, Malaysia; aso.hameed@garmian.edu.krd
[2]Department of Chemistry, College of Science, University of Garmian, Kalar 46021, Kurdistan Region, Iraq
[3]Department of Pharmacy, Kalar Private Technical Institute, Kalar 46021, Kurdistan Region, Iraq; farouqpharma85@gmail.com
[4]Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh 11451, Saudi Arabia; aobaidullah@ksu.edu.sa (A.J.O.); mmalanazi@ksu.edu.sa (M.M.A.)
[5]Department of Pharmaceutical Sciences, College of Pharmacy, Princess Nourah bint AbdulRahman University, Riyadh 11671, Saudi Arabia; hfalotaibi@pnu.edu.sa
[6]Mathematics Department, Faculty of Science, Cairo University, Giza 12613, Egypt; noamaan@sci.cu.edu.eg
[7]Medicinal Chemistry Research Laboratory, Birla Institute of Technology & Science Pilani (BITS Pilani), Pilani Campus, Pilani 333031, Rajasthan, India; murugesan@pilani.bits-pilani.ac.in
[8]Department of Biosciences, Faculty of Science, Universiti Teknologi Malaysia, Johor Bahru 81310, Johor, Malaysia; syazwaniitri@utm.my
[9]Department of Chemistry, R.T.M. Nagpur University, 440033, Nagpur, India; bhatajmal@gmail.com

*Corresponding author E-mail: joazaizulfazli@utm.my (Joazaizulfazli Jamalis).

EXPERIMENTAL

In vitro inhibition study on AChE

The assay for AChE inhibitory activity was done based on a modified protocol [1-5]. Acetylcholinesterase (Type VI-S, from Electrophorus electricus), 5,5′-dithiobis-2-nitrobenzoic acid (Ellman's reagent, DTNB) and acetylthiocholine chloride (ATCI) were purchased from Sigma Aldrich. Enzyme solutions were prepared to give 0.28 units/mL aliquots. Stock solutions were prepared by dissolving 1 mg of tested compounds in 1 mL of DMSO and diluted to a final concentration of 1000, 800, 600, 400, 200, 100, and 50 µg/mL. The assay buffer solution A (pH = 8.0) was prepared by taking 93.2 mL of solution (6 g of sodium dihydrogen phosphate was dissolved in 500 mL of deionized water) and mixed with 6.8 mL of solution (7 g of sodium hydrogen phosphate was dissolved in 500 mL of deionized water) and adjusted. 57.7 mL of sodium dihydrogen phosphate and 42.3 mL of sodium hydrogen phosphate were mixed and adjusted to prepare the buffer B (pH = 7.0). Furthermore, fresh solutions of 0.01 M DTNB (0.396 g of DTNB and 15 mg $NaHCO_3$ were dissolved in 100 mL of the buffer B) in a dark place, and 0.075 M ATCI (0.2048 g of ATCI was dissolved in 10 mL of deionized water), were prepared. In 96-well plates, 20 µL of the test compounds, 10 µL of DTNB, 15 µL of the enzyme (AChE) and 140 µL of the buffer solution A, were added in dark conditions and incubated for 15 min, followed by the addition of ATCI (10 µL) and incubated again for the same period. The activity was measured by reading the absorbance of the solution at 412 nm. Blanks containing all the components except the enzyme were carried out. IC_{50} values were calculated as the concentration of a compound that produces 50% enzyme activity inhibition using the GraphPad Prism 8 programme package. Results are expressed as the mean ± SD of at least three different experiments performed in triplicate.

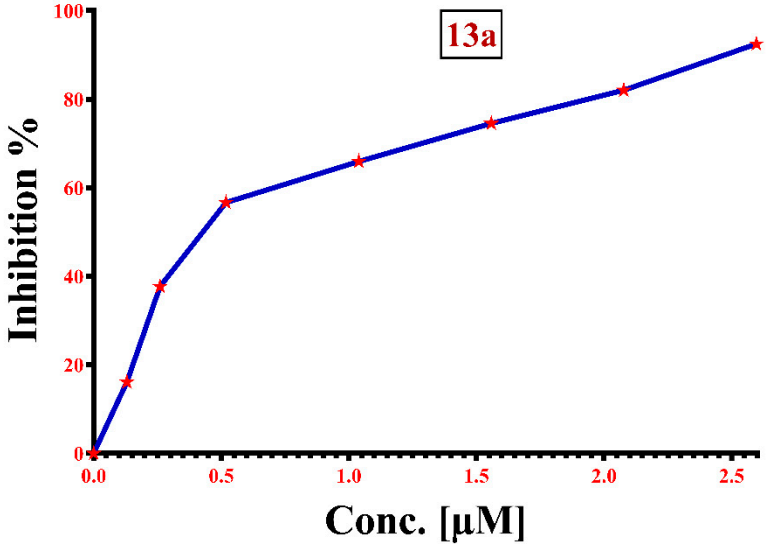
IC_{50} Calculations

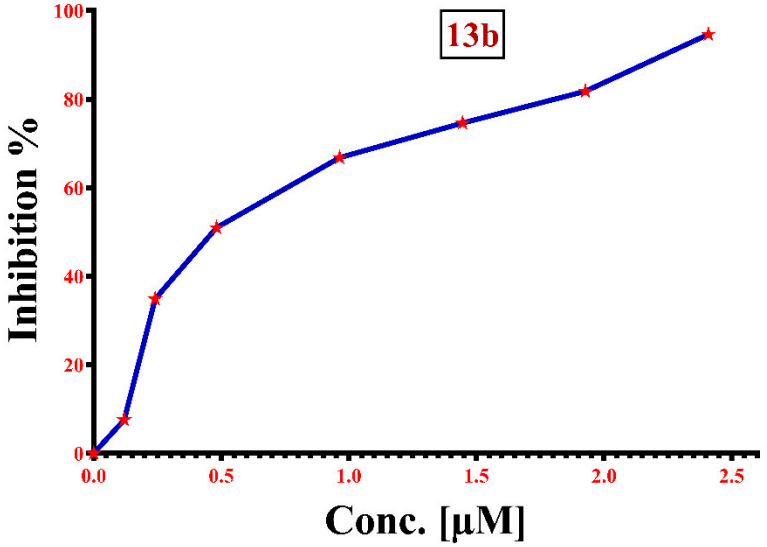
Percentage inhibition was calculated by this formula:

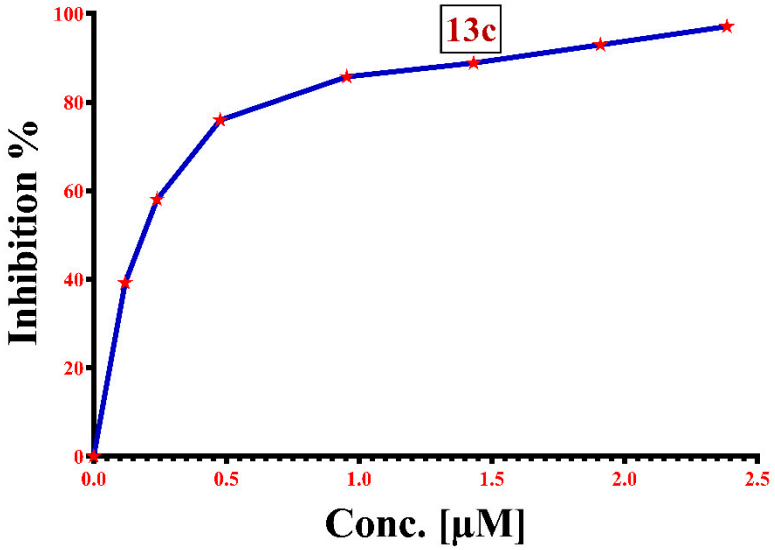
$$\%\ (\text{Inhibition}) = \frac{B - A}{B} X\ 100$$

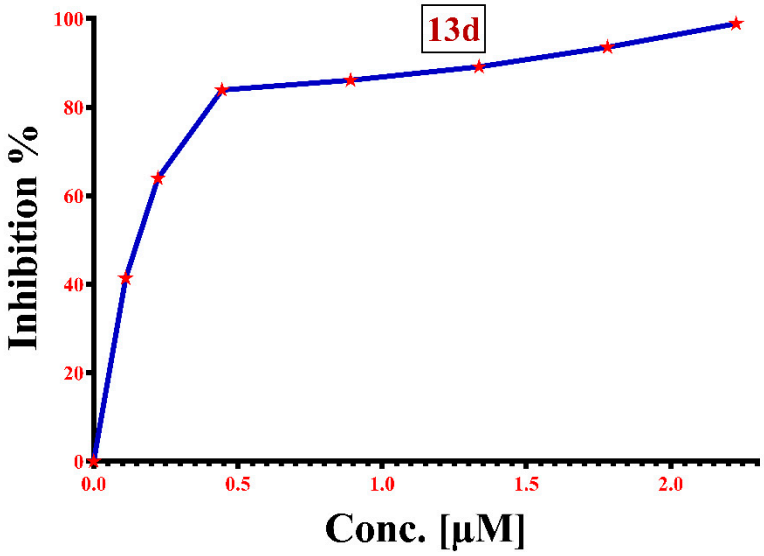
- A= absorbance of the enzyme with the test sample;
- B = absorbance of the enzyme without test sample.
- Each experiment was repeated thrice.

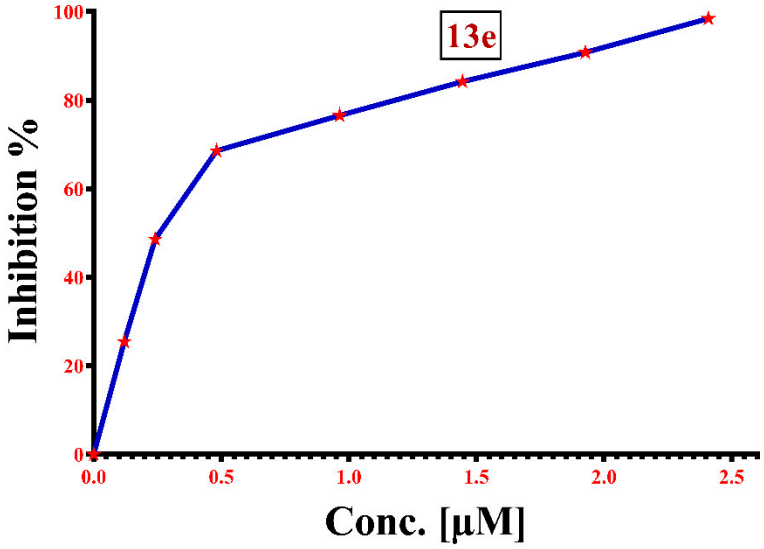
- Concentrations were converted from µg/mL to µM.
- IC_{50} value was calculated by GraphPad Prism.
- Galantamine was used as a reference compound.

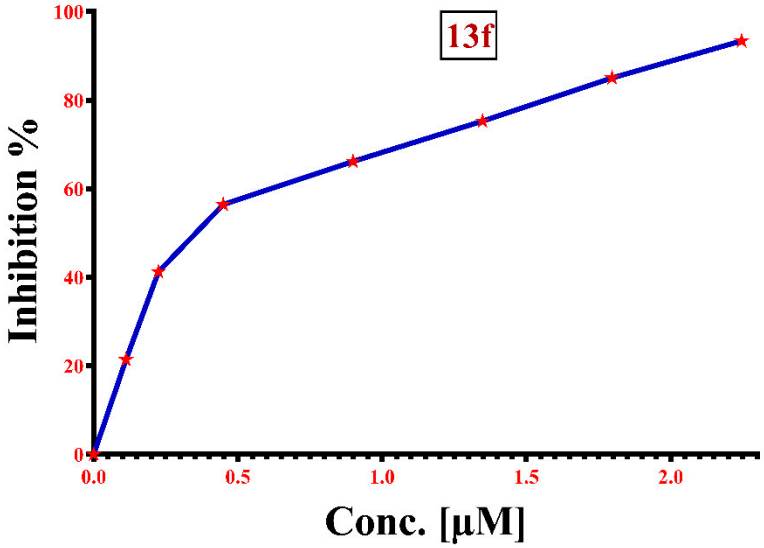


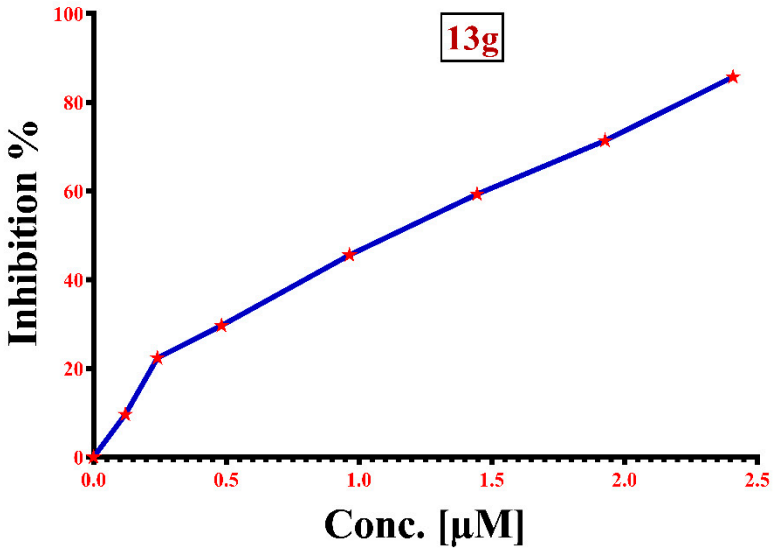


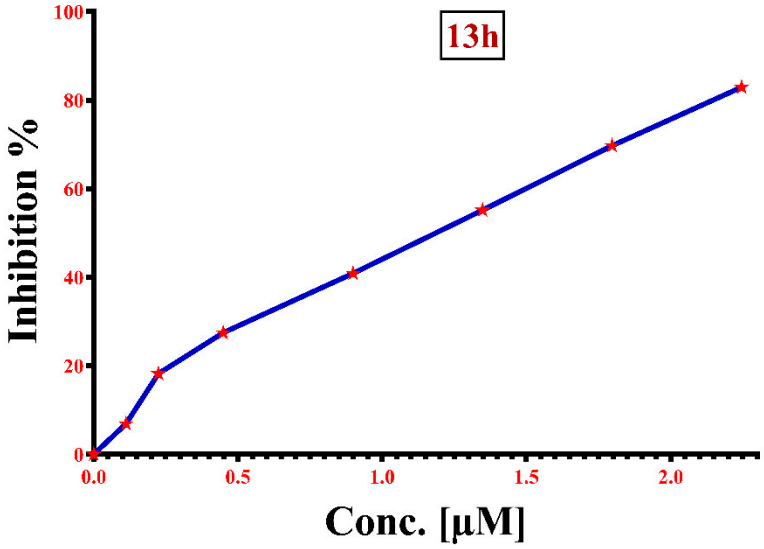


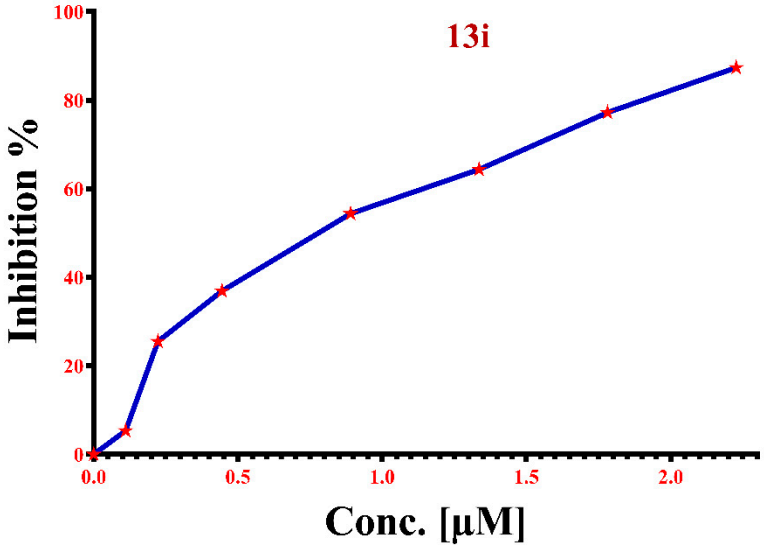

13d
Inhibition %
100
80
60
40
20
0
0.0
0.5
1.0
1.5
2.0
Conc. [µM]

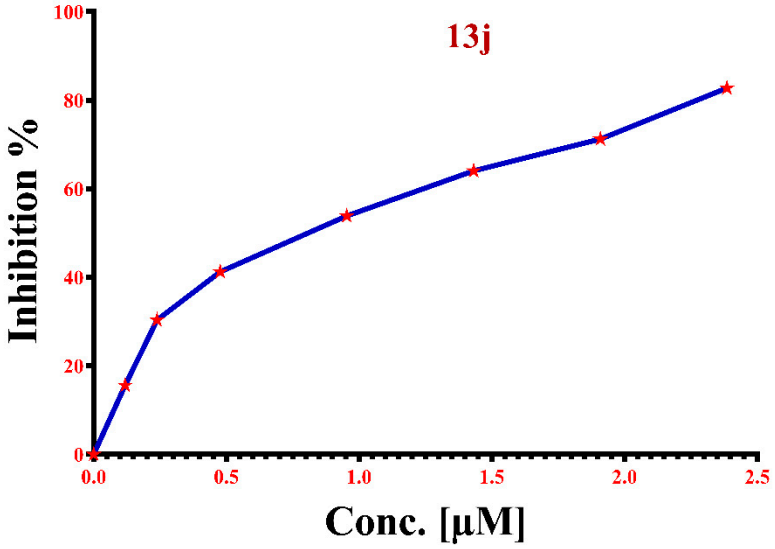

13e
Inhibition %
100
80
60
40
20
0
0.0
0.5
1.0
1.5
2.0
2.5
Conc. [µM]

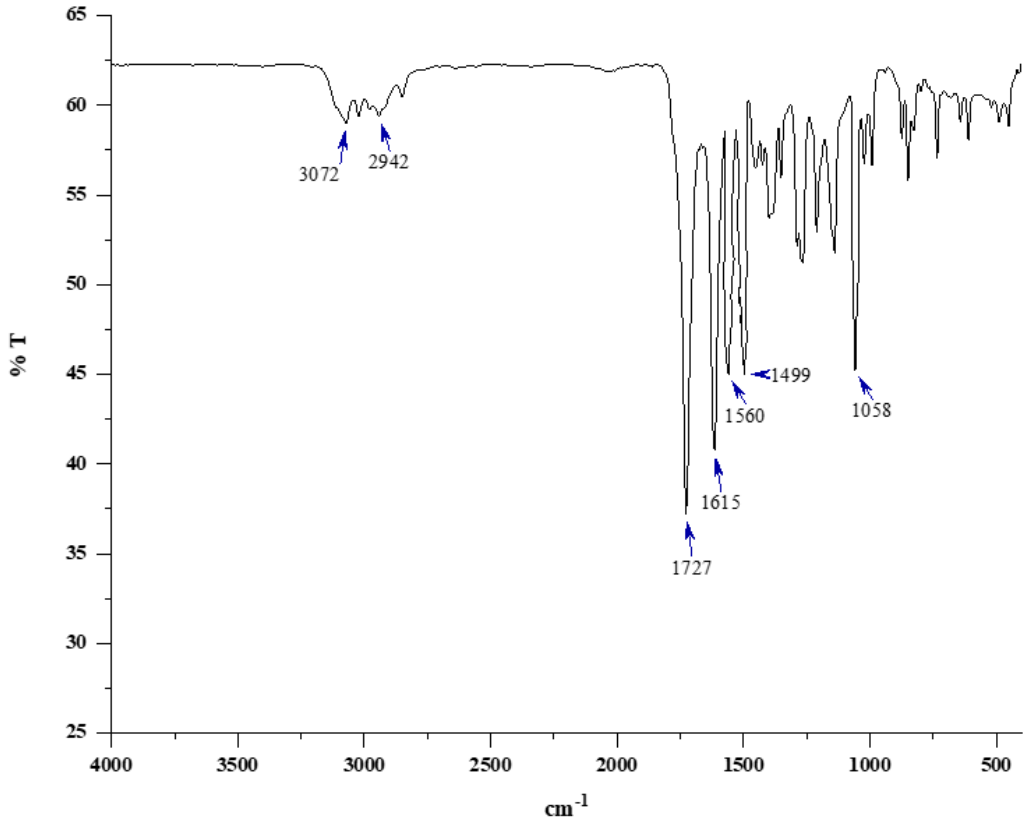

13f
Inhibition %
100
80
60
40
20
0
0.0
0.5
1.0
1.5
2.0
Conc. [µM]


13g
Inhibition %
Conc. [µM]
0
20
40
60
80
100
0.0
0.5
1.0
1.5
2.0
2.5

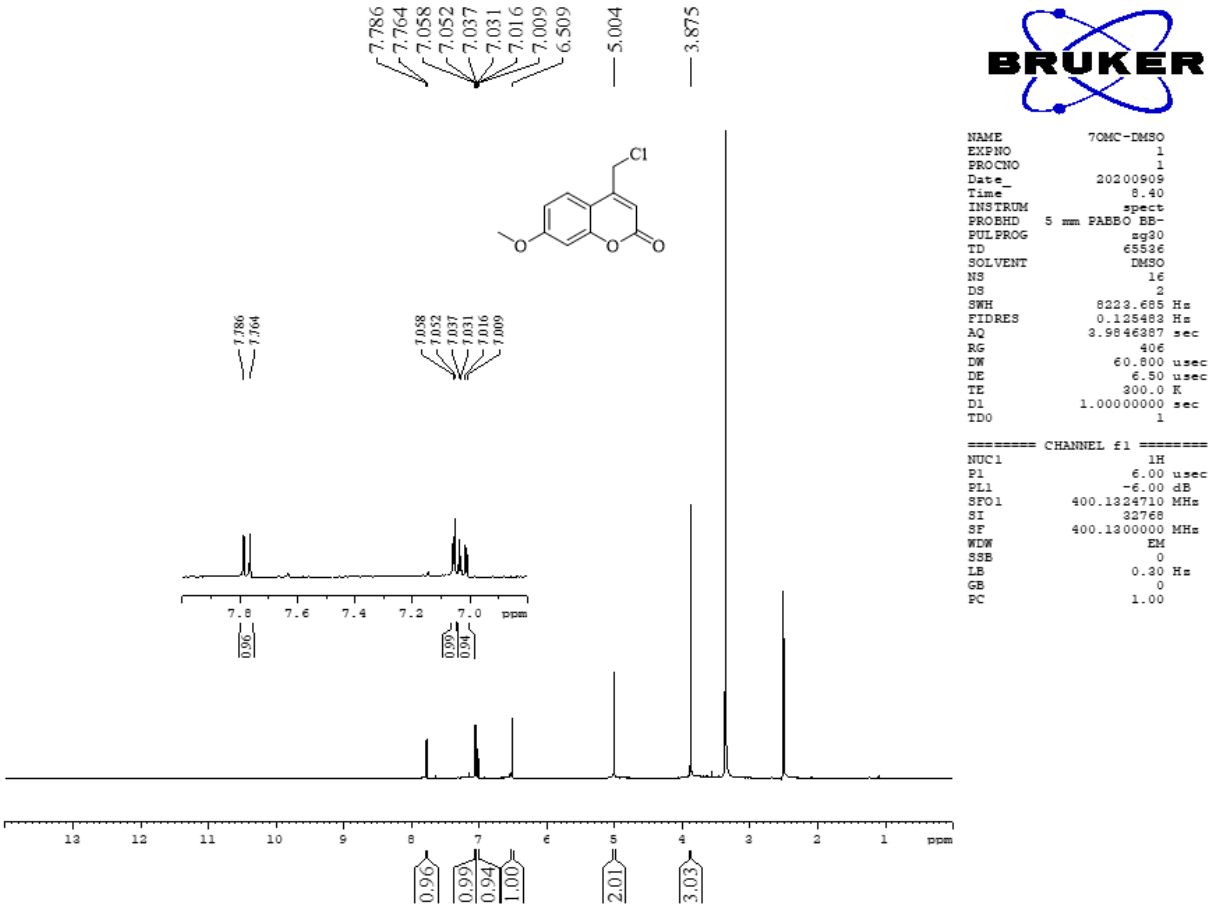

13h
Inhibition %
Conc. [µM]
0
20
40
60
80
100
0.0
0.5
1.0
1.5
2.0


13i
Inhibition %
Conc. [µM]
0
20
40
60
80
100
0.0
0.5
1.0
1.5
2.0

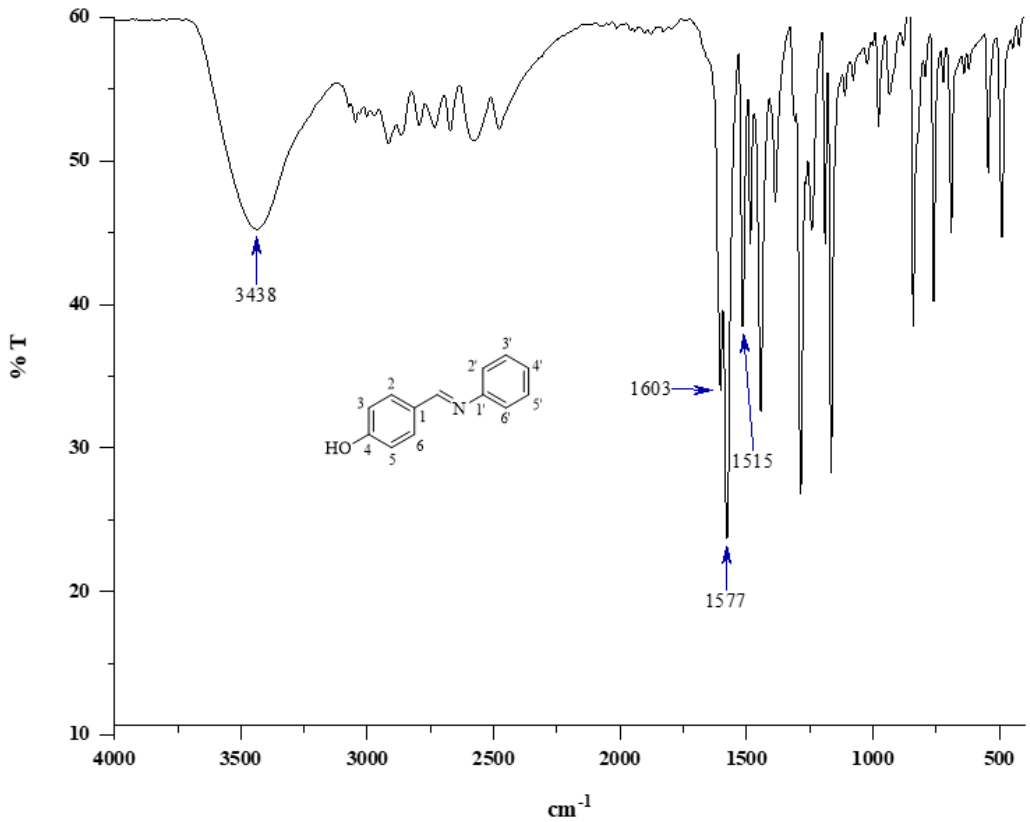




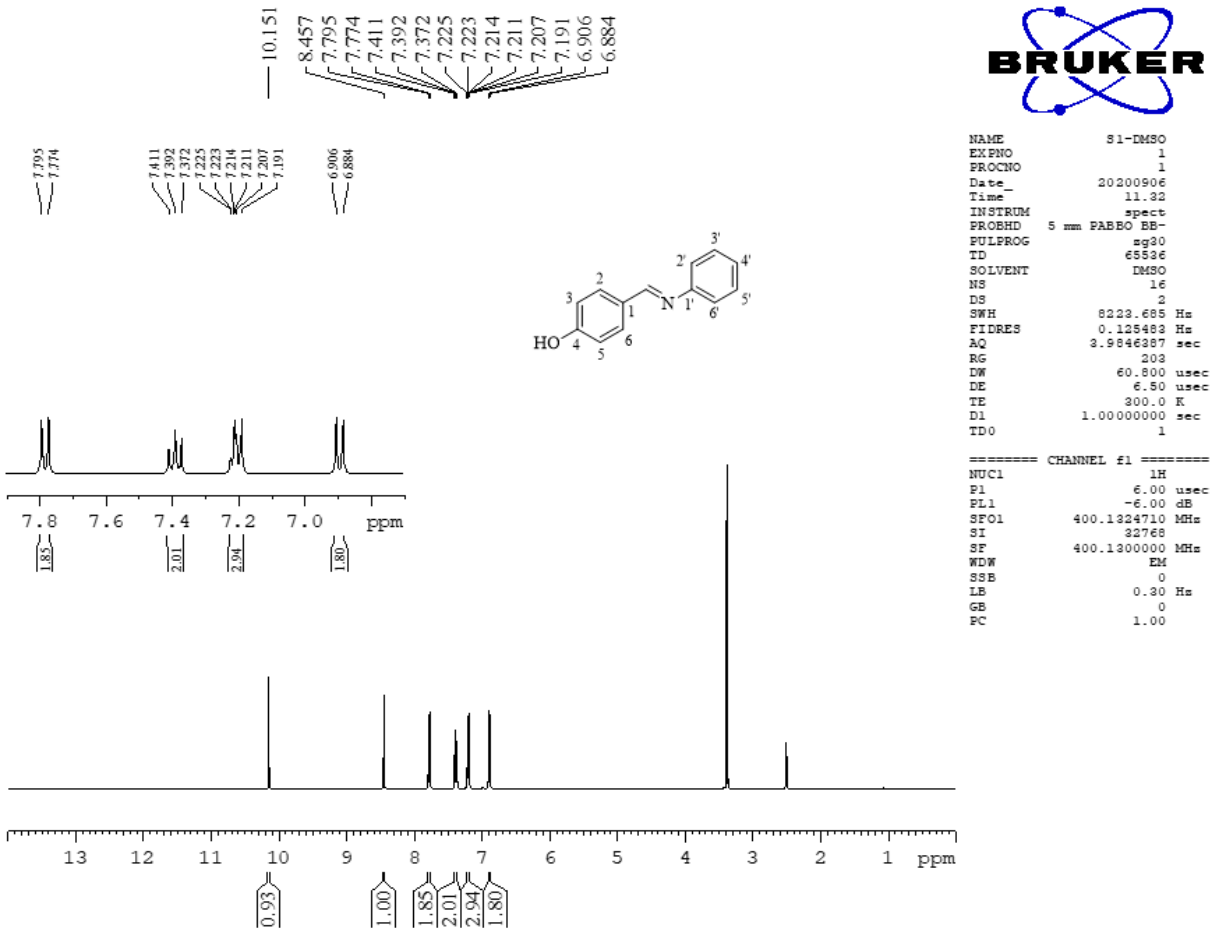
IR spectrum of 4-(chloromethyl)-7-methoxy-2*H*-chromen-2-one **(9)**



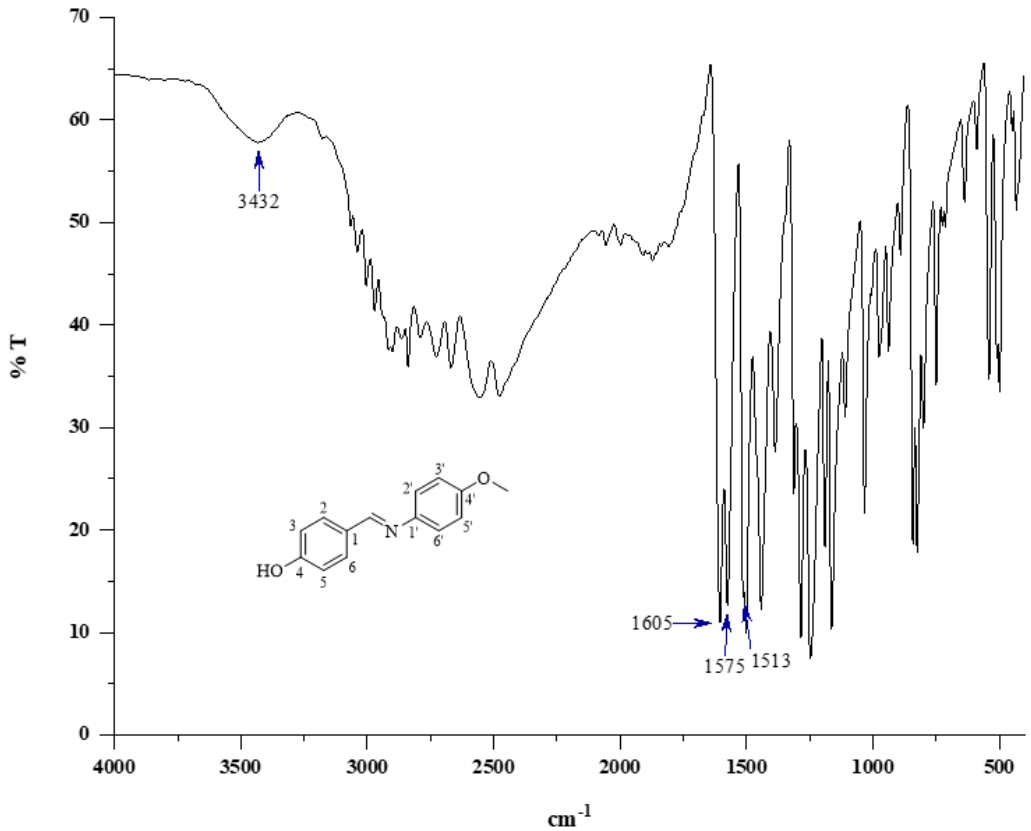
^{1}H NMR spectrum of 4-(chloromethyl)-7-methoxy-2*H*-chromen-2-one **(9)**



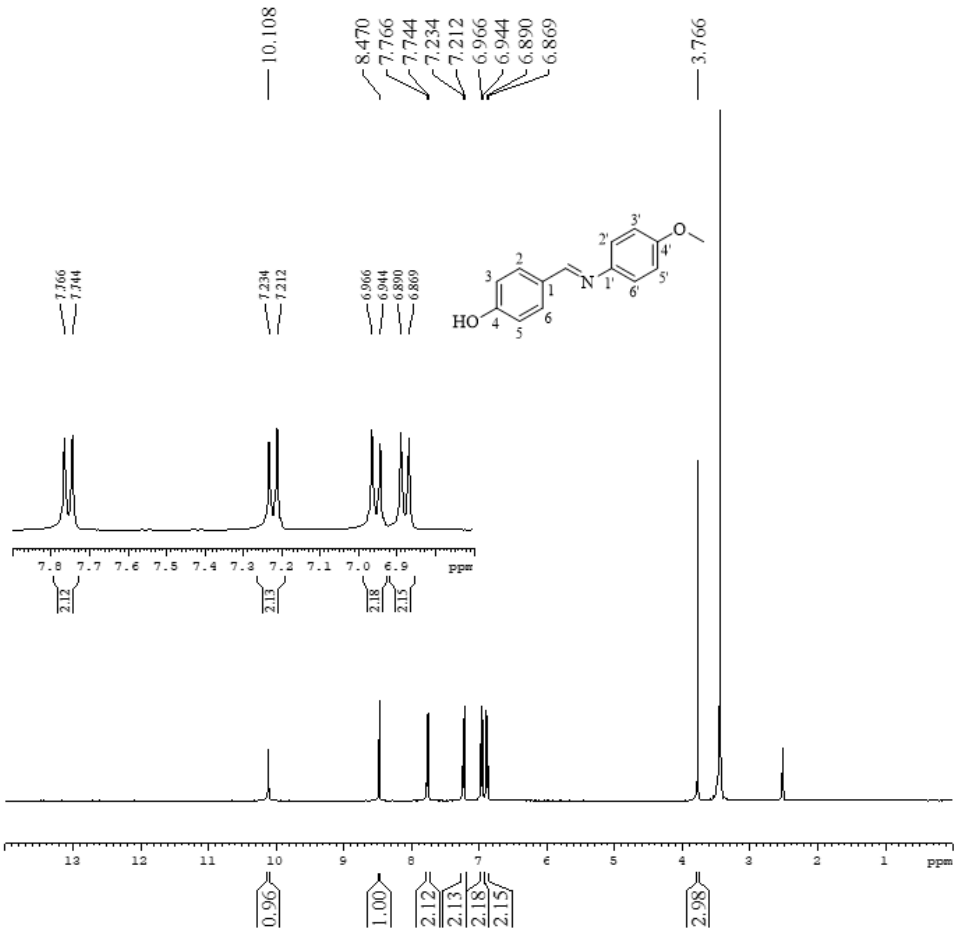
IR spectrum of (*E*)-4-((phenylimino)methyl)phenol **(12a)**



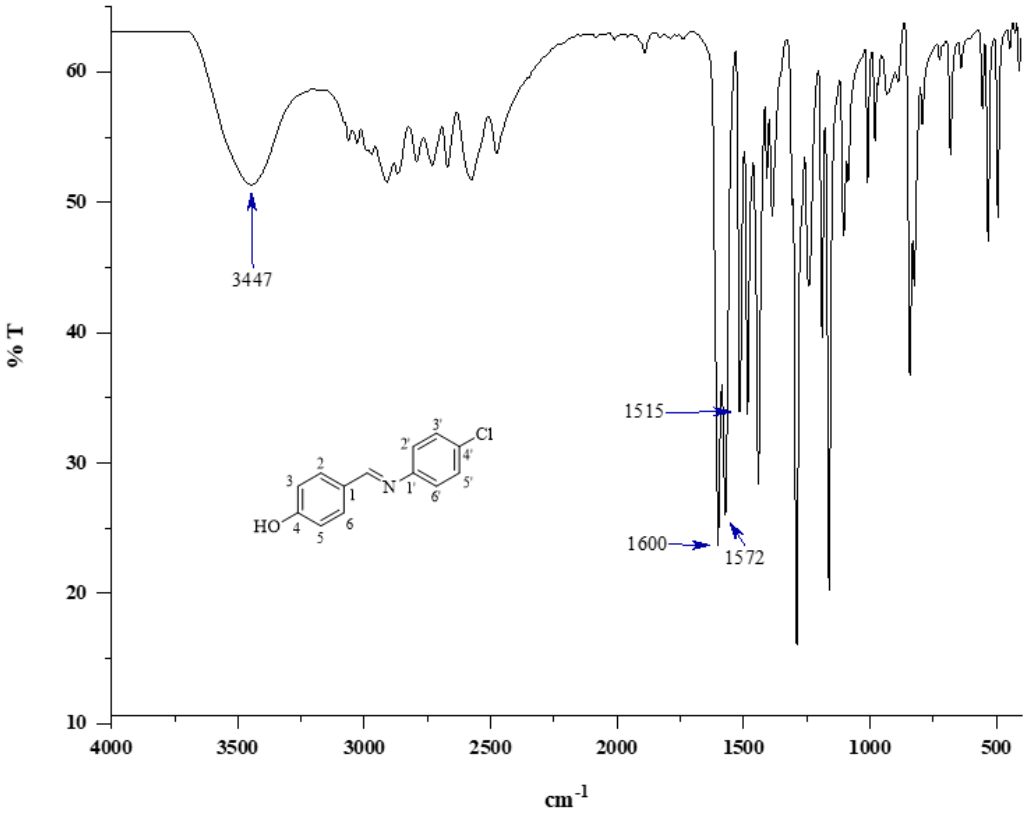
^{1}H NMR spectrum of 4-((phenylimino)methyl)phenol **(12a)**



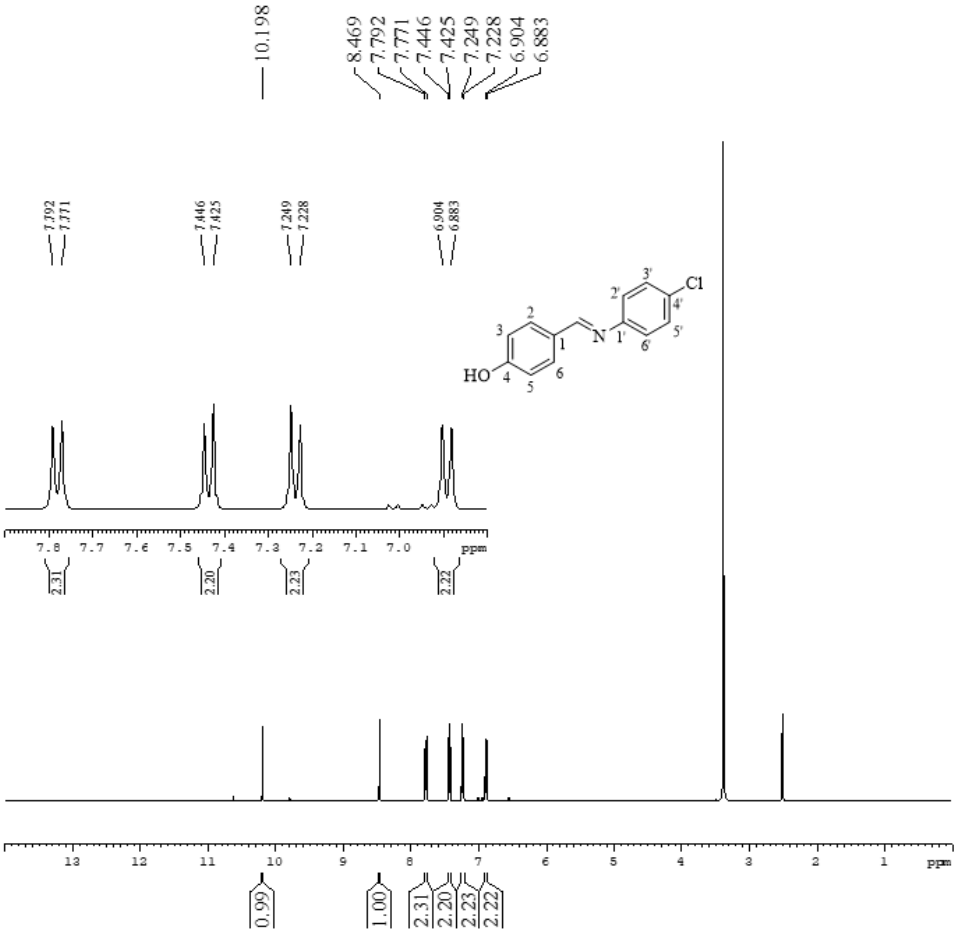
IR spectrum of (*E*)-4-(((4-methoxyphenyl)imino)methyl)phenol **(12b)**

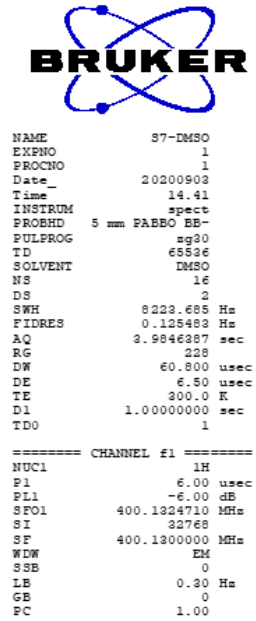


^{1}H NMR spectrum of (*E*)-4-(((4-methoxyphenyl)imino)methyl)phenol **(12b)**

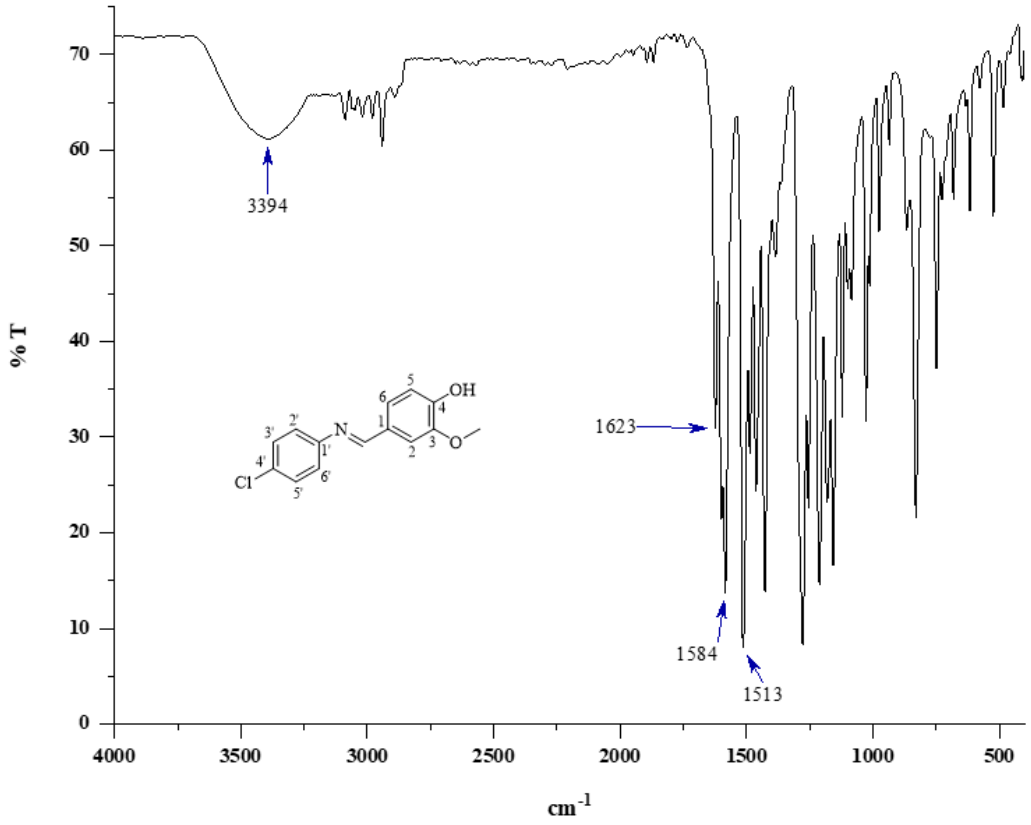


IR spectrum of (*E*)-4-(((4-chlorophenyl)imino)methyl)phenol **(12c)**

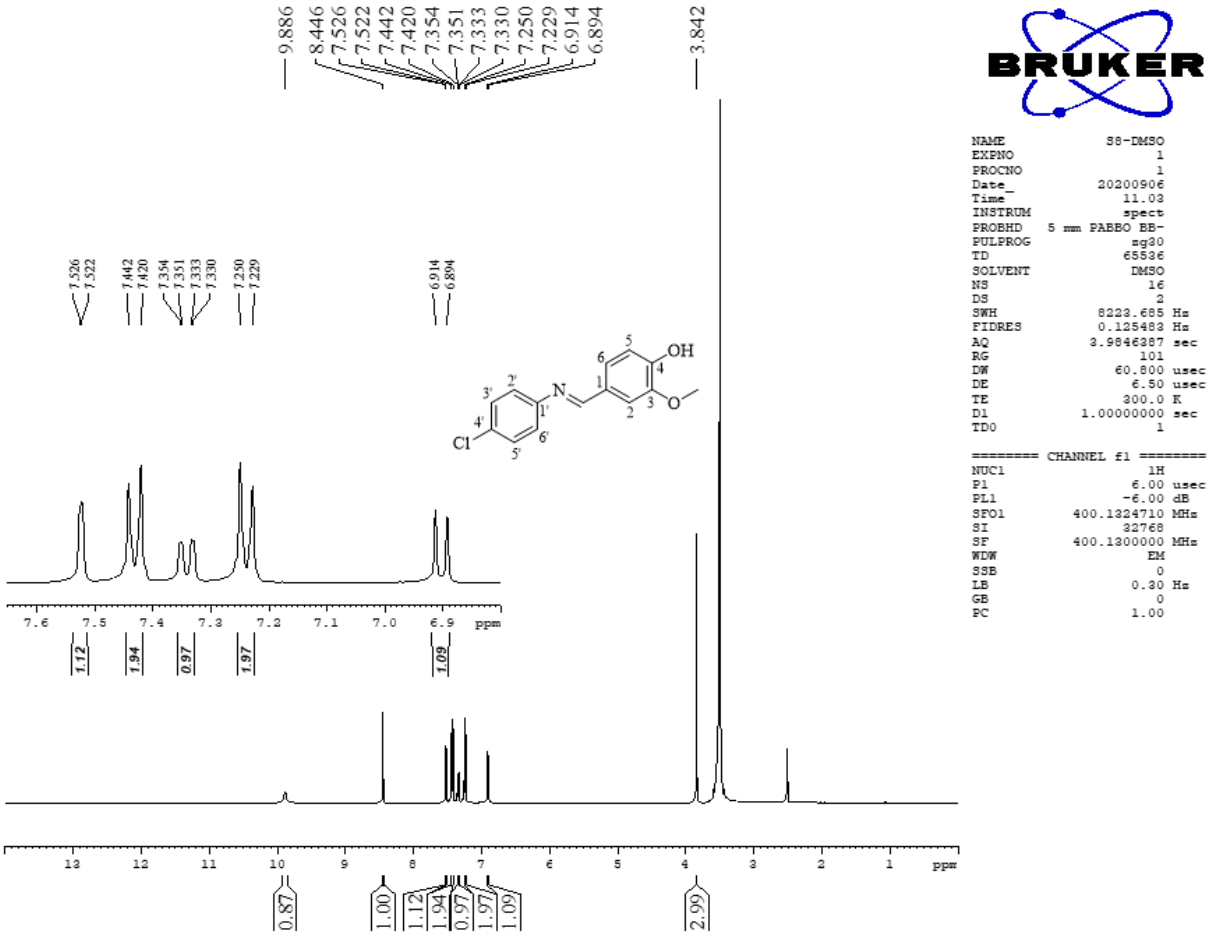




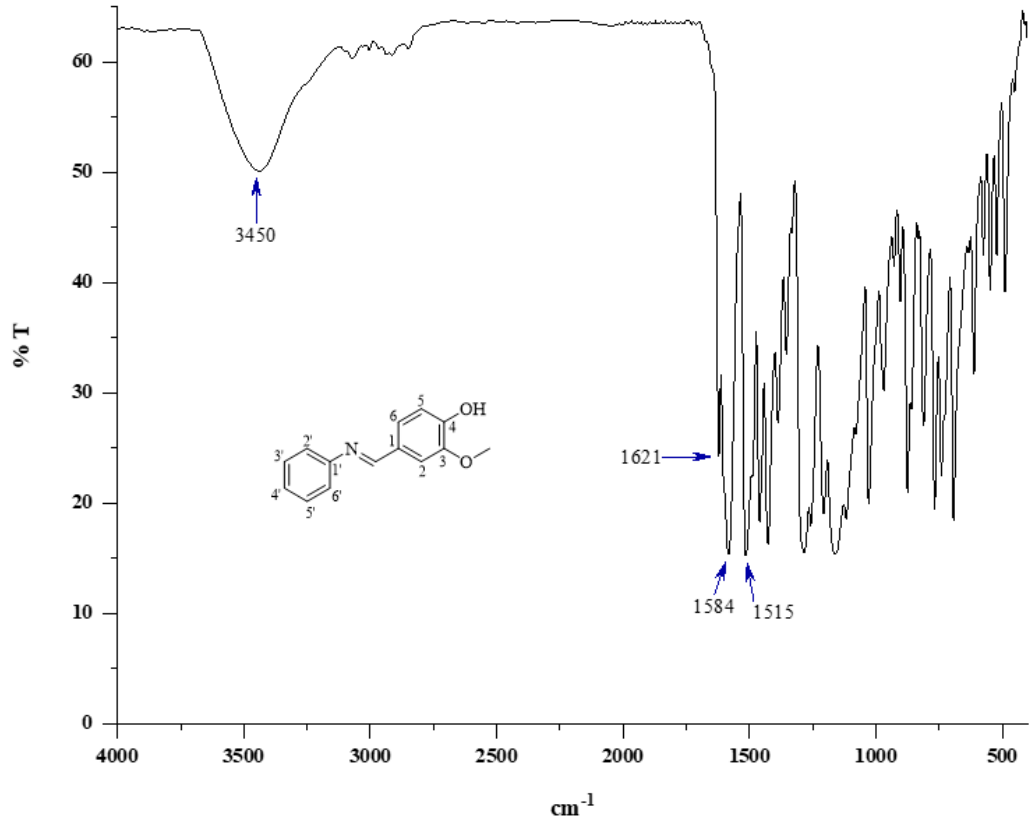
^{1}H NMR spectrum of (*E*)-4-(((4-chlorophenyl)imino)methyl)phenol **(12c)**



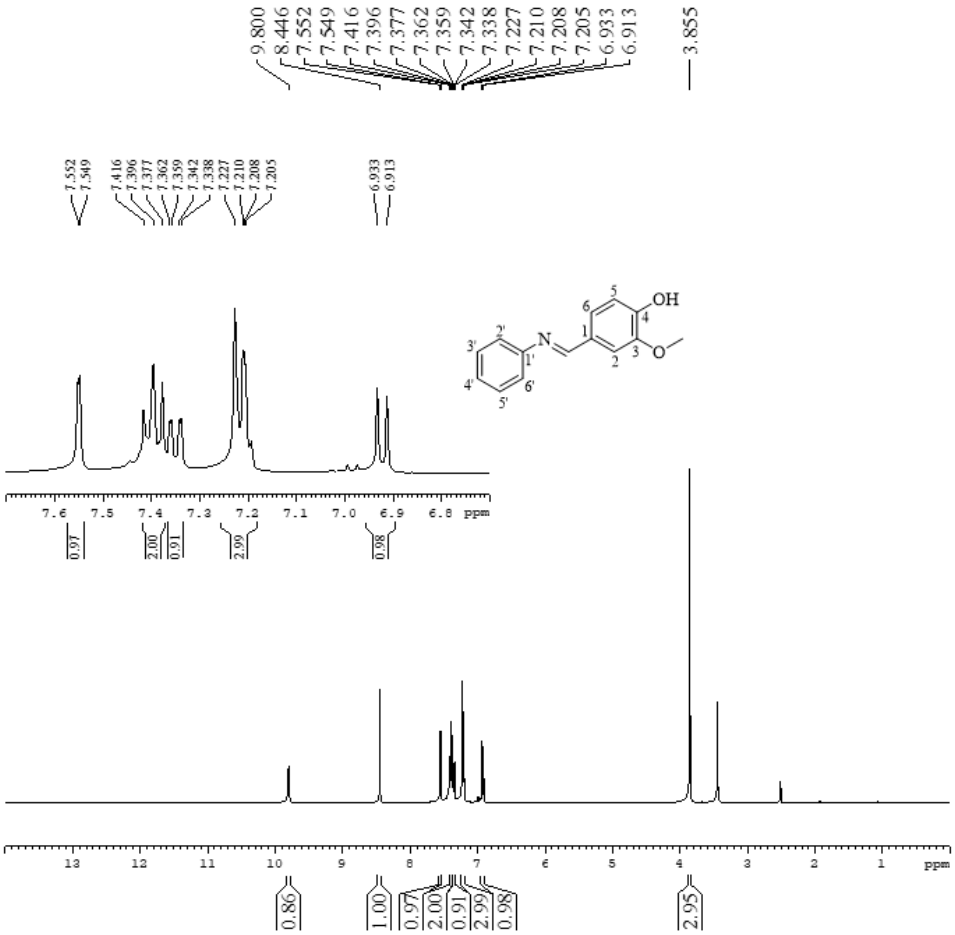
IR spectrum of (*E*)-4-(((4-chlorophenyl)imino)methyl)-2-methoxyphenol **(12d)**



^{1}H NMR spectrum of (*E*)-4-(((4-chlorophenyl)imino)methyl)-2-methoxyphenol **(12d)**

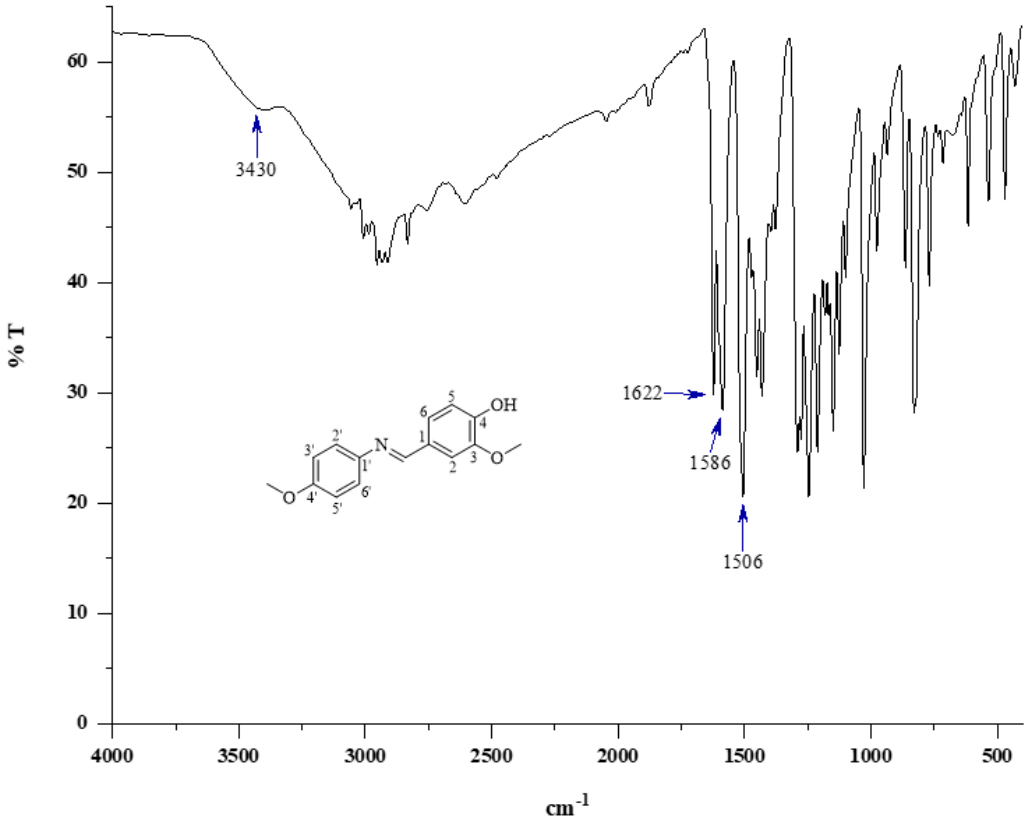


IR spectrum of (*E*)-2-methoxy-4-((phenylimino)methyl)phenol **(12e)**

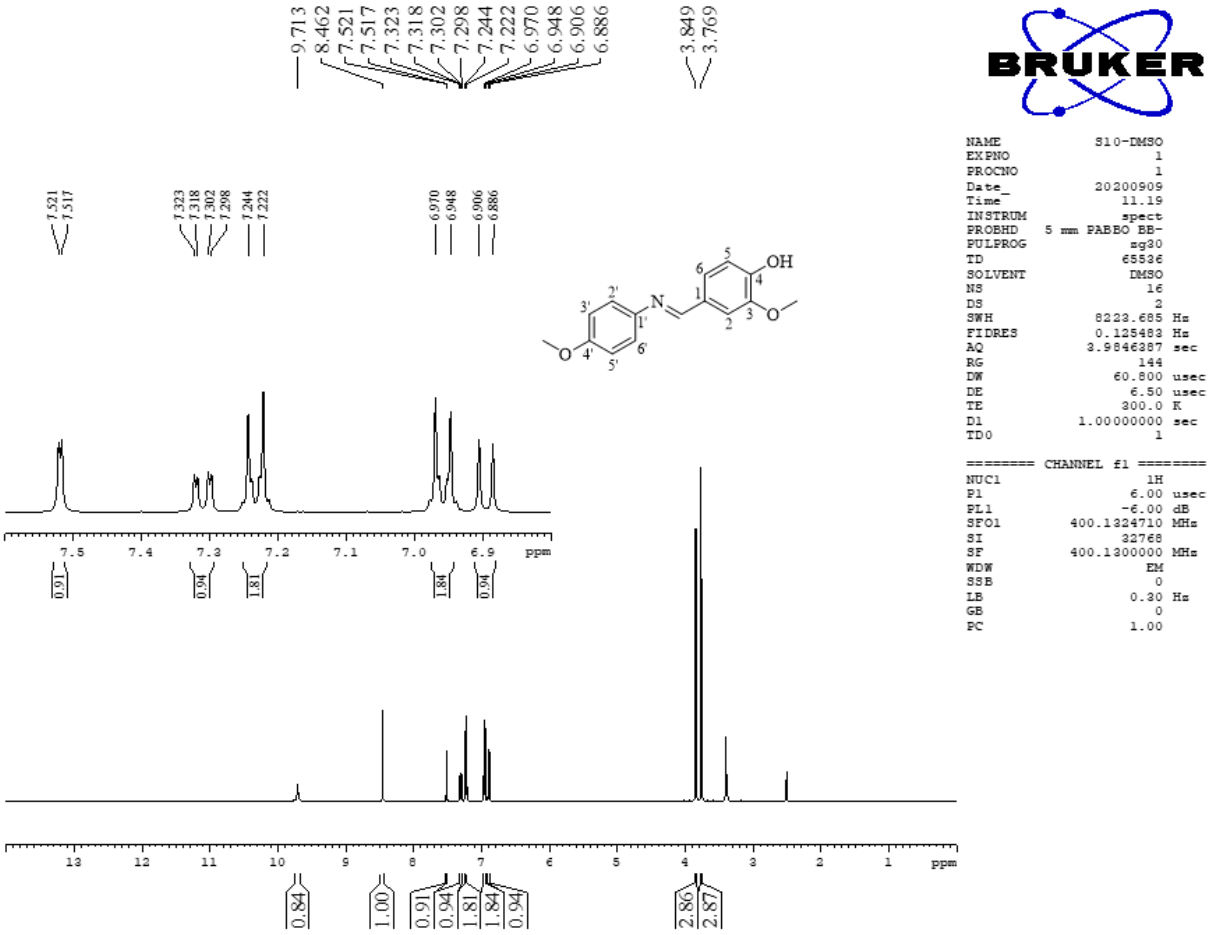



```
NAME                SS-DMSO
EXPNO                     1
PROCNO                    1
Date_              20200909
Time                  11.38
INSTRUM                spect
PROBHD     5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                        16
DS                         2
SWH                8223.685 Hz
FIDRES             0.125483 Hz
AQ                 3.9846387 sec
RG                       101
DW                    60.800 usec
DE                     6.50 usec
TE                    300.0 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     6.00 usec
PL1                   -6.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300000 MHz
WDW                       EM
SSB                        0
LB                     0.30 Hz
GB                         0
PC                      1.00
```

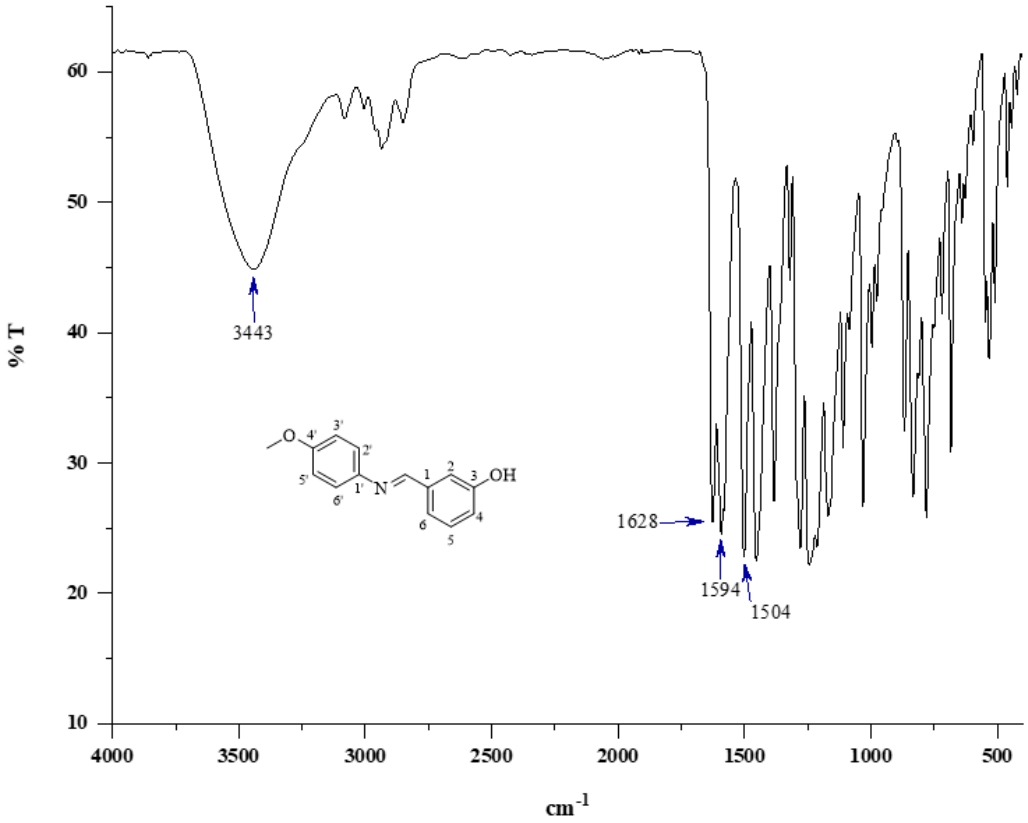
^{1}H NMR spectrum of (*E*)-2-methoxy-4-((phenylimino)methyl)phenol **(12e)**



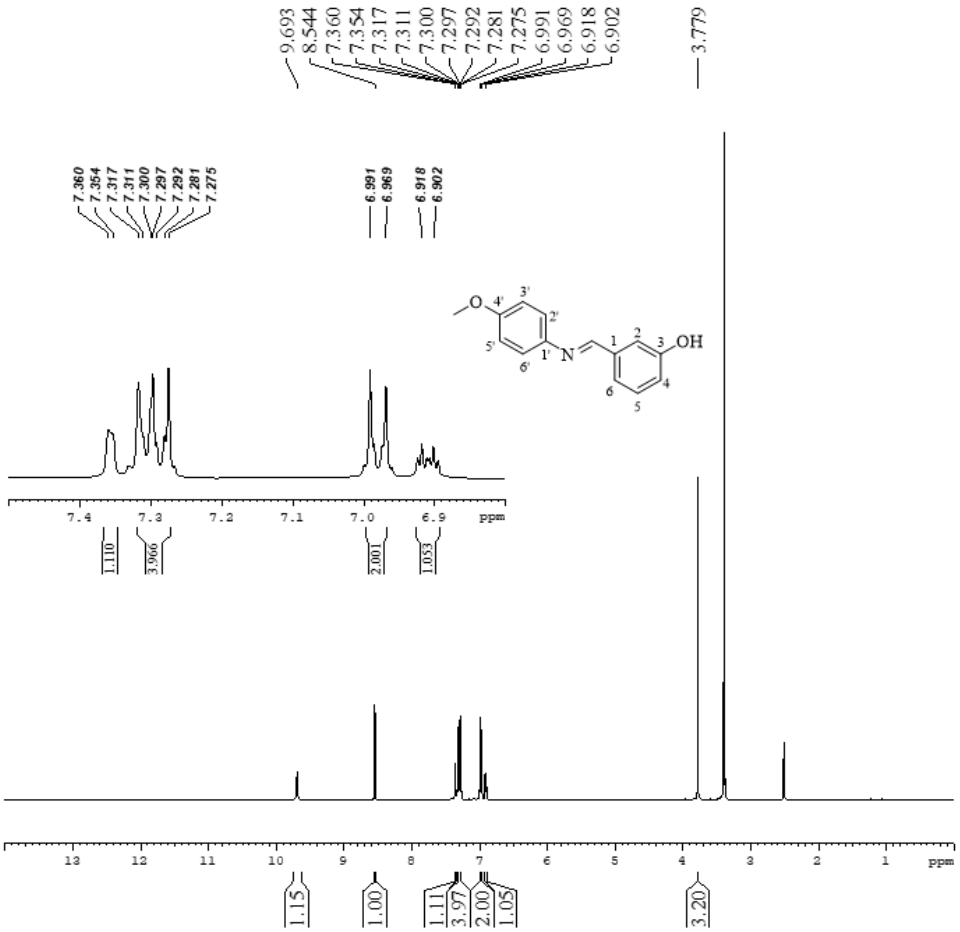
IR spectrum of (*E*)-2-methoxy-4-(((4-methoxyphenyl)imino)methyl)phenol **(12f)**

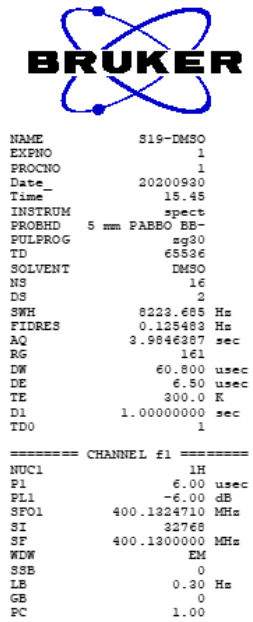


^{1}H NMR spectrum of (*E*)-2-methoxy-4-(((4-methoxyphenyl)imino)methyl)phenol **(12f)**

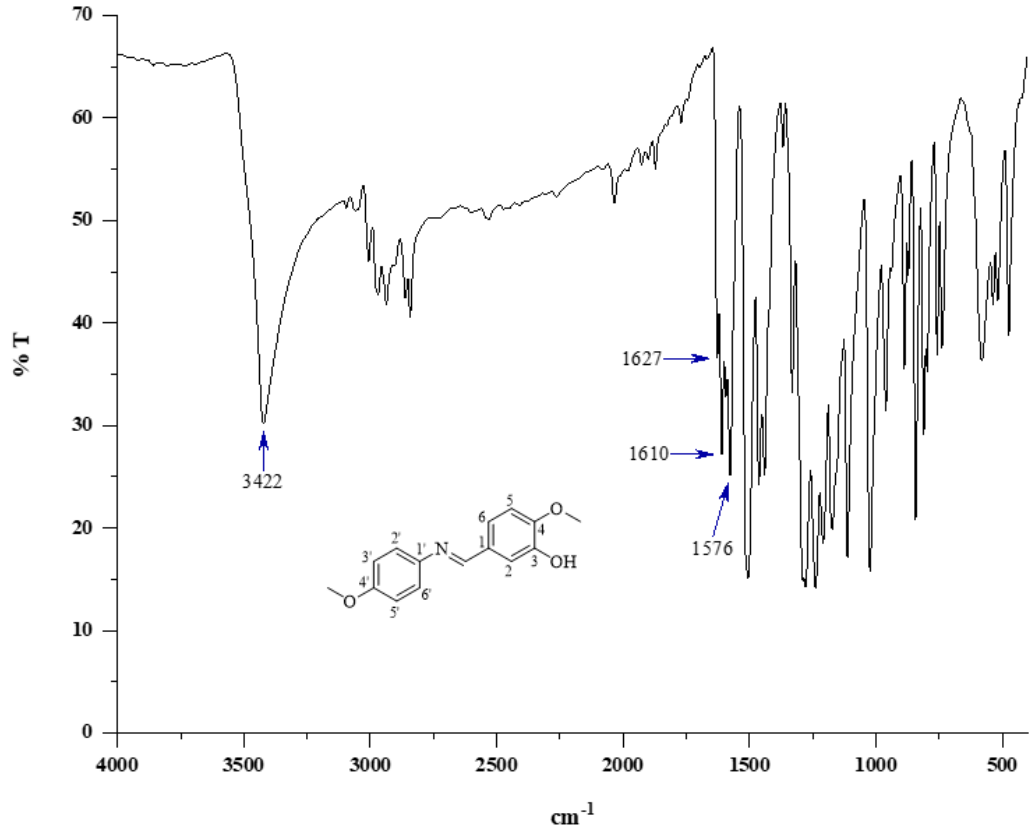


IR spectrum of (*E*)-3-(((4-methoxyphenyl)imino)methyl)phenol **(12g)**

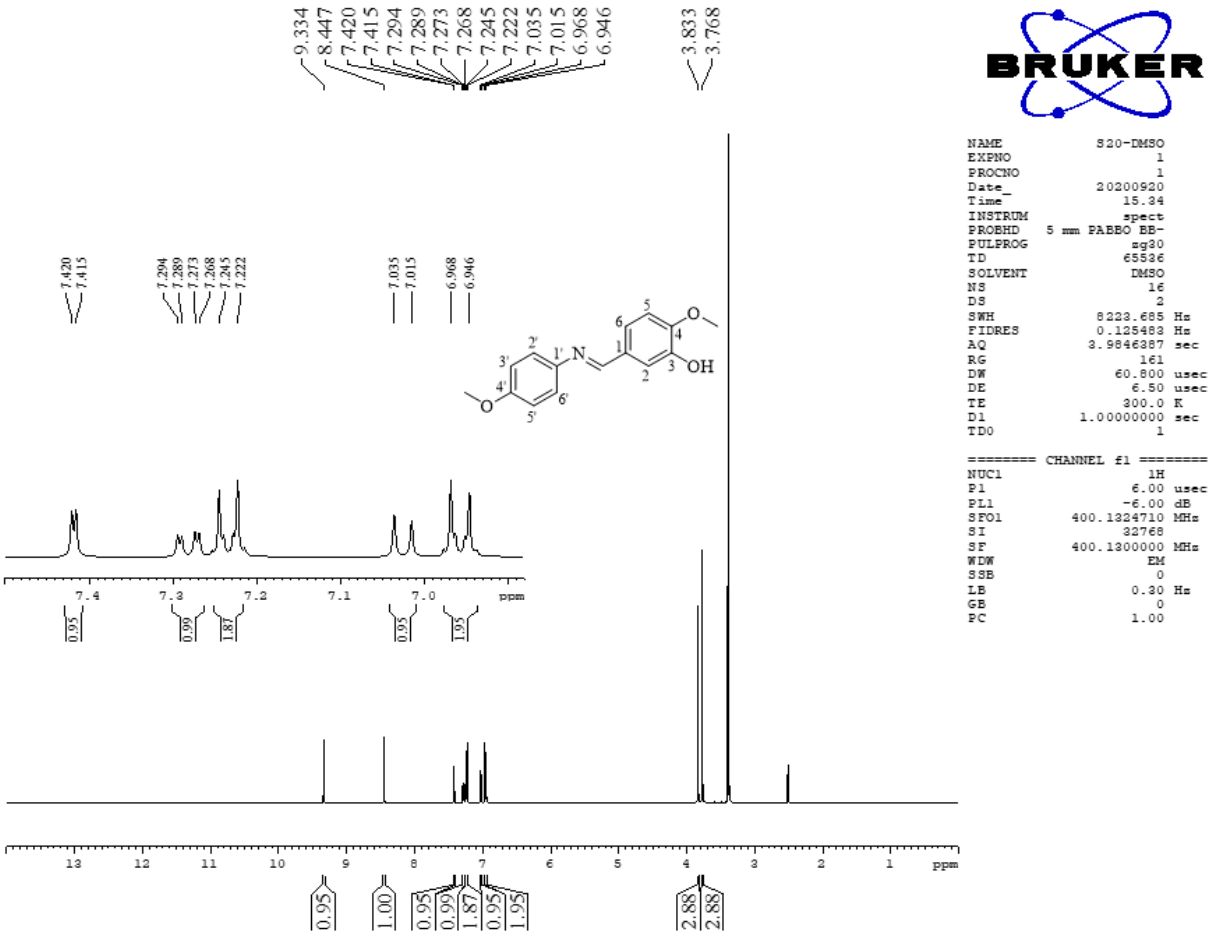




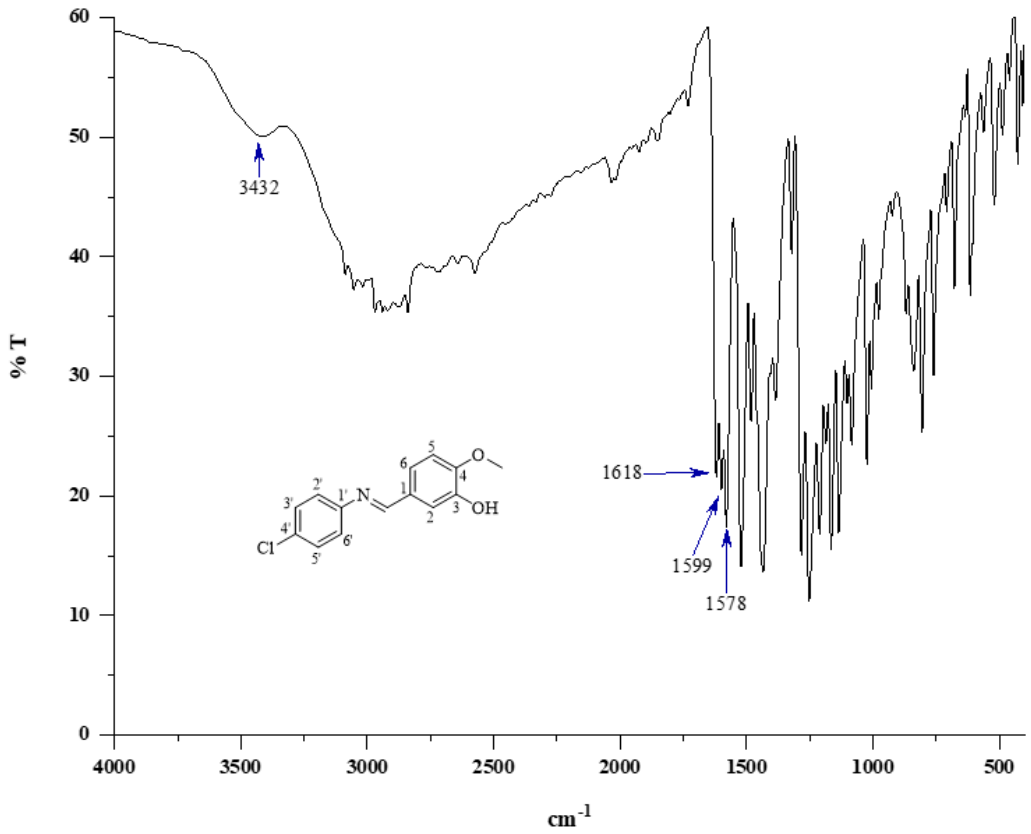
^{1}H NMR spectrum of (*E*)-3-(((4-methoxyphenyl)imino)methyl)phenol **(12g)**



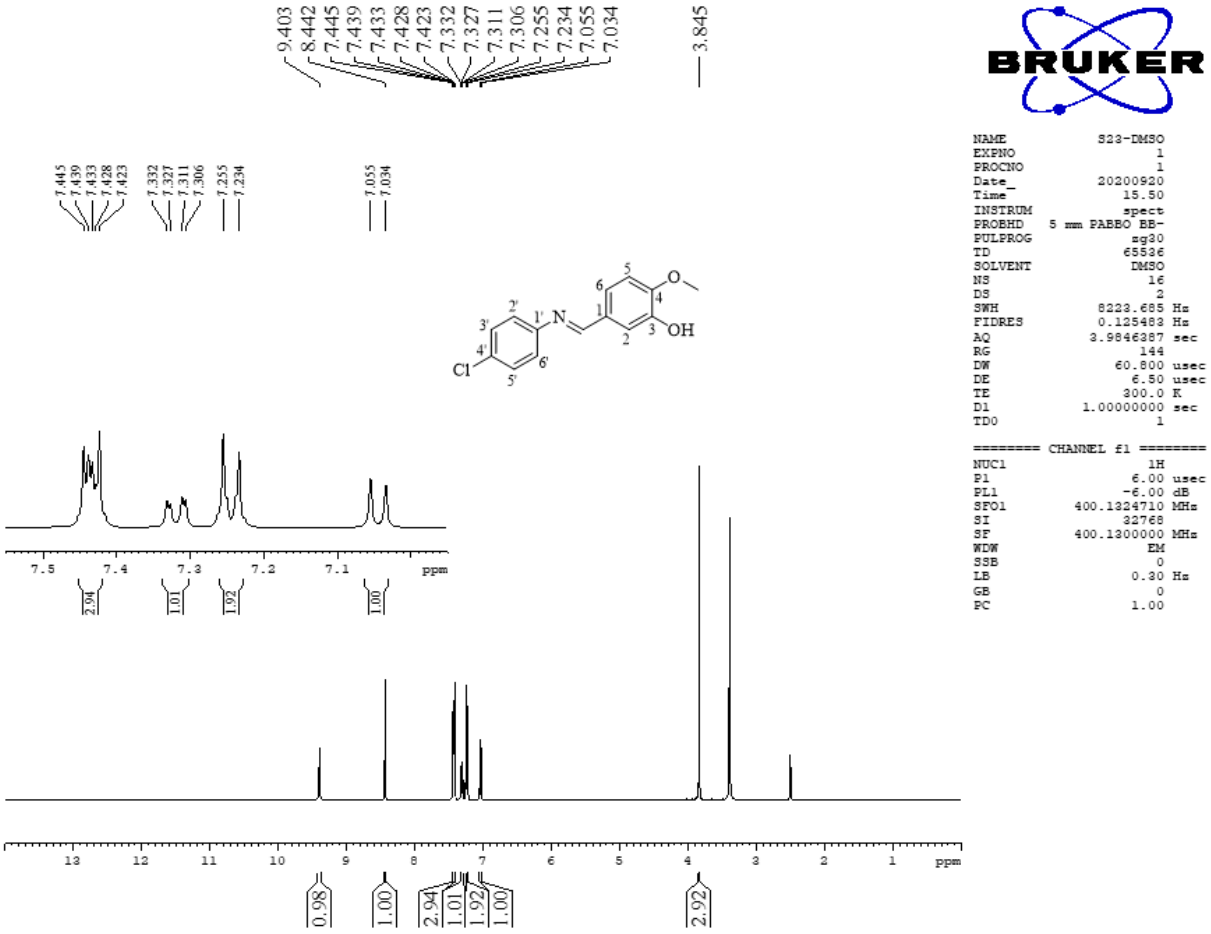
IR spectrum of (*E*)-2-methoxy-5-(((4-methoxyphenyl)imino)methyl) phenol **(12h)**



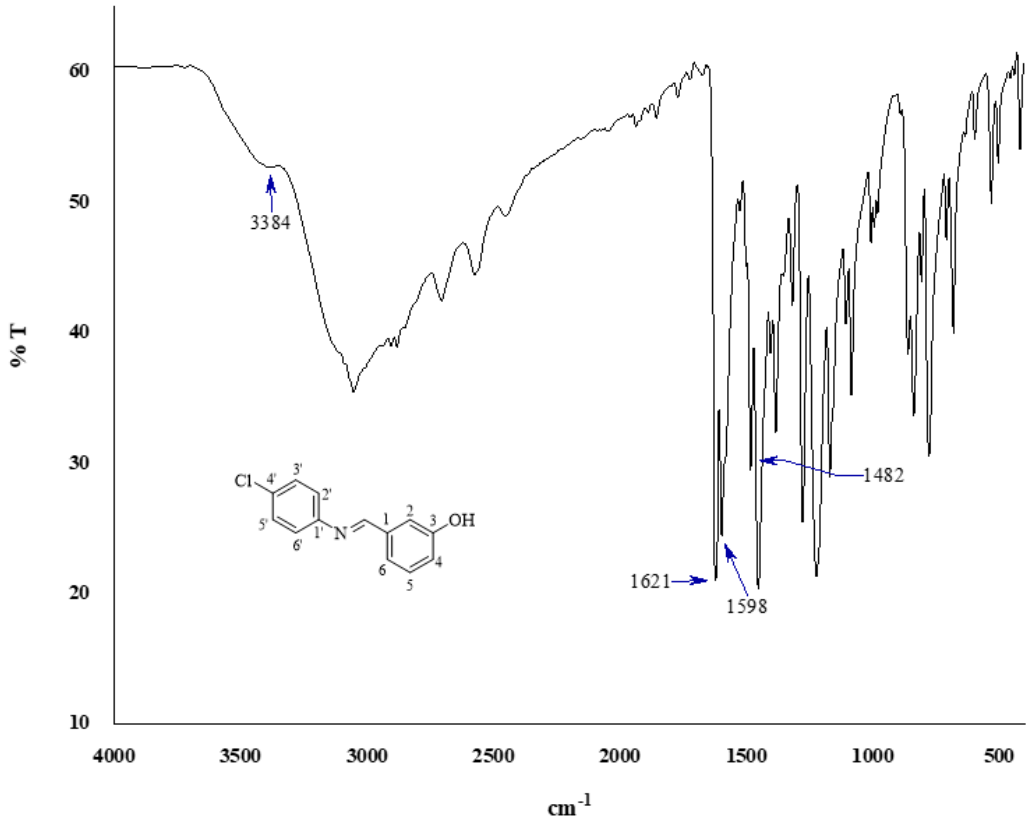
^{1}H NMR spectrum of (*E*)-2-methoxy-5-(((4-methoxyphenyl)imino)methyl) phenol **(12h)**



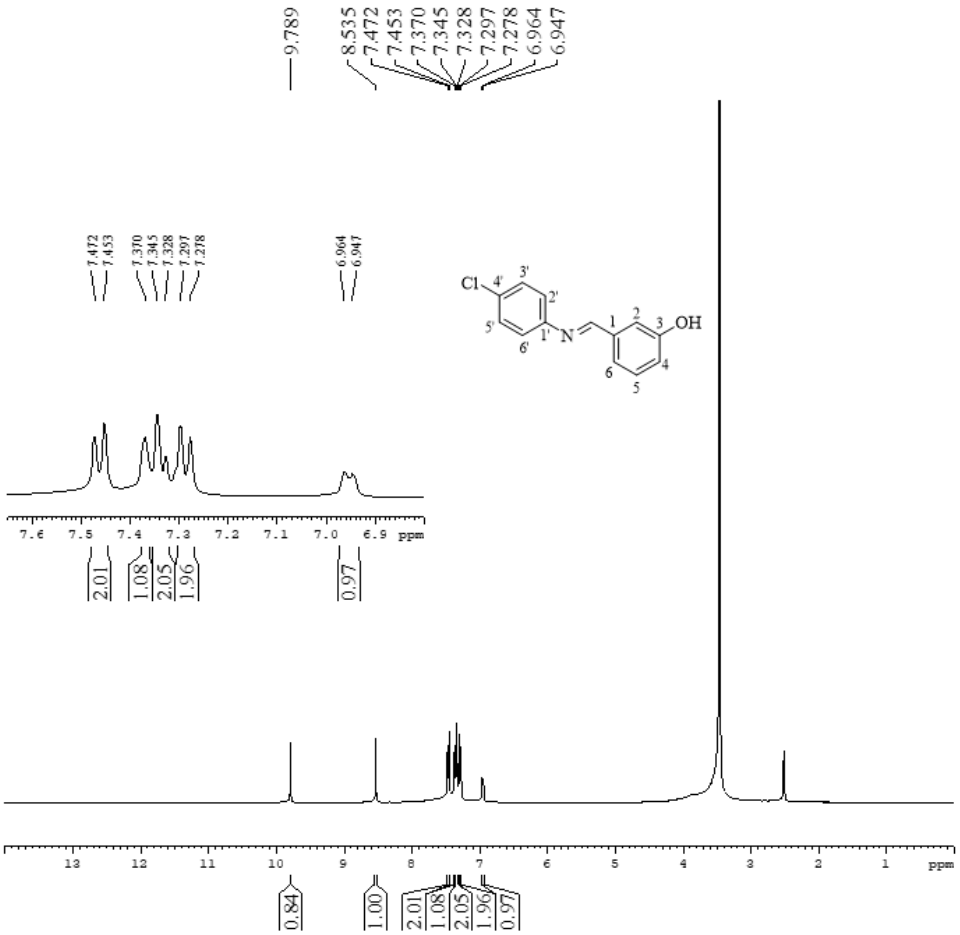
IR spectrum of (*E*)-5-(((4-chlorophenyl)imino)methyl)-2-methoxyphenol **(12i)**

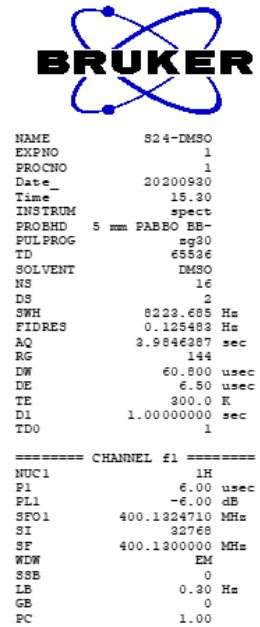


^{1}H NMR spectrum of (*E*)-5-(((4-chlorophenyl)imino)methyl)-2-methoxyphenol **(12i)**

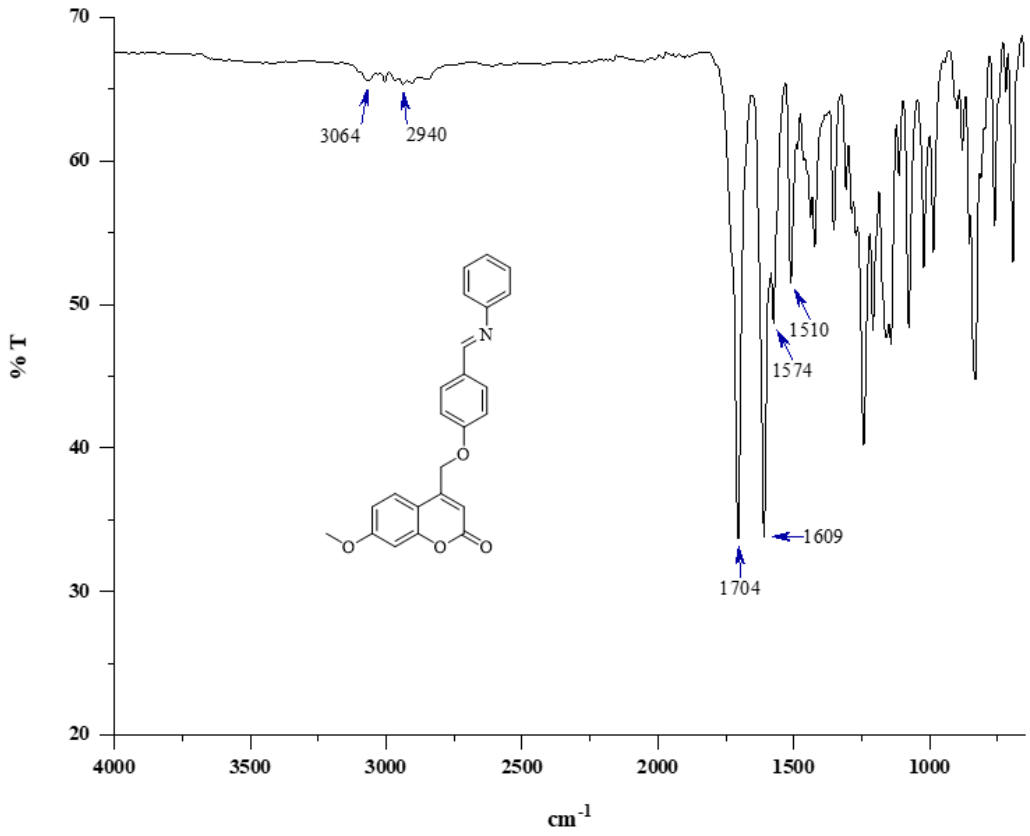


IR spectrum of (*E*)-3-(((4-chlorophenyl)imino)methyl)phenol **(12j)**

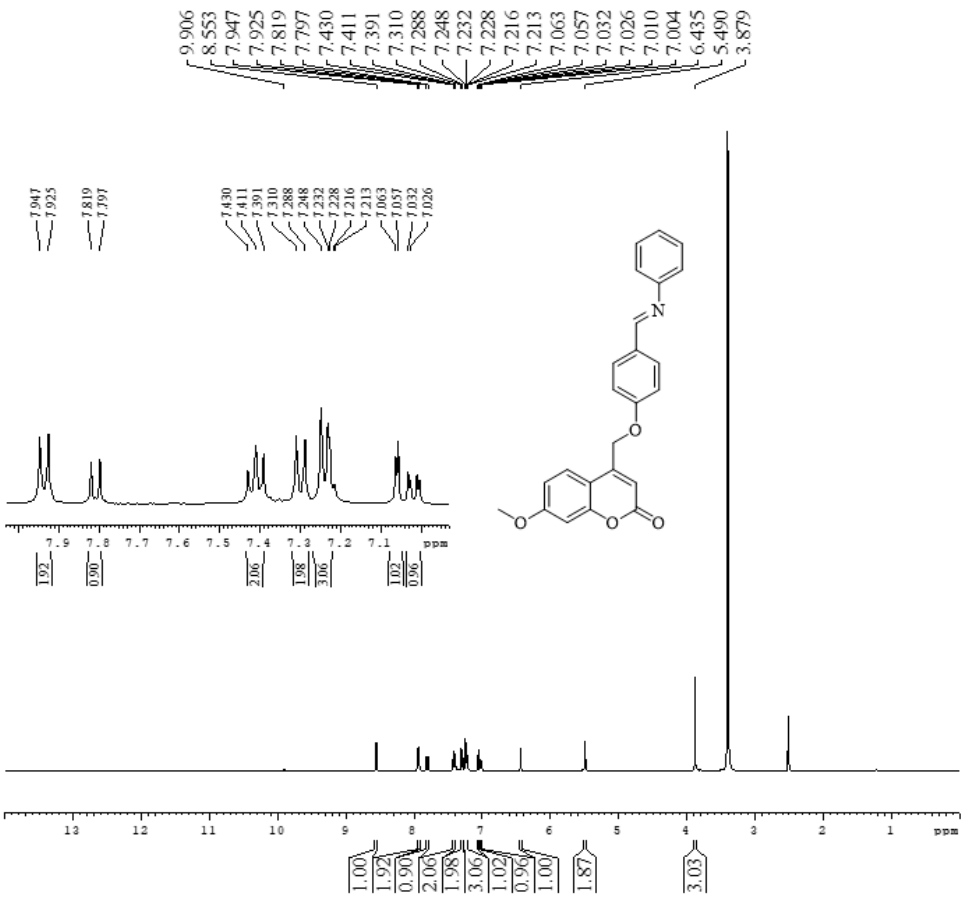




^{1}H NMR spectrum of (*E*)-3-(((4-chlorophenyl)imino)methyl)phenol **(12j)**

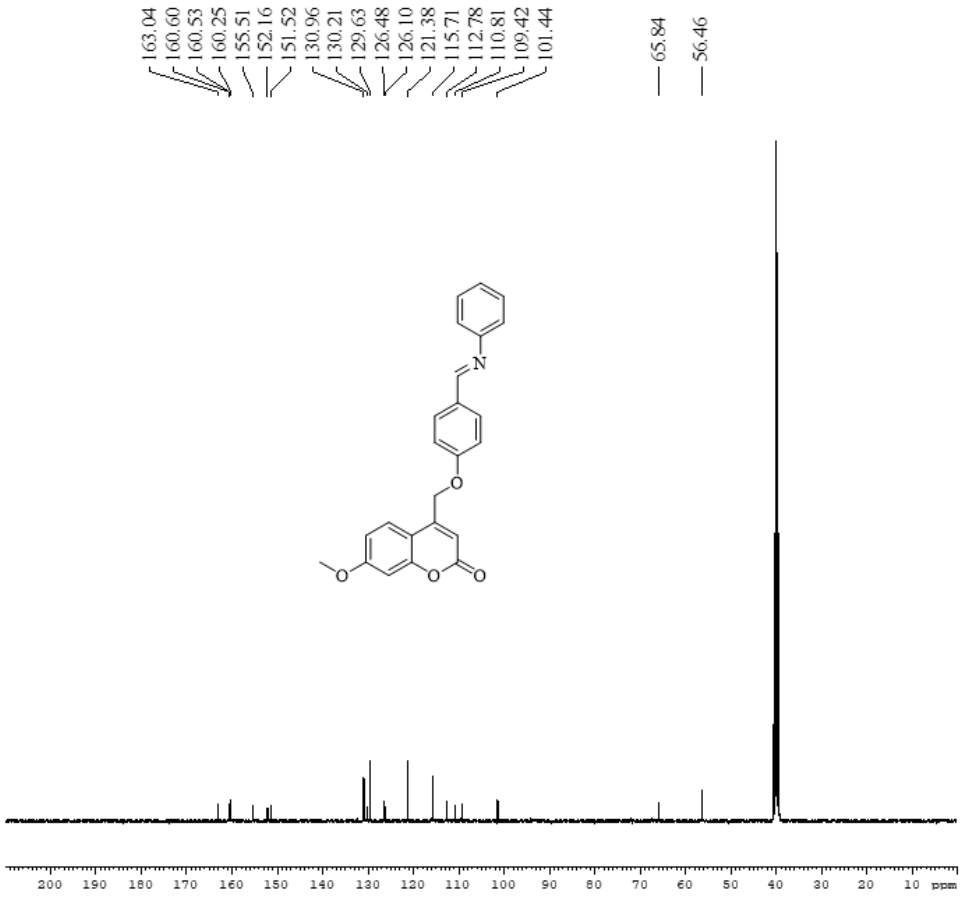


IR spectrum of (*E*)-7-methoxy-4-((4-((phenylimino)methyl)phenoxy)methyl) -2*H*-chromen-2-one **(13a)**




```
NAME          S17OMC-DMSO
EXPNO                   1
PROCNO                  1
Date_            20200909
Time                11.05
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                    181
DW                60.800 usec
DE                 6.50 usec
TE                300.0 K
D1            1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   6.00 usec
PL1                 -6.00 dB
SFO1          400.1324710 MHz
SI                  32768
SF            400.1300000 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

^{1}H NMR spectrum of (*E*)-7-methoxy-4-((4-((phenylimino)methyl)phenoxy)methyl) -2*H*-chromen-2-one **(13a)**



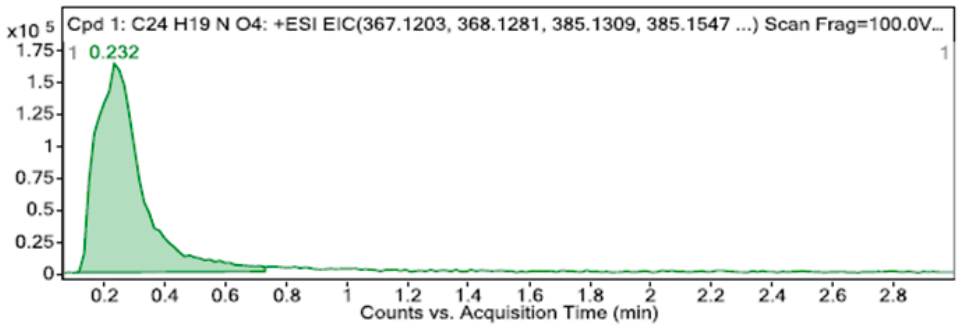

```
NAME          S17OMC-DMSO
EXPNO                   3
PROCNO                  1
Date_            20200909
Time                11.54
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG            sgpg30
TD                  65536
SOLVENT              DMSO
NS                   2048
DS                      4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                  12.00 usec
PL1                 -1.00 dB
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz65
NUC2                   1H
PCPD2                80.00 usec
PL2                 -6.00 dB
PL12                19.50 dB
PL13                19.50 dB
SFO2          400.1316005 MHz
SI                  32768
SF            100.6127690 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

^{13}C NMR spectrum of (*E*)-7-methoxy-4-((4-((phenylimino)methyl)phenoxy)methyl) -2*H*-chromen-2-one **(13a)**

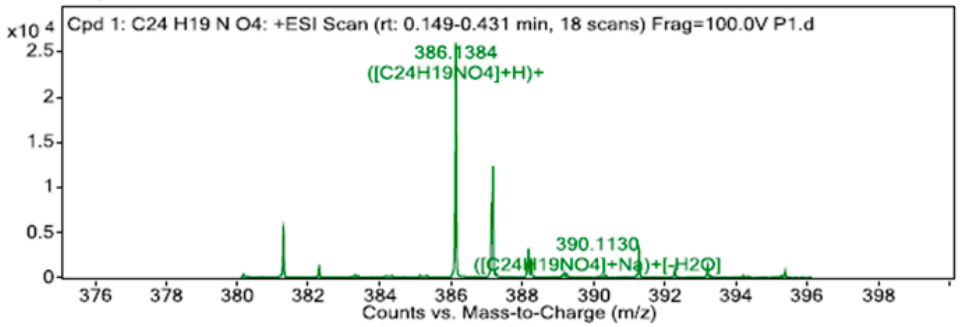
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C24 H19 N O4	0.232	385.1312	113	C24 H19 N O4	385.1314	-0.56

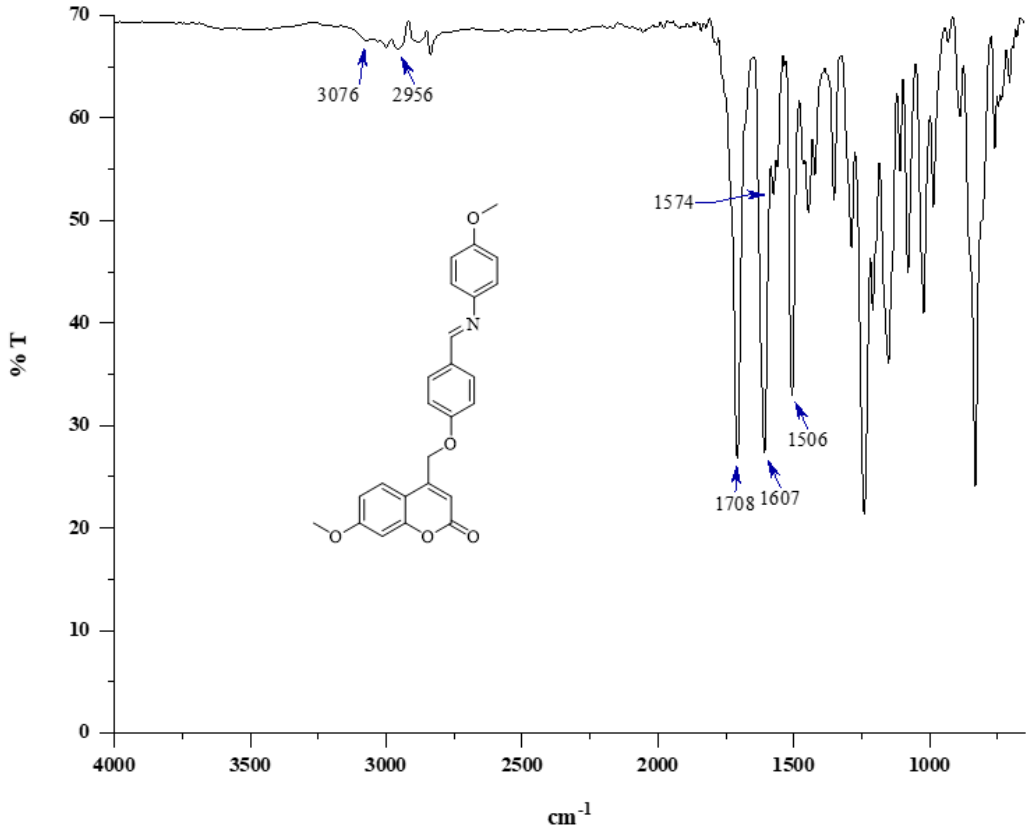
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C24 H19 N O4	390.113	0.232	Find By Formula	385.1312



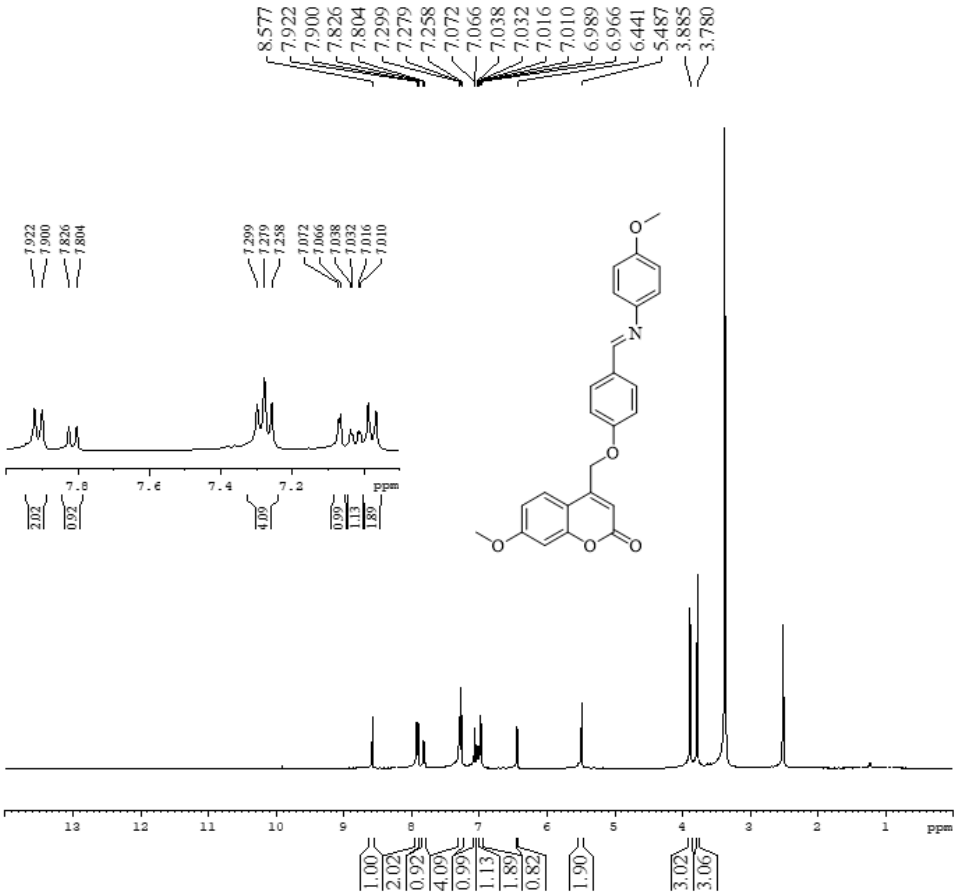
MS Zoomed Spectrum



HRMS of (*E*)-7-methoxy-4-((4-((phenylimino)methyl)phenoxy)methyl) -2*H*-chromen-2-one **(13a)**



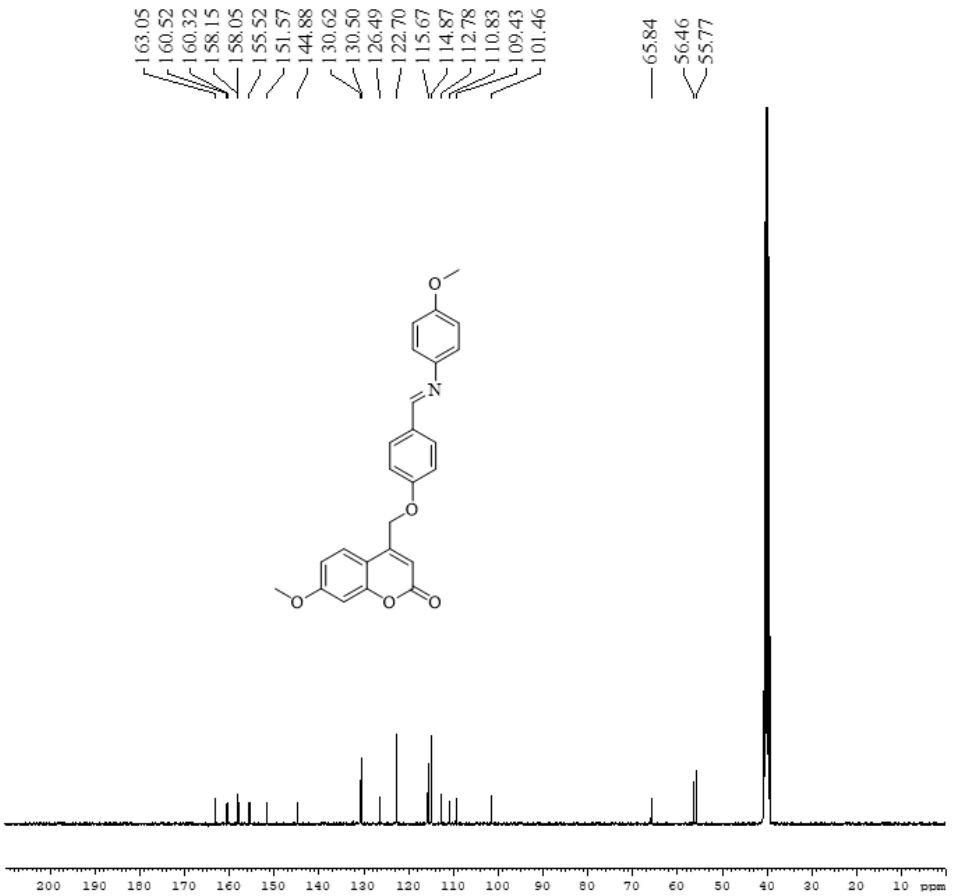
IR spectrum of (*E*)-7-methoxy-4-((4-(((4-methoxyphenyl)imino)methyl) phenoxy)methyl)-2*H*-chromen-2-one **(13b)**




```
NAME          S270MC-DMSO
EXPNO                   1
PROCNO                  1
Date_            20200917
Time_               12.14
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                    228
DW                60.800 usec
DE                 6.50 usec
TE                300.0 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  1H
P1                 6.00 usec
PL1               -6.00 dB
SFO1         400.1324710 MHz
SI                  32768
SF           400.1300000 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

^{1}H NMR spectrum of (*E*)-7-methoxy-4-((4-(((4-methoxyphenyl)imino)methyl) phenoxy)methyl)-2*H*-chromen-2-one

(13b)




```
NAME          S270MC-DMSO
EXPNO                   2
PROCNO                  1
Date_            20200917
Time_               12.29
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                  15360
DS                      4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                12.00 usec
PL1               -1.00 dB
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz65
NUC2                  1H
PCPD2             80.00 usec
PL2               -6.00 dB
PL12              19.50 dB
PL13              19.50 dB
SFO2         400.1316005 MHz
SI                  32768
SF           100.6127690 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                1.40
```

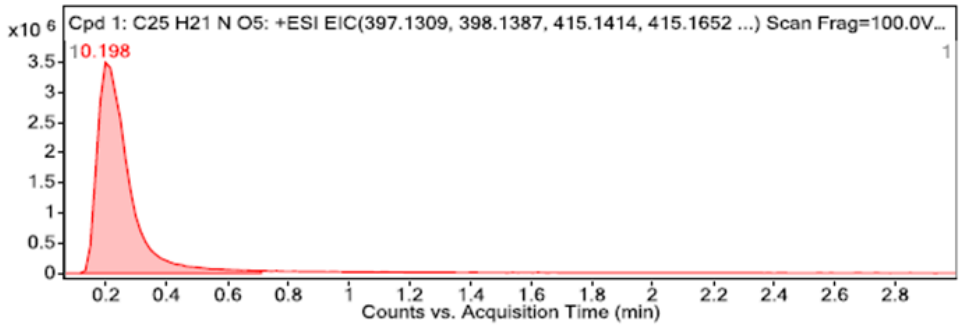
^{13}C NMR spectrum of (*E*)-7-methoxy-4-((4-(((4-methoxyphenyl)imino)methyl) phenoxy)methyl)-2*H*-chromen-2-one

(13b)

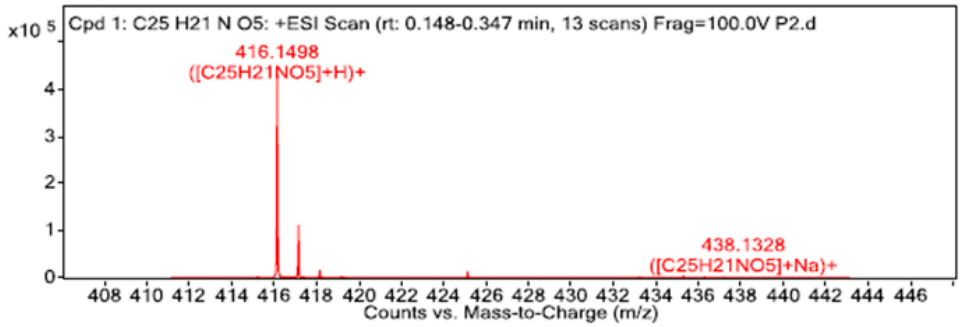
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C25 H21 N O5	0.198	415.1424	432183	C25 H21 N O5	415.142	1.13

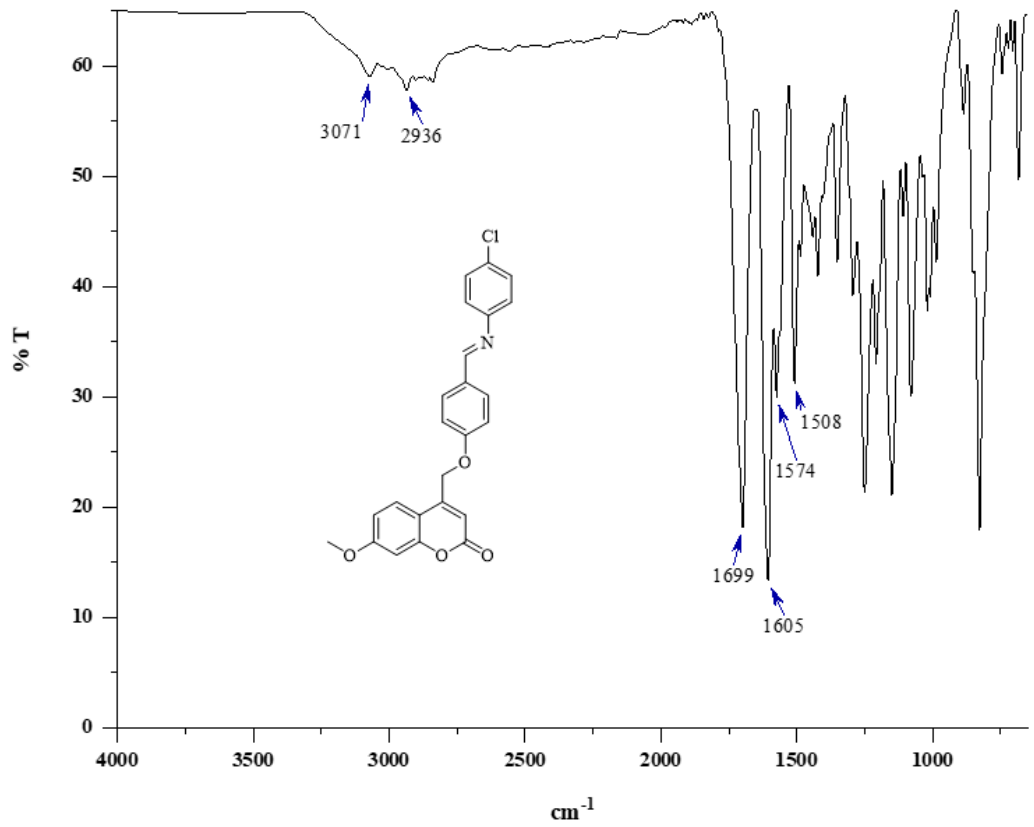
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C25 H21 N O5	416.1498	0.198	Find By Formula	415.1424



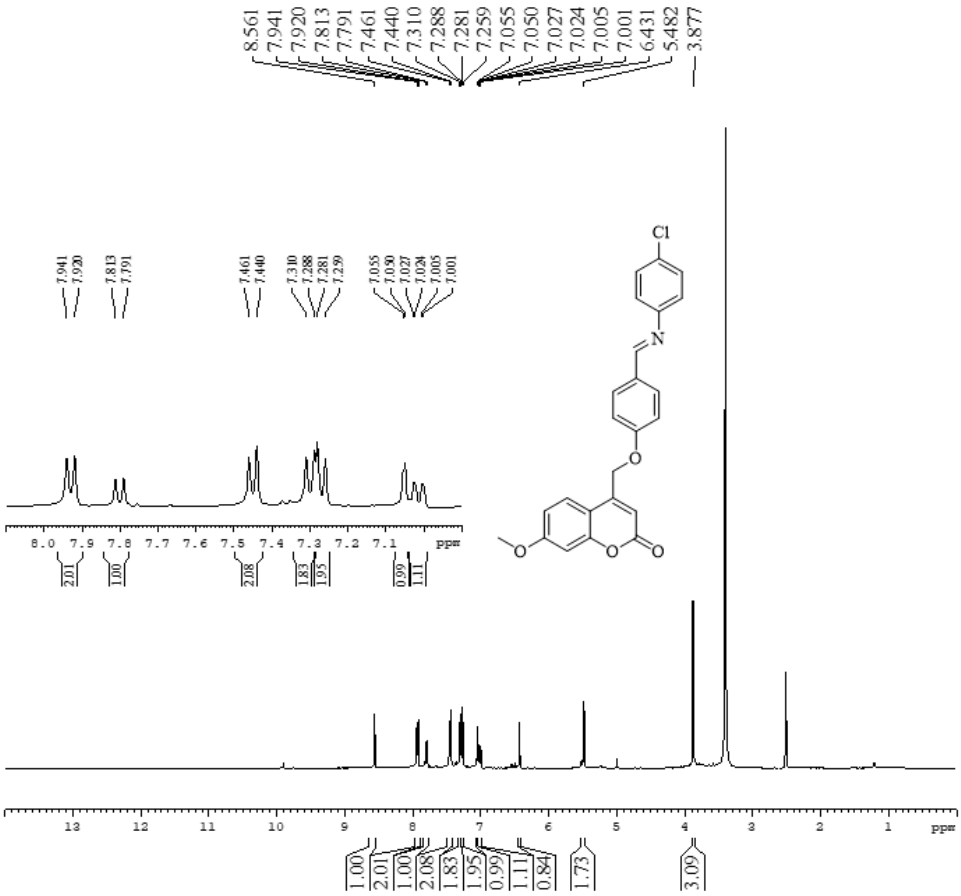
MS Zoomed Spectrum



HRMS of (*E*)-7-methoxy-4-((4-(((4-methoxyphenyl)imino)methyl) phenoxy)methyl)-2*H*-chromen-2-one **(13b)**



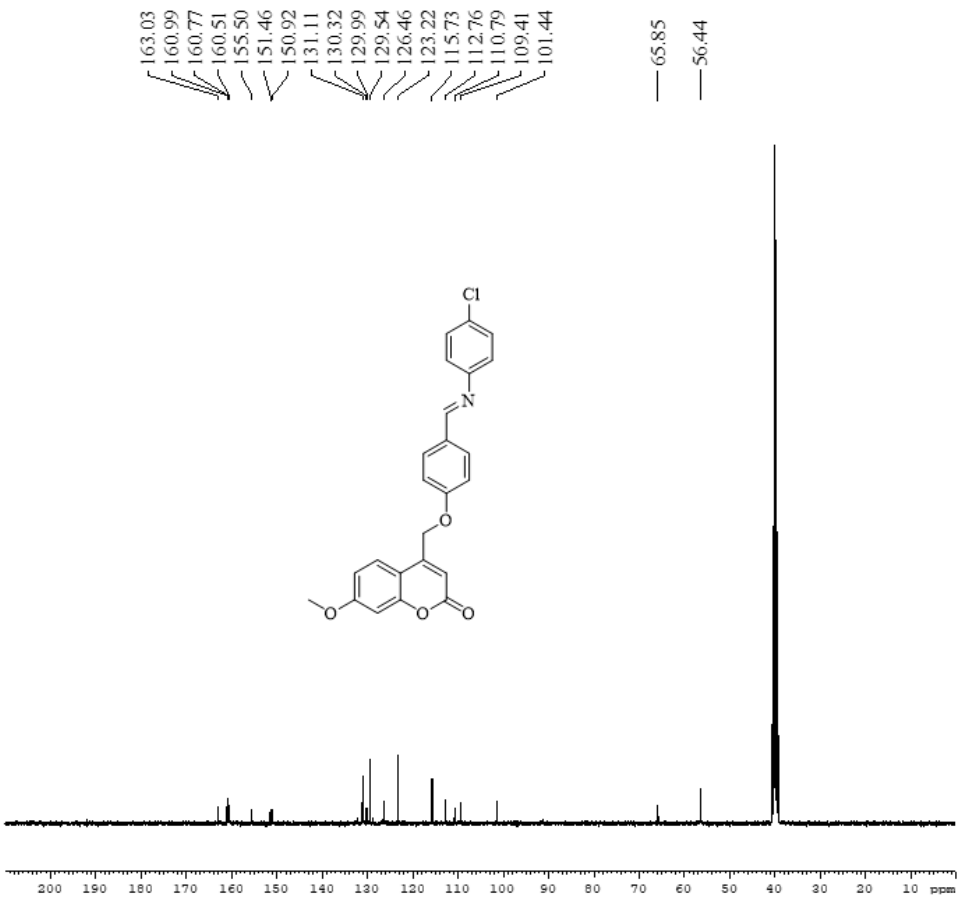
IR spectrum of (*E*)-4-((4-(((4-chlorophenyl)imino)methyl)phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13c)**




```
NAME            S77OMC-DMSO
EXPNO                     1
PROCNO                    1
Date_              20200909
Time_                 8.58
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH               8223.685 Hz
FIDRES               0.125483 Hz
AQ                3.9846387 sec
RG                      161
DW                   60.800 usec
DE                    6.50 usec
TE                   300.0 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    6.00 usec
PL1                  -6.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300000 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.00
```

^{1}H NMR spectrum of (*E*)-4-((4-(((4-chlorophenyl)imino)methyl)phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one

(13c)




```
NAME            S77OMC-DMSO
EXPNO                     2
PROCNO                    1
Date_              20200909
Time_                18.02
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG             sgpg30
TD                    65536
SOLVENT                DMSO
NS                     2048
DS                        4
SWH              24038.461 Hz
FIDRES               0.366798 Hz
AQ                1.3631988 sec
RG                      203
DW                   20.800 usec
DE                    6.50 usec
TE                   300.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      13C
P1                   12.00 usec
PL1                  -1.00 dB
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz65
NUC2                      1H
PCPD2                80.00 usec
PL2                  -6.00 dB
PL12                 19.50 dB
PL13                 19.50 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127690 MHz
WDW                      EM
SSB                       0
LB                    1.00 Hz
GB                        0
PC                    1.40
```

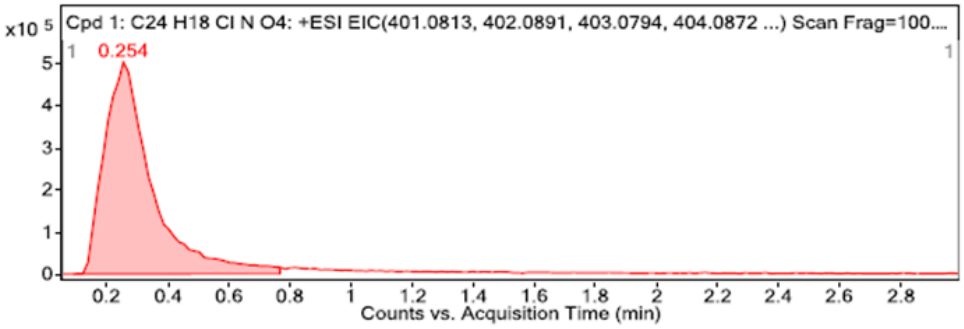
^{13}C NMR spectrum of (*E*)-4-((4-(((4-chlorophenyl)imino)methyl)phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one

(13c)

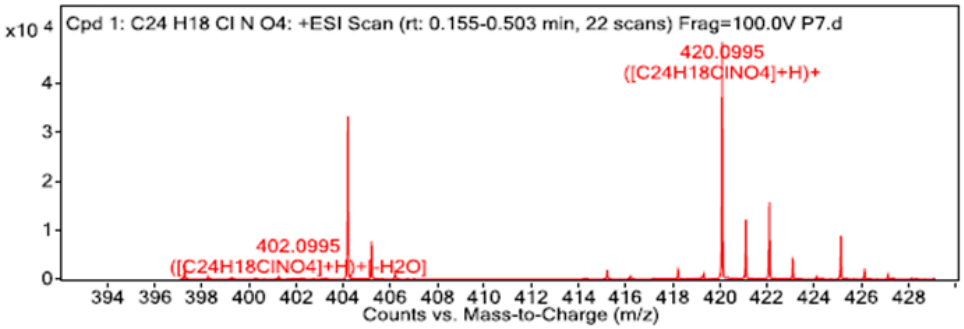
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C24 H18 Cl N O4	0.254	419.092	49039	C24 H18 Cl N O4	419.0924	-1.06

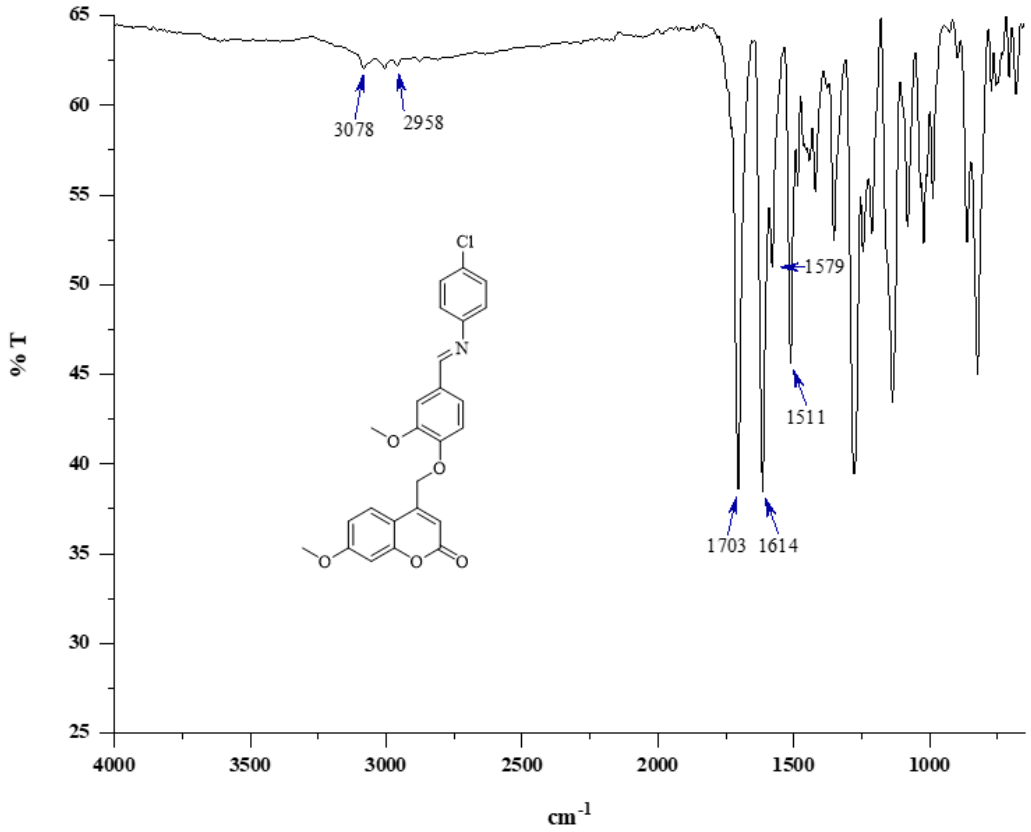
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C24 H18 Cl N O4	420.0995	0.254	Find By Formula	419.092



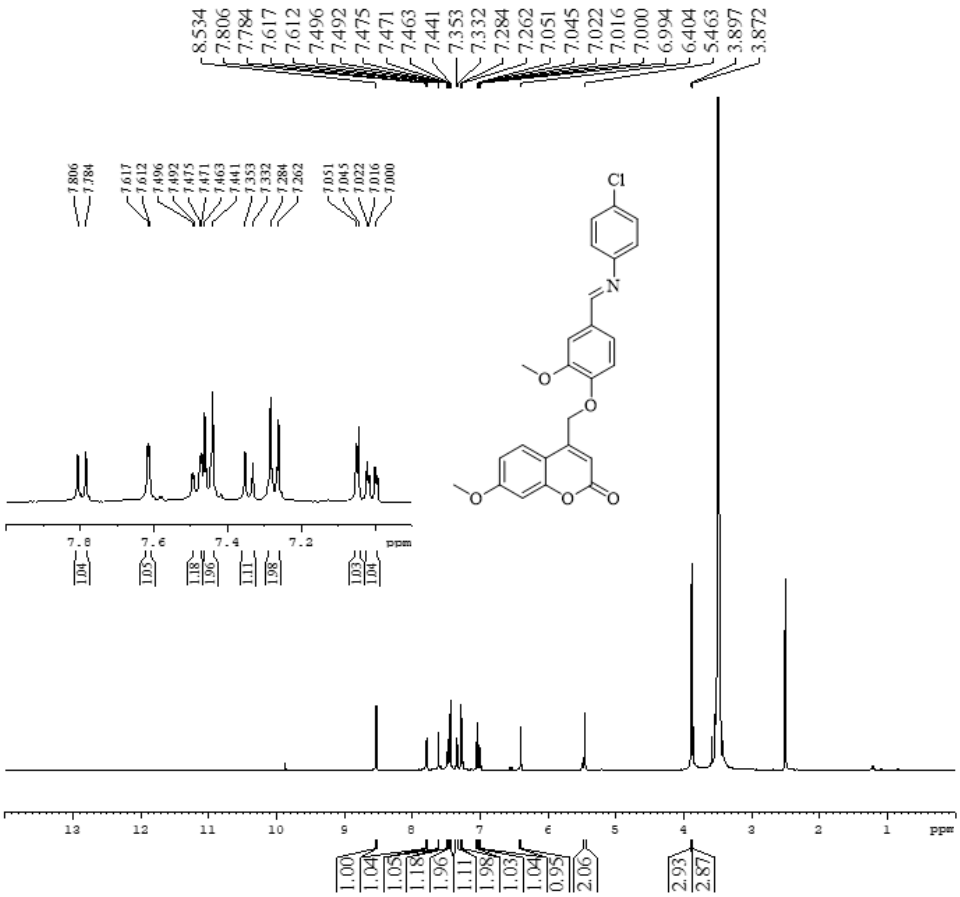
MS Zoomed Spectrum



HRMS of (*E*)-4-((4-(((4-chlorophenyl)imino)methyl)phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13c)**

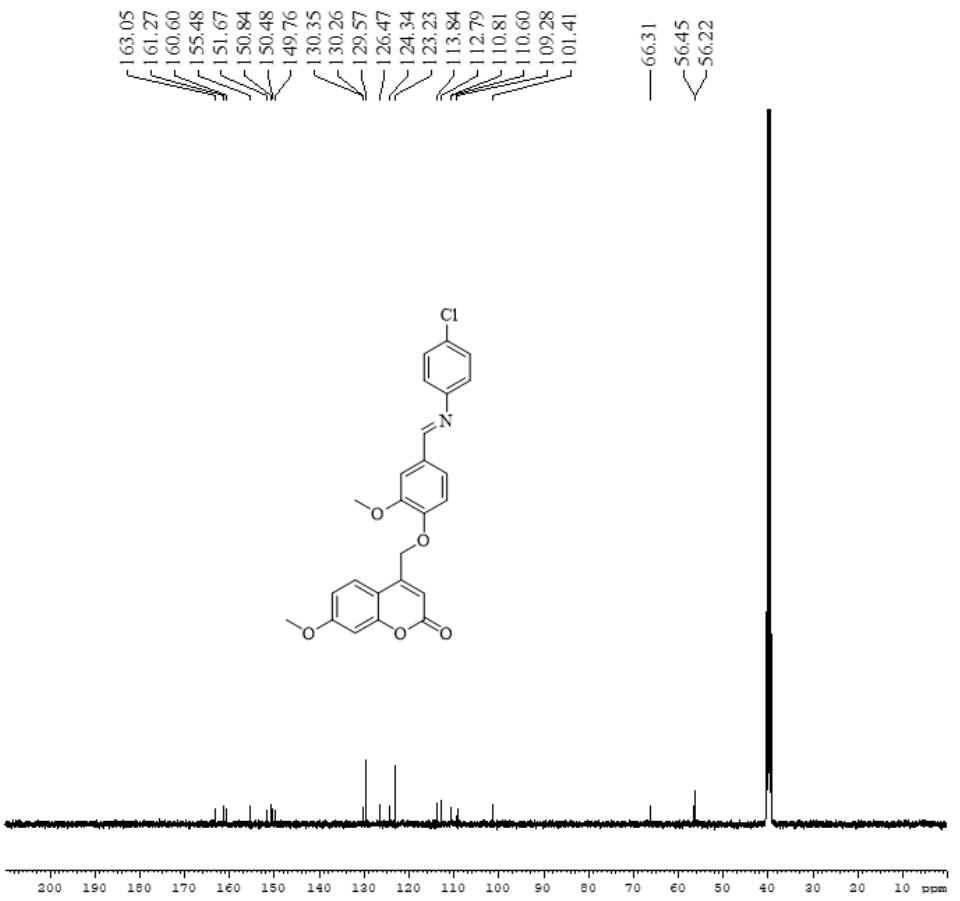


IR spectrum of (*E*)-4-((4-(((4-chlorophenyl)imino)methyl)-2-methoxy phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13d)**




```
NAME          S870MC-DMSO
EXPNO                   1
PROCNO                  1
Date_          20200909
Time               9.16
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT            DMSO
NS                   16
DS                    2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG                  114
DW             60.800 usec
DE              6.50 usec
TE             300.0 K
D1          1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                  1H
P1              6.00 usec
PL1             -6.00 dB
SFO1       400.1324710 MHz
SI                32768
SF         400.1300000 MHz
WDW                  EM
SSB                   0
LB              0.30 Hz
GB                    0
PC                 1.00
```

^{1}H NMR spectrum of (*E*)-4-((4-(((4-chlorophenyl)imino)methyl)-2-methoxy phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13d)**



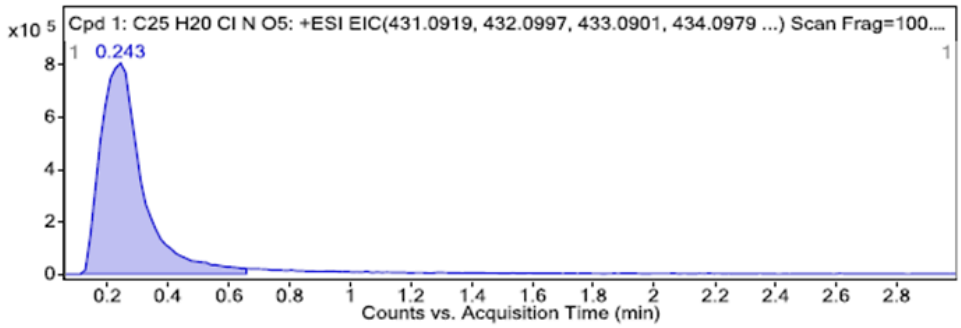

```
NAME          S870MC-DMSO
EXPNO                   2
PROCNO                  1
Date_          20200909
Time              17.20
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                 1984
DS                    4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG                  203
DW             20.800 usec
DE              6.50 usec
TE             300.0 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                  13C
P1              12.00 usec
PL1             -1.00 dB
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz65
NUC2                  1H
PCPD2           80.00 usec
PL2             -6.00 dB
PL12            19.50 dB
PL13            19.50 dB
SFO2       400.1316005 MHz
SI                32768
SF         100.6127690 MHz
WDW                  EM
SSB                   0
LB              1.00 Hz
GB                    0
PC                 1.40
```

^{13}C NMR spectrum of (*E*)-4-((4-(((4-chlorophenyl)imino)methyl)-2-methoxy phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13d)**

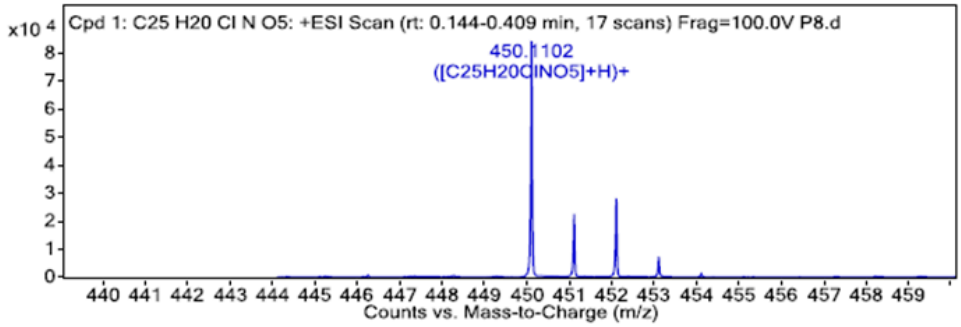
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C25 H20 Cl N O5	0.243	449.1028	87486	C25 H20 Cl N O5	449.103	-0.47

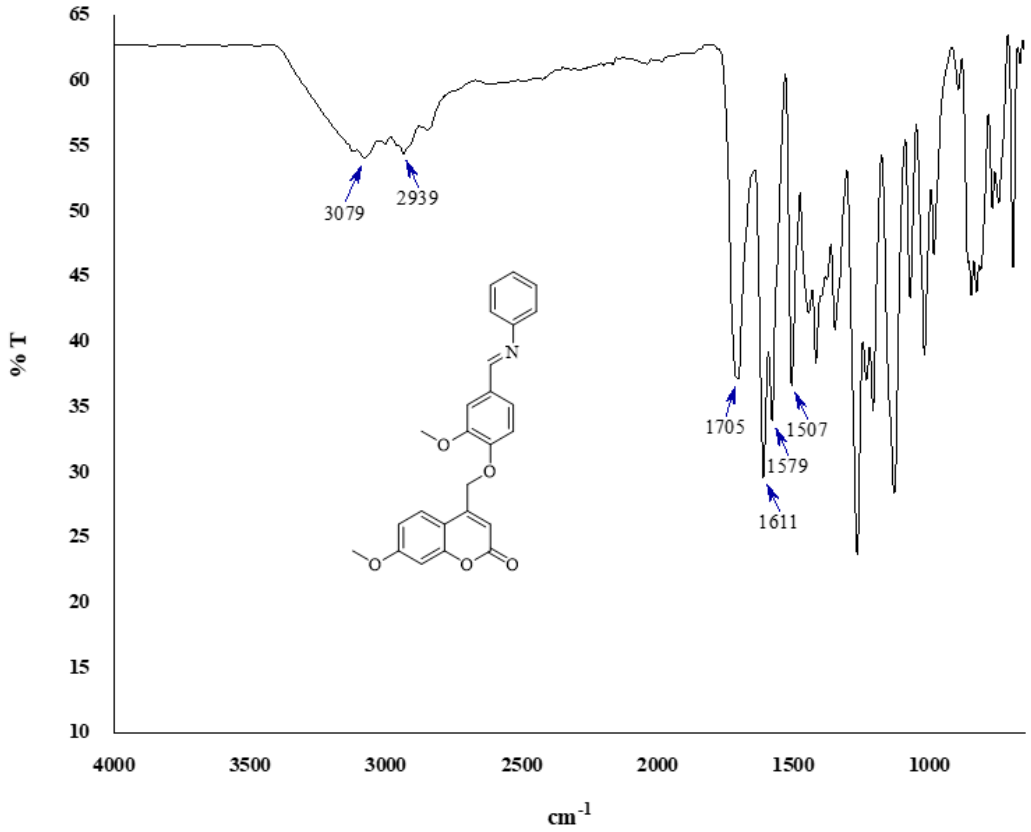
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C25 H20 Cl N O5	450.1102	0.243	Find By Formula	449.1028



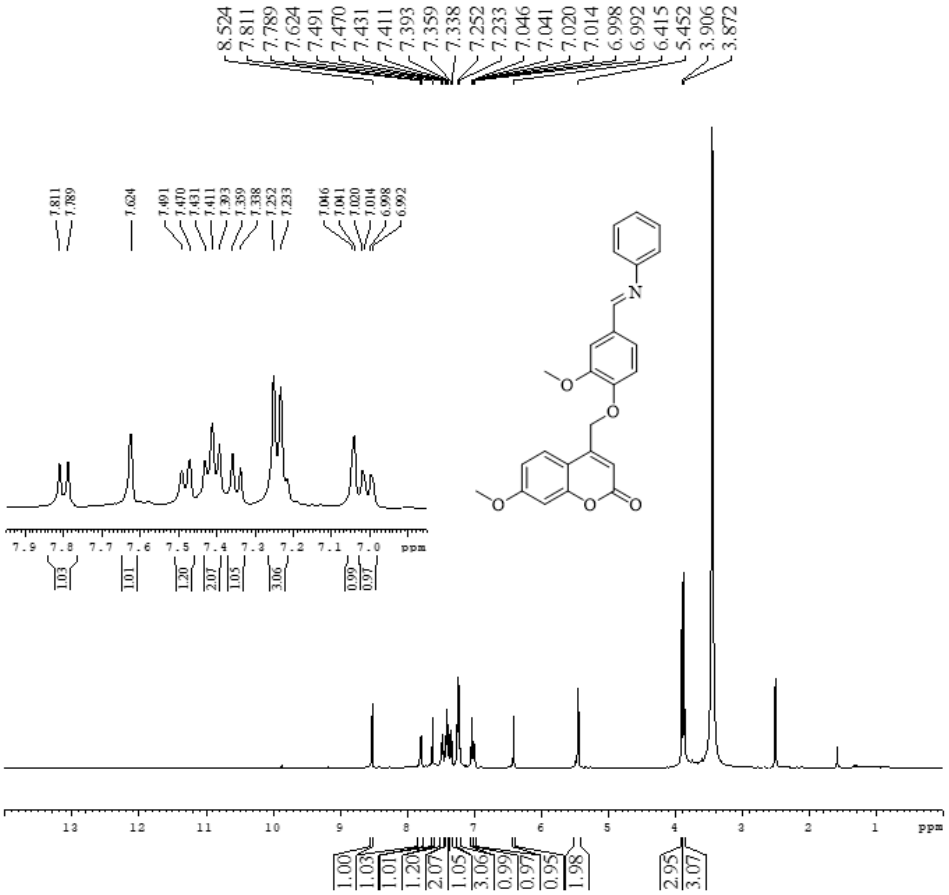
MS Zoomed Spectrum



HRMS of (*E*)-4-((4-(((4-chlorophenyl)imino)methyl)-2-methoxy phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13d)**



IR spectrum of (*E*)-7-methoxy-4-((2-methoxy-4-((phenylimino)methyl) phenoxy)methyl)-2*H*-chromen-2-one **(13e)**

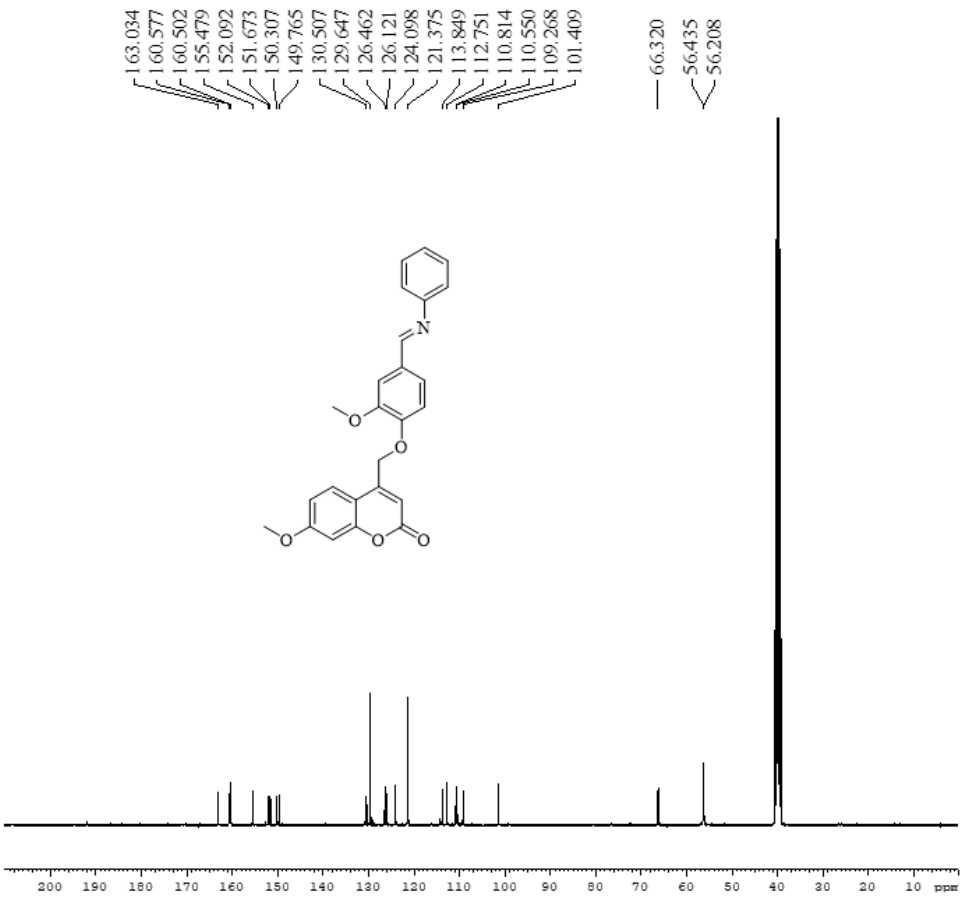


BRUKER

```
NAME          S97OMC-DMSO
EXPNO                   1
PROCNO                  1
Date_            20201007
Time                16.43
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                    144
DW                60.800 usec
DE                 6.50 usec
TE                300.0 K
D1            1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  6.00 usec
PL1                -6.00 dB
SFO1         400.1324710 MHz
SI                  32768
SF           400.1300000 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.00
```

^{1}H NMR spectrum of (*E*)-7-methoxy-4-((2-methoxy-4-((phenylimino)methyl) phenoxy)methyl)-2*H*-chromen-2-one

(13e)



BRUKER

```
NAME          S97OMC-DMSO
EXPNO                   2
PROCNO                  1
Date_            20201008
Time                15.27
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT              DMSO
NS                  20480
DS                      4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 12.00 usec
PL1                -1.00 dB
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz65
NUC2                   1H
PCPD2              80.00 usec
PL2                -6.00 dB
PL12               19.50 dB
PL13               19.50 dB
SFO2         400.1316005 MHz
SI                  32768
SF           100.6127690 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                   1.40
```

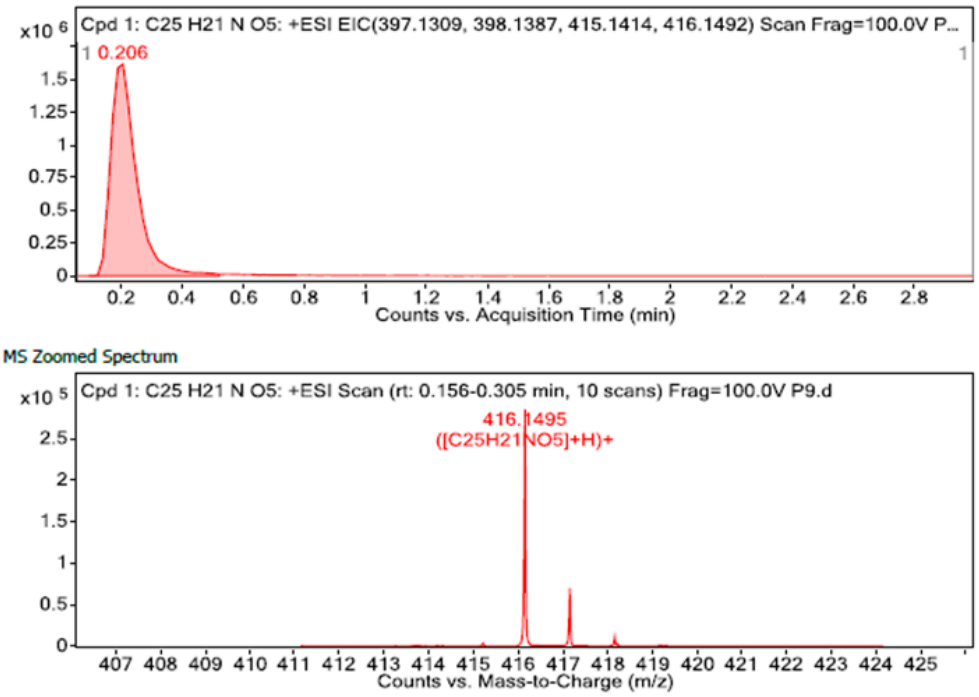
^{13}C NMR spectrum of (*E*)-7-methoxy-4-((2-methoxy-4-((phenylimino)methyl) phenoxy)methyl)-2*H*-chromen-2-one

(13e)

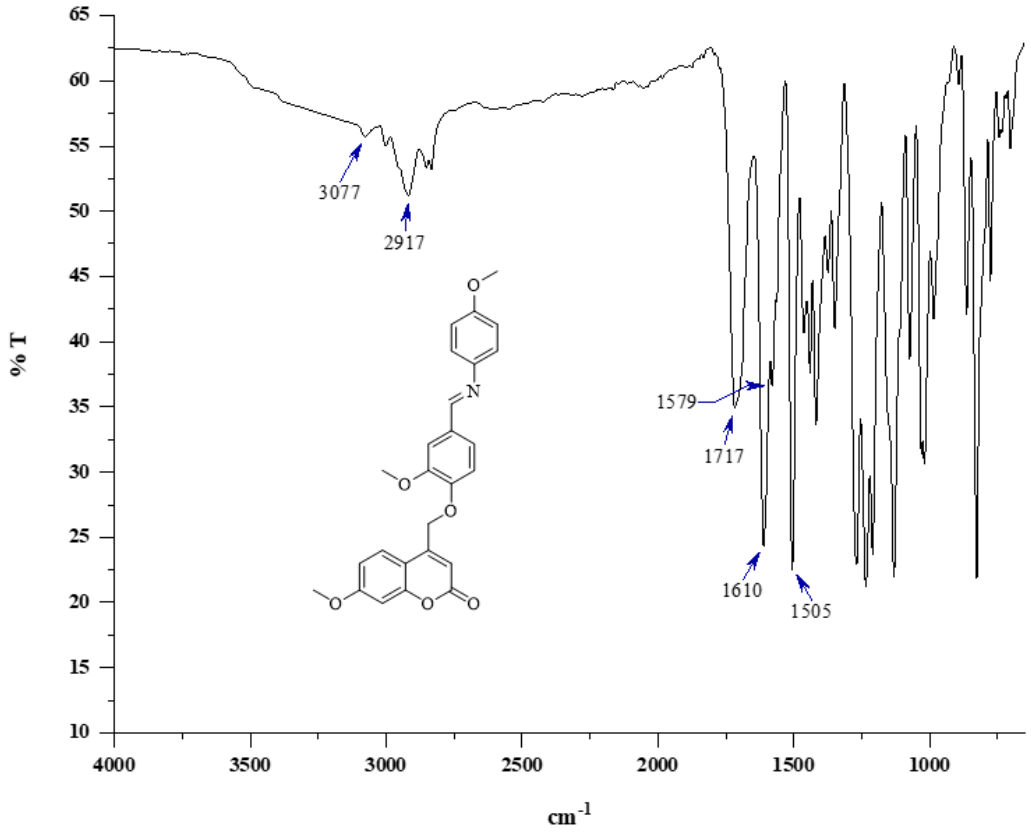
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C25 H21 N O5	0.206	415.1421	287628	C25 H21 N O5	415.142	0.37

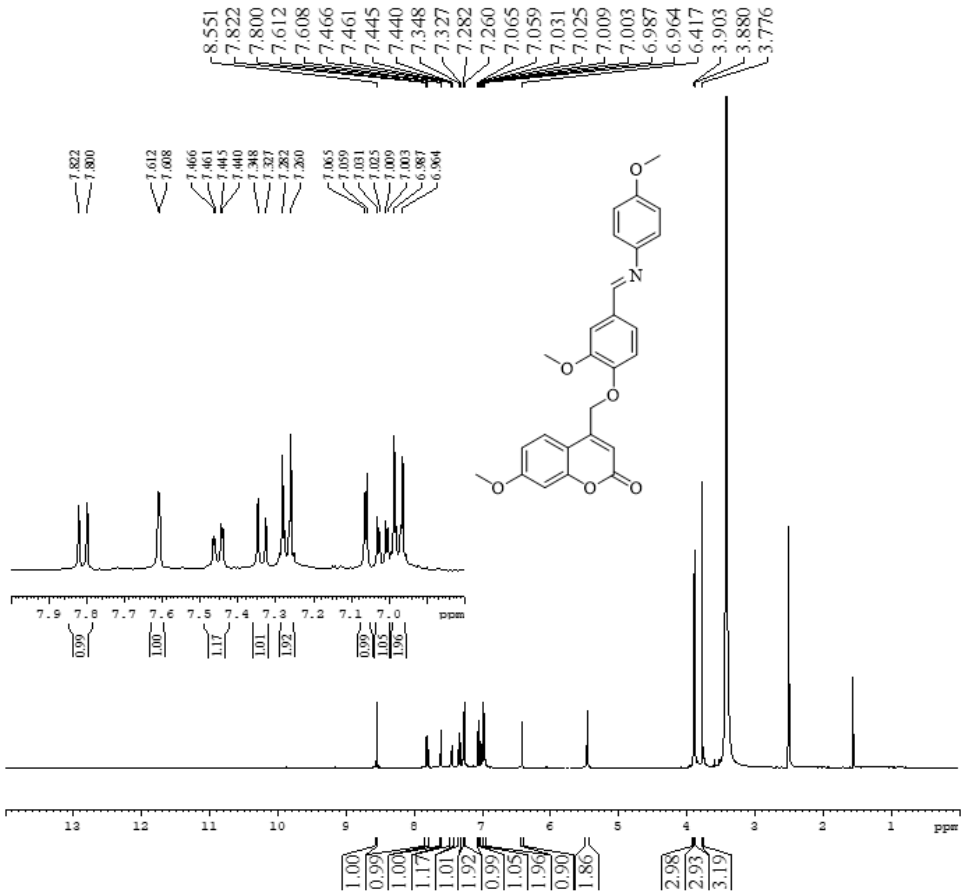
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C25 H21 N O5	416.1495	0.206	Find By Formula	415.1421



HRMS of (*E*)-7-methoxy-4-((2-methoxy-4-((phenylimino)methyl) phenoxy)methyl)-2*H*-chromen-2-one **(13e)**

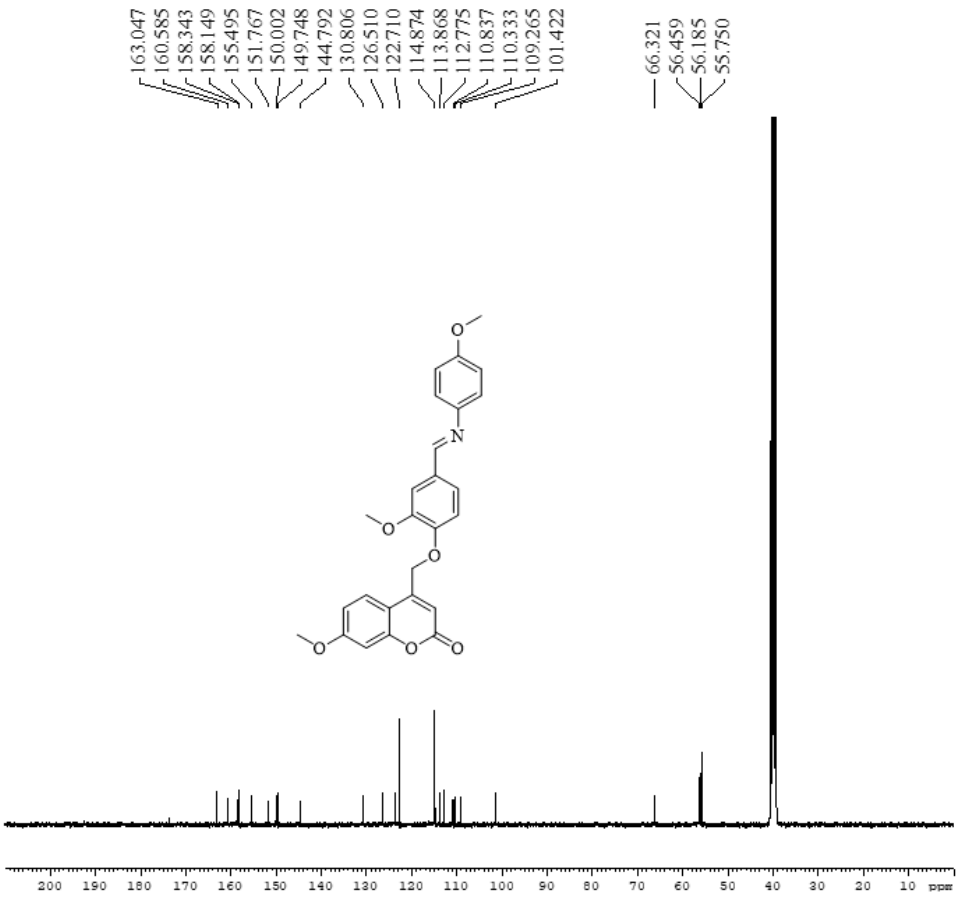


IR spectrum of (*E*)-7-methoxy-4-((2-methoxy-4-(((4-methoxyphenyl)imino) methyl)phenoxy)methyl)-2*H*-chromen-2-one **(13f)**




```
NAME          S107OMC-DMSO
EXPNO                    3
PROCNO                   1
Date_             20201007
Time_                16.23
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG               zg30
TD                   65536
SOLVENT               DMSO
NS                      16
DS                       2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846287 sec
RG                     203
DW                60.800 usec
DE                 6.50 usec
TE                300.0 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   1H
P1                 6.00 usec
PL1                -6.00 dB
SFO1         400.1324710 MHz
SI                   32768
SF           400.1300000 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                 1.00
```

^{1}H NMR spectrum of (*E*)-7-methoxy-4-((2-methoxy-4-(((4-methoxyphenyl)imino) methyl)phenoxy)methyl)-2*H*-chromen-2-one **(13f)**



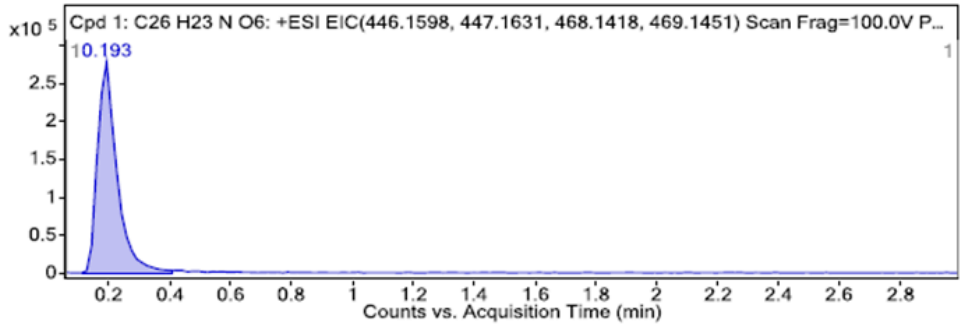

```
NAME          S107OMC-DMSO
EXPNO                    3
PROCNO                   1
Date_             20201007
Time_                17.15
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT               DMSO
NS                    16384
DS                       4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                     203
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                12.00 usec
PL1                -1.00 dB
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz65
NUC2                   1H
PCPD2             80.00 usec
PL2                -6.00 dB
PL12               19.50 dB
PL13               19.50 dB
SFO2         400.1316005 MHz
SI                   32768
SF           100.6127690 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                 1.40
```

^{13}C NMR spectrum of (*E*)-7-methoxy-4-((2-methoxy-4-(((4-methoxyphenyl)imino) methyl)phenoxy)methyl)-2*H*-chromen-2-one **(13f)**

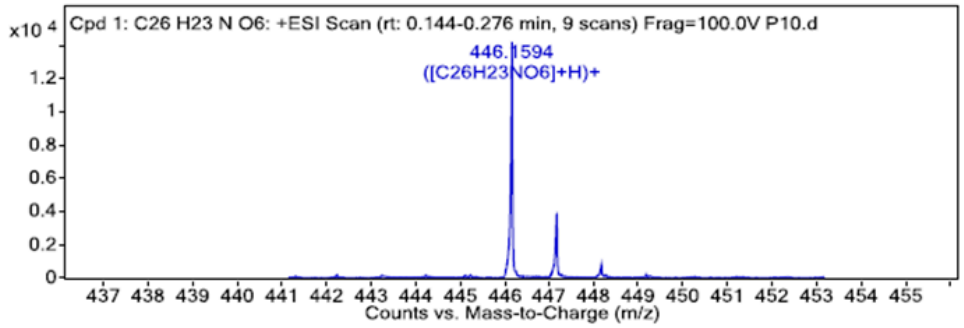
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C26 H23 N O6	0.193	445.1519	14309	C26 H23 N O6	445.1525	-1.53

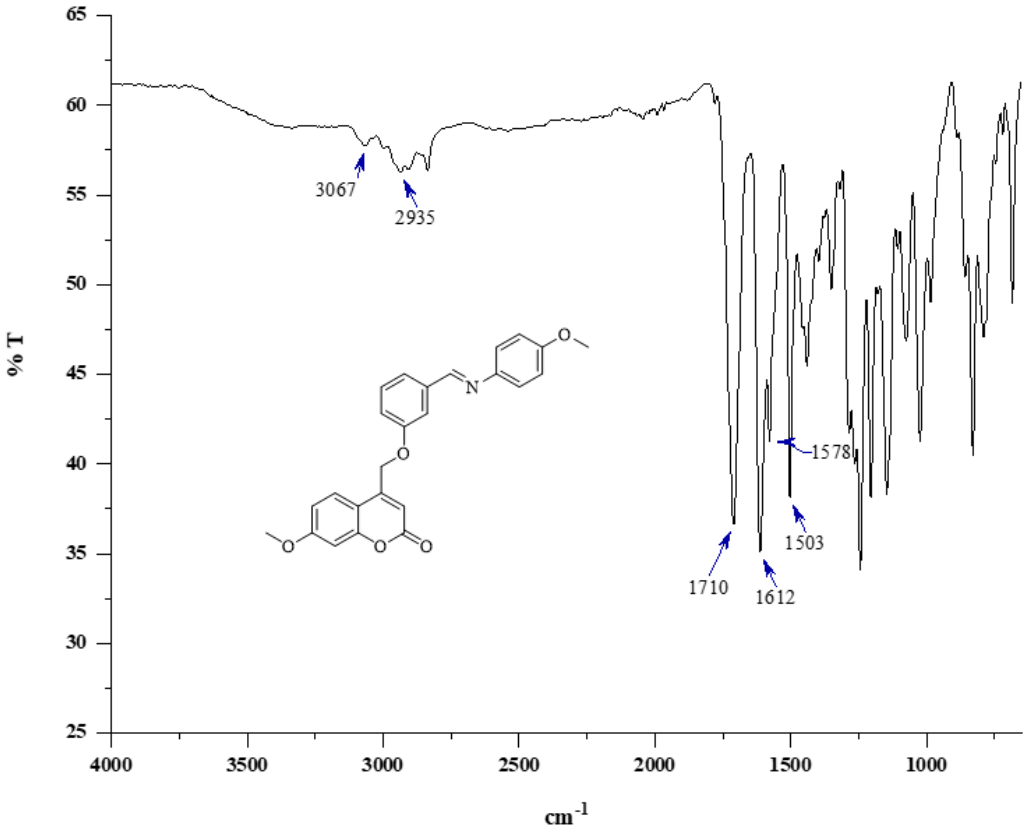
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C26 H23 N O6	446.1594	0.193	Find By Formula	445.1519



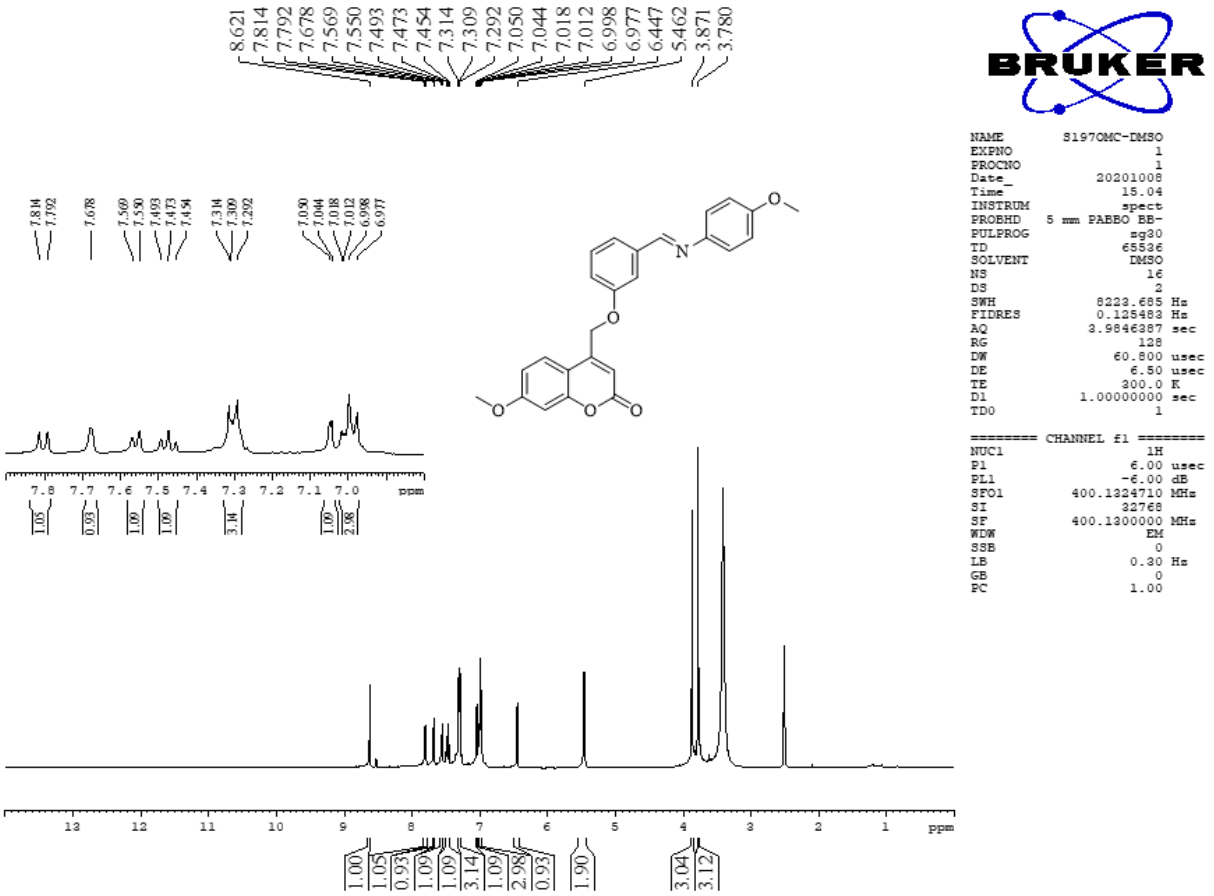
MS Zoomed Spectrum



HRMS of (*E*)-7-methoxy-4-((2-methoxy-4-(((4-methoxyphenyl)imino) methyl)phenoxy)methyl)-2*H*-chromen-2-one **(13f)**



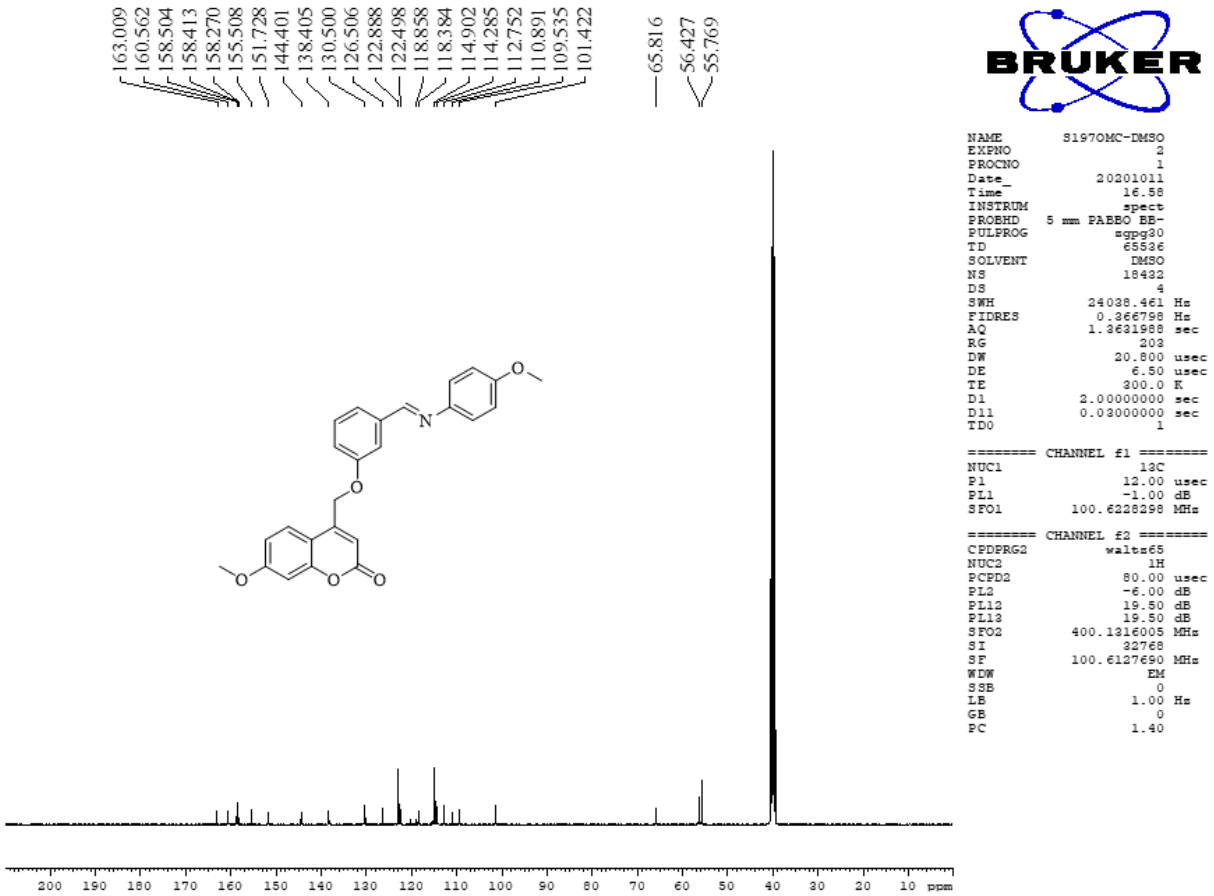
IR spectrum of (*E*)-7-methoxy-4-((3-(((4-methoxyphenyl)imino)methyl) phenoxy)methyl)-2*H*-chromen-2-one **(13g)**



NAME S197OMC-DMSO
EXPNO 1
PROCNO 1
Date_ 20201008
Time 15.04
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 128
DW 60.800 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 6.00 usec
PL1 -6.00 dB
SFO1 400.1324710 MHz
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

^{1}H NMR spectrum of (*E*)-7-methoxy-4-((3-(((4-methoxyphenyl)imino)methyl) phenoxy)methyl)-2*H*-chromen-2-one
(13g)



NAME S197OMC-DMSO
EXPNO 2
PROCNO 1
Date_ 20201011
Time 16.58
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 18432
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 12.00 usec
PL1 -1.00 dB
SFO1 100.6228298 MHz

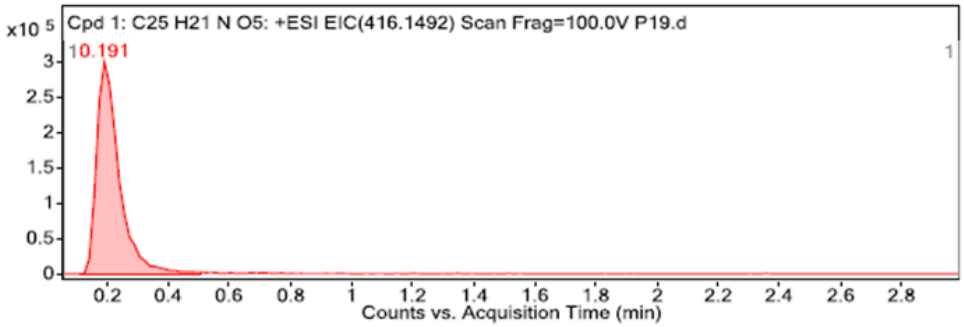
======== CHANNEL f2 ========
CPDPRG2 waltz65
NUC2 1H
PCPD2 80.00 usec
PL2 -6.00 dB
PL12 19.50 dB
PL13 19.50 dB
SFO2 400.1316005 MHz
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

^{13}C NMR spectrum of (*E*)-7-methoxy-4-((3-(((4-methoxyphenyl)imino)methyl) phenoxy)methyl)-2*H*-chromen-2-one
(13g)

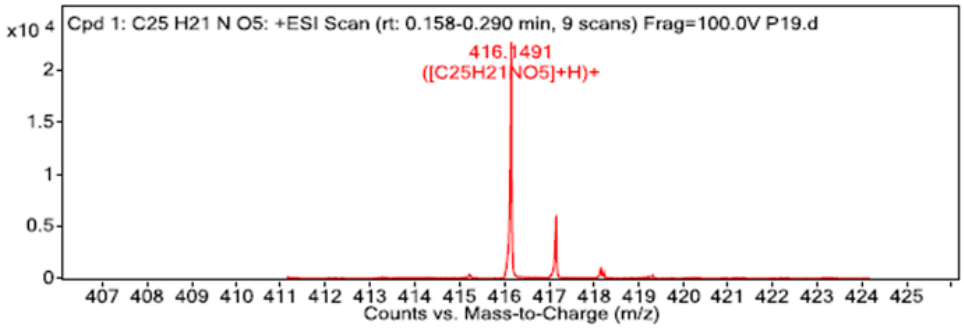
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C25 H21 N O5	0.191	415.1417	22797	C25 H21 N O5	415.142	-0.69

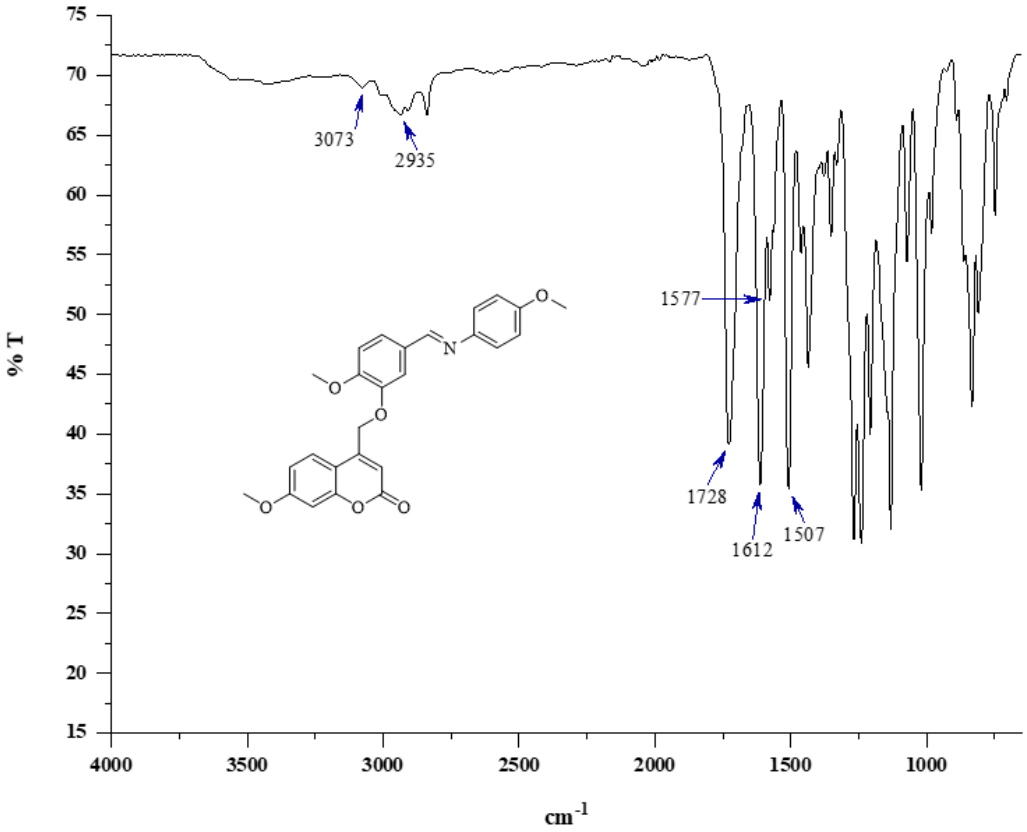
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C25 H21 N O5	416.1491	0.191	Find By Formula	415.1417



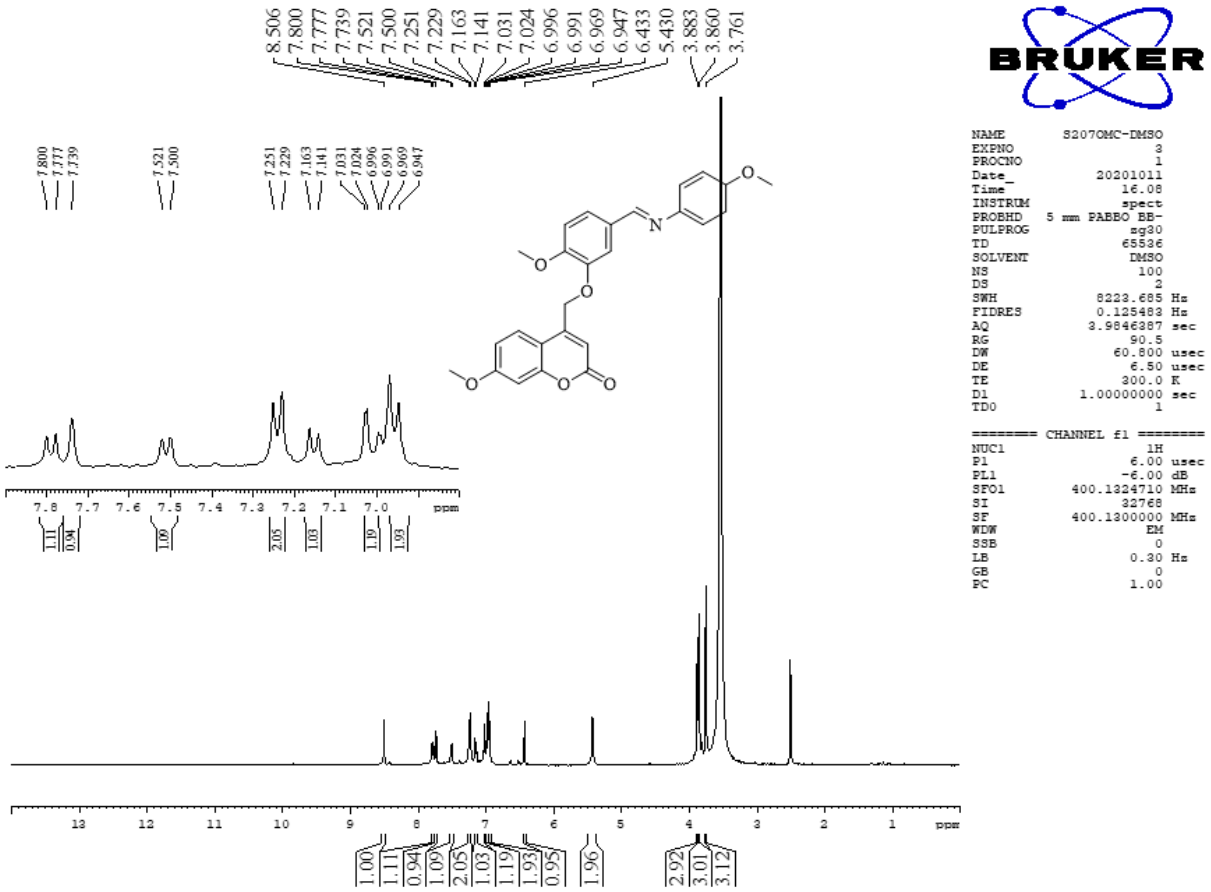
MS Zoomed Spectrum



HRMS of (*E*)-7-methoxy-4-((3-(((4-methoxyphenyl)imino)methyl) phenoxy)methyl)-2*H*-chromen-2-one **(13g)**

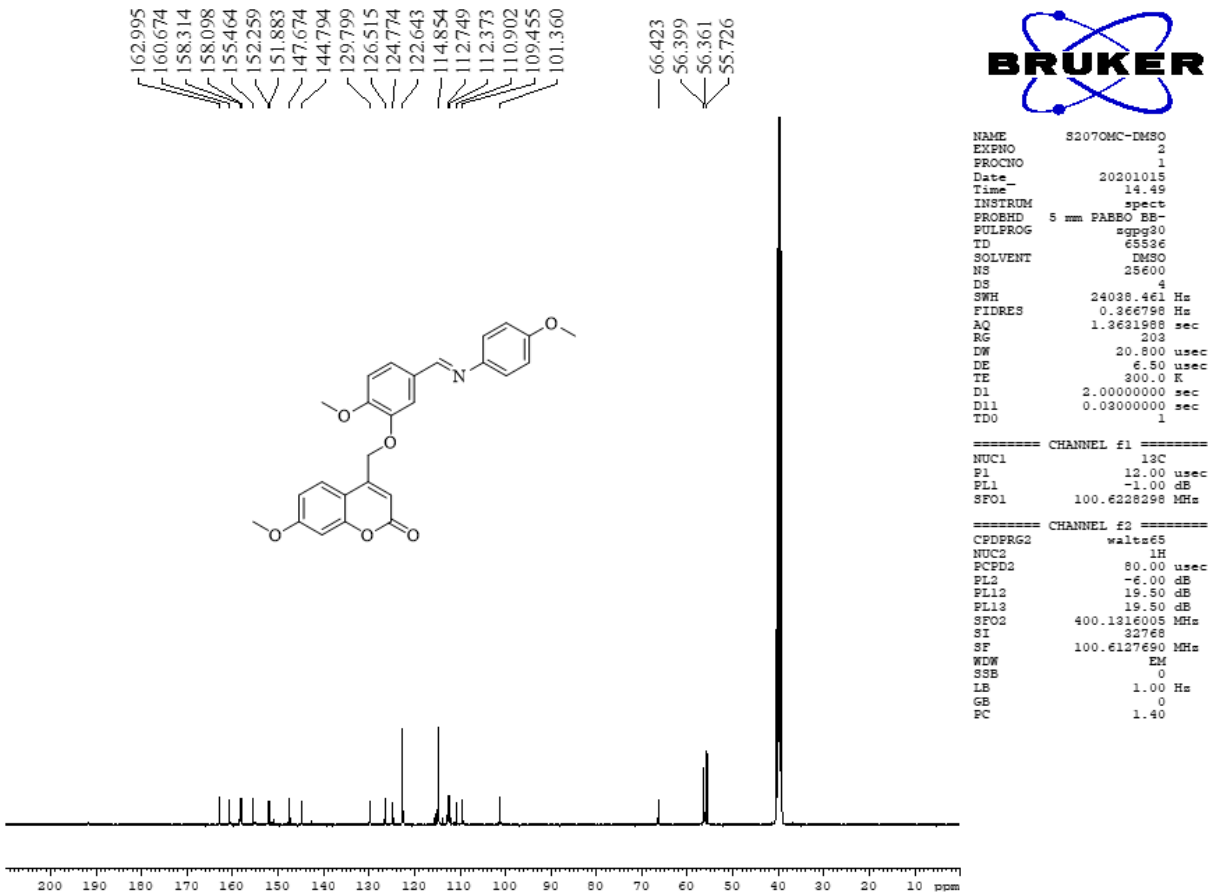


IR spectrum of (*E*)-7-methoxy-4-((2-methoxy-5-(((4-methoxyphenyl)imino) methyl)phenoxy)methyl)-2*H*-chromen-2-one **(13h)**




```
NAME          S207OMC-DMSO
EXPNO                    3
PROCNO                   1
Date_             20201011
Time                 16.08
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                    100
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                   90.5
DW                 60.800 usec
DE                  6.50 usec
TE                 300.0 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  6.00 usec
PL1                -6.00 dB
SFO1         400.1324710 MHz
SI                  32768
SF           400.1300000 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

^{1}H NMR spectrum of (*E*)-7-methoxy-4-((2-methoxy-5-(((4-methoxyphenyl)imino) methyl)phenoxy)methyl)-2*H*-chromen-2-one **(13h)**



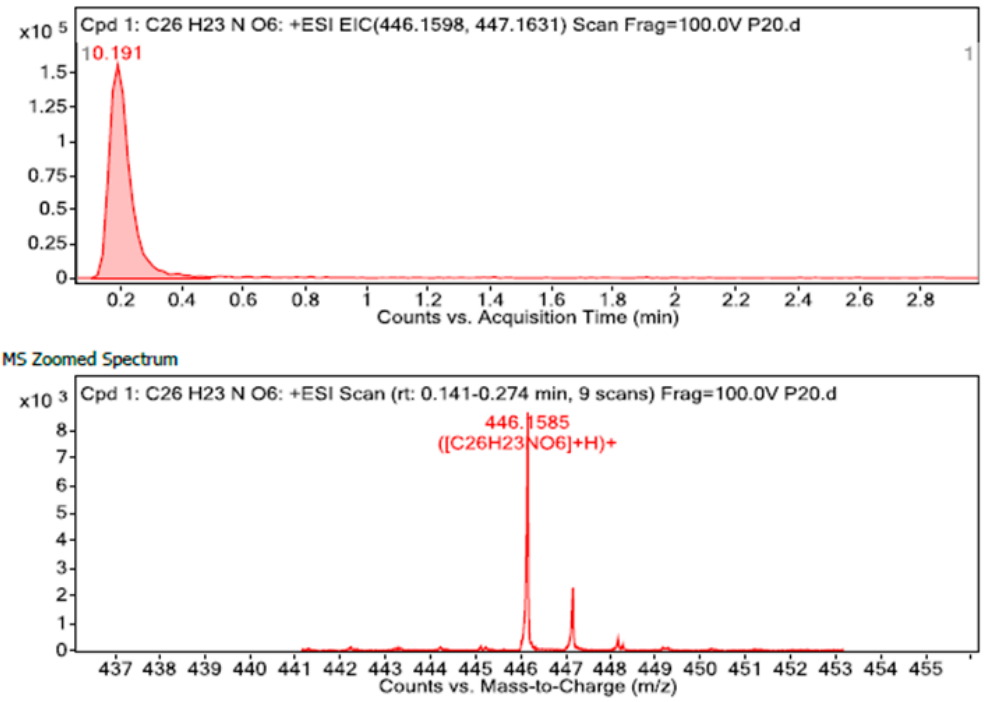

```
NAME          S207OMC-DMSO
EXPNO                    2
PROCNO                   1
Date_             20201015
Time                 14.49
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   25600
DS                       4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                     203
DW                 20.800 usec
DE                  6.50 usec
TE                 300.0 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 12.00 usec
PL1                -1.00 dB
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz65
NUC2                   1H
PCPD2              80.00 usec
PL2                -6.00 dB
PL12               19.50 dB
PL13               19.50 dB
SFO2         400.1316005 MHz
SI                  32768
SF           100.6127690 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

^{13}C NMR spectrum of (*E*)-7-methoxy-4-((2-methoxy-5-(((4-methoxyphenyl)imino) methyl)phenoxy)methyl)-2*H*-chromen-2-one **(13h)**

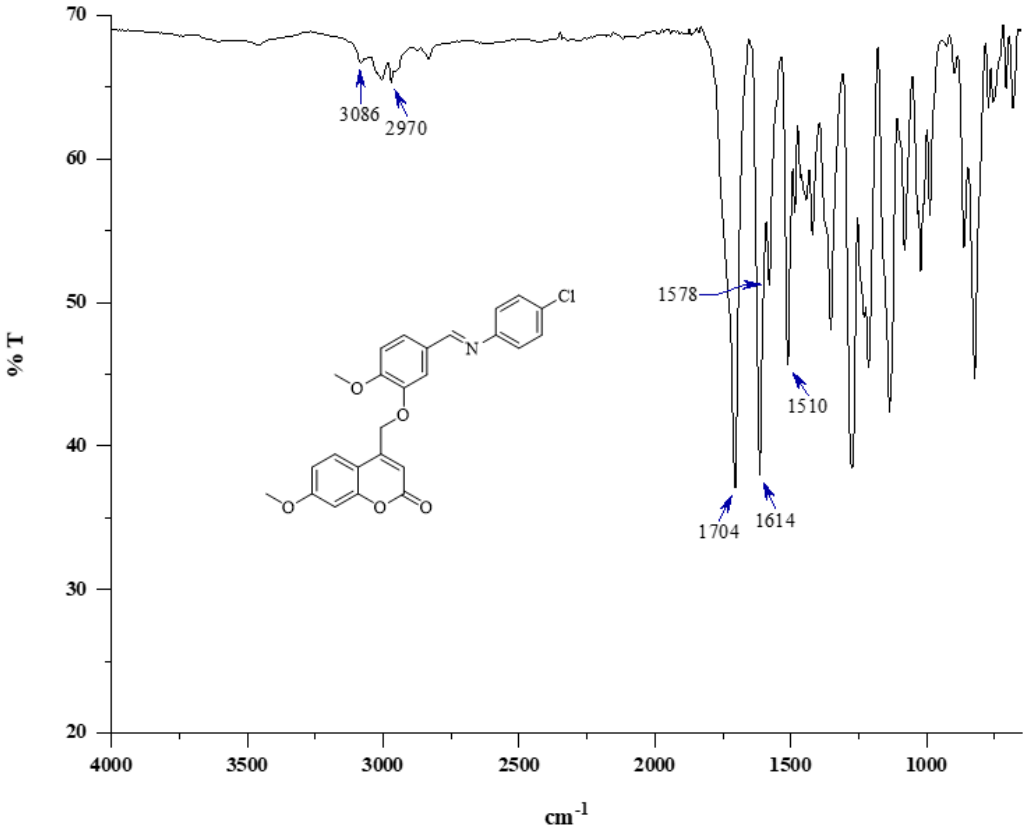
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C26 H23 N O6	0.191	445.1512	8662	C26 H23 N O6	445.1525	-3

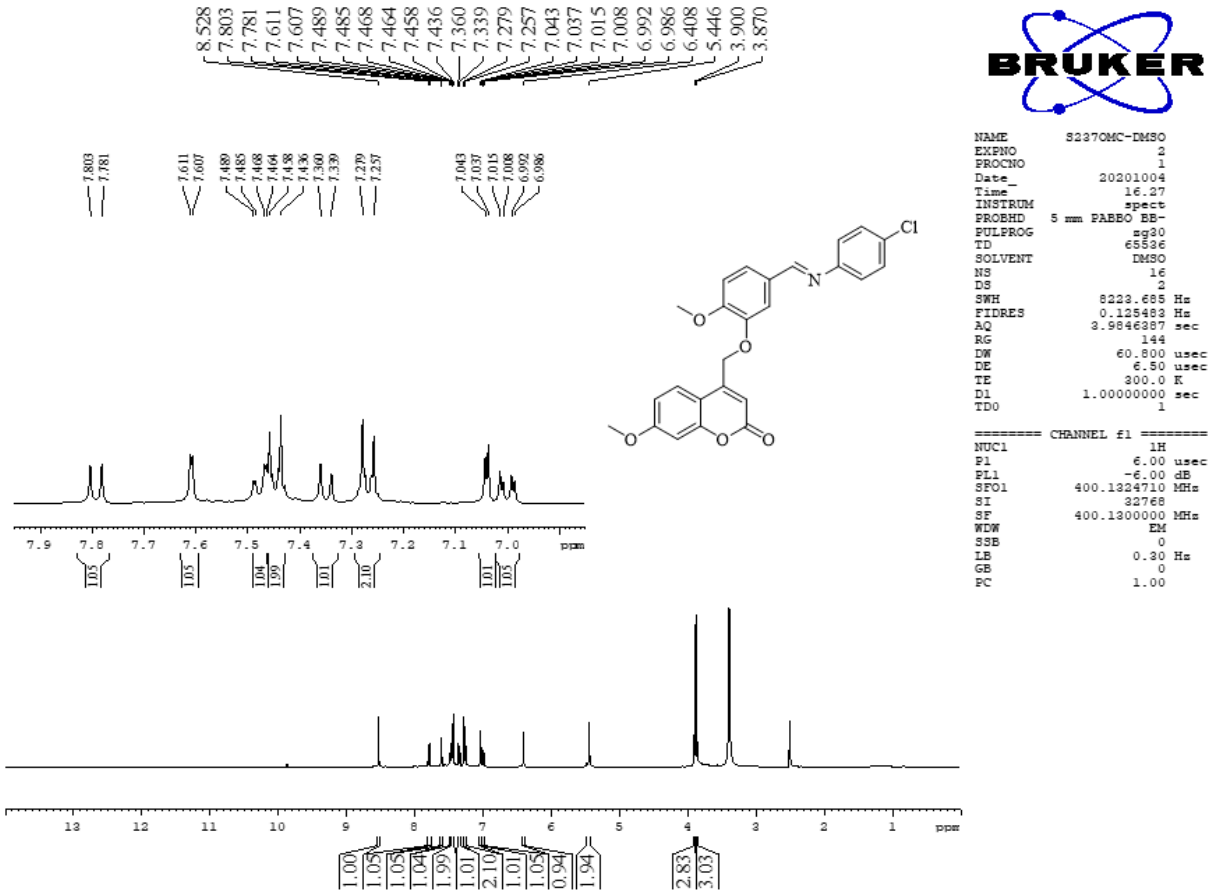
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C26 H23 N O6	446.1585	0.191	Find By Formula	445.1512



HRMS of (*E*)-7-methoxy-4-((2-methoxy-5-(((4-methoxyphenyl)imino) methyl)phenoxy)methyl)-2*H*-chromen-2-one **(13h)**

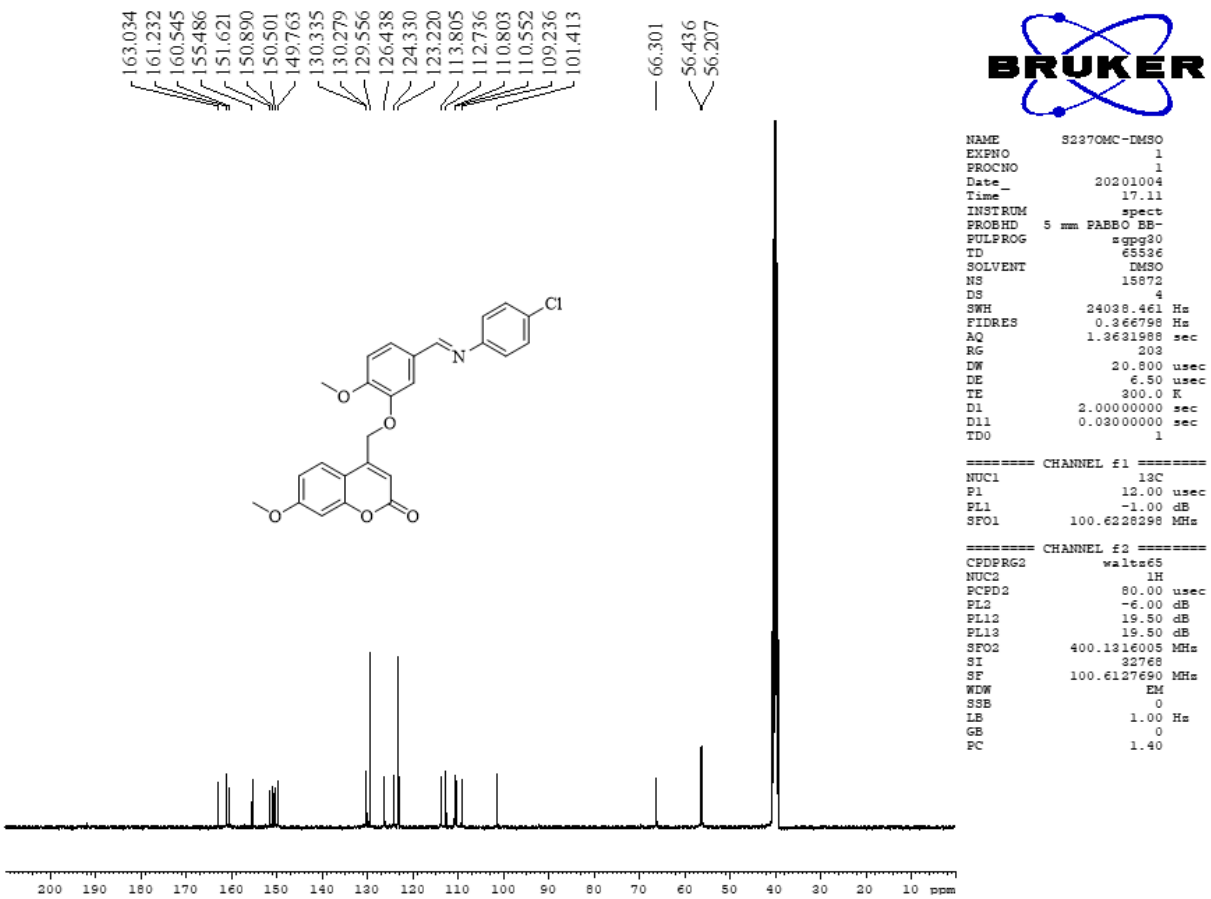


IR spectrum of (*E*)-4-((5-(((4-chlorophenyl)imino)methyl)-2-methoxy phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13i)**




```
NAME          S2370MC-DMSO
EXPNO                    2
PROCNO                   1
Date_             20201004
Time                 16.27
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                    144
DW                60.800 usec
DE                 6.50 usec
TE                300.0 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 6.00 usec
PL1                -6.00 dB
SFO1         400.1324710 MHz
SI                  32768
SF           400.1300000 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.00
```

^{1}H NMR spectrum of (*E*)-4-((5-(((4-chlorophenyl)imino)methyl)-2-methoxy phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13i)**



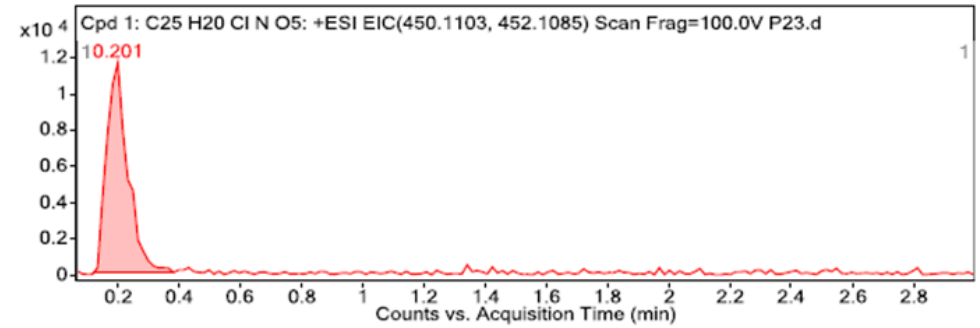

```
NAME          S2370MC-DMSO
EXPNO                    1
PROCNO                   1
Date_             20201004
Time                 17.11
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                  15872
DS                      4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                12.00 usec
PL1                -1.00 dB
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz65
NUC2                   1H
PCPD2             80.00 usec
PL2                -6.00 dB
PL12               19.50 dB
PL13               19.50 dB
SFO2         400.1316005 MHz
SI                  32768
SF           100.6127690 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                   1.40
```

^{13}C NMR spectrum of (*E*)-4-((5-(((4-chlorophenyl)imino)methyl)-2-methoxy phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13i)**

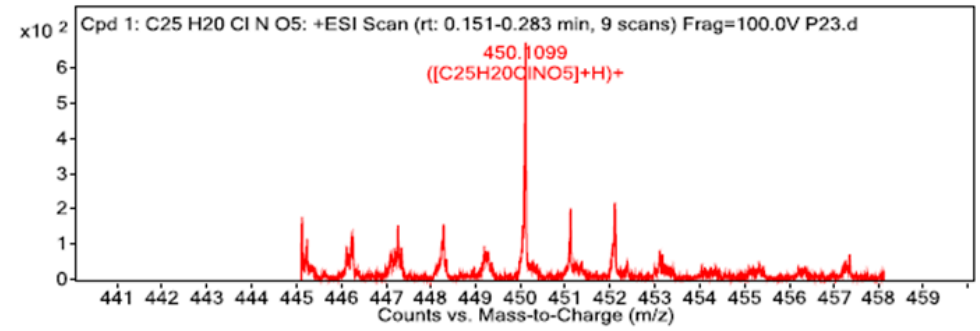
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C25 H20 Cl N O5	0.201	449.1029	691	C25 H20 Cl N O5	449.103	-0.19

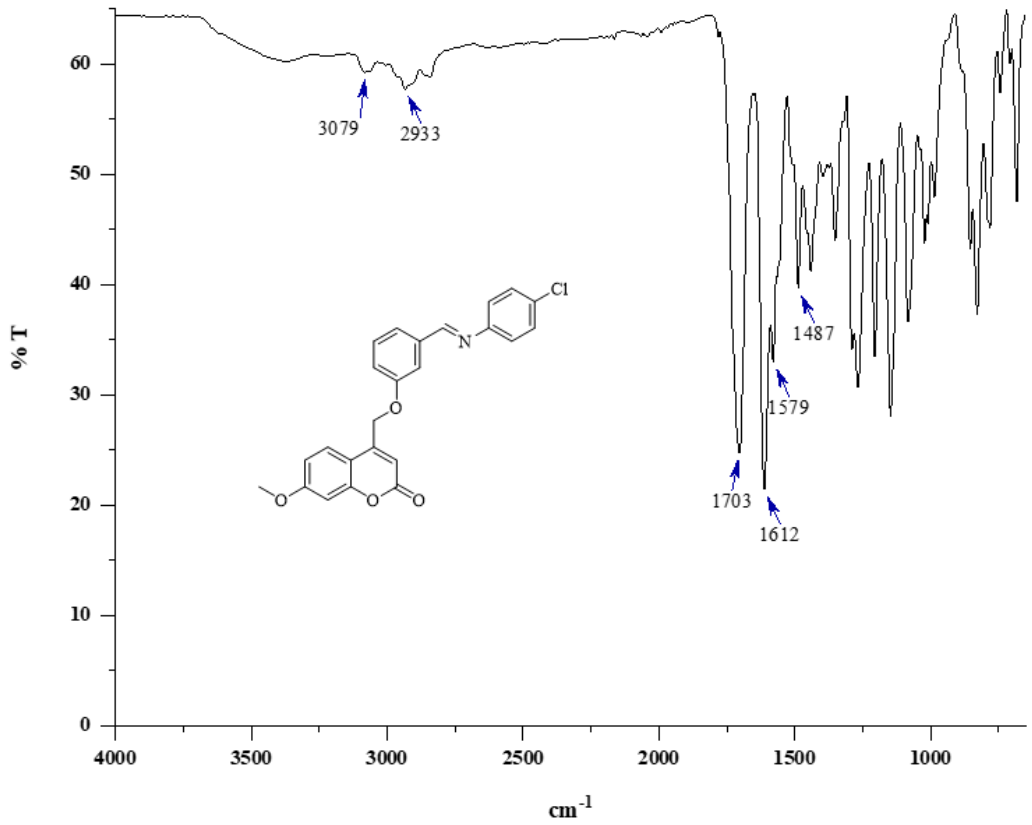
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C25 H20 Cl N O5	450.1099	0.201	Find By Formula	449.1029



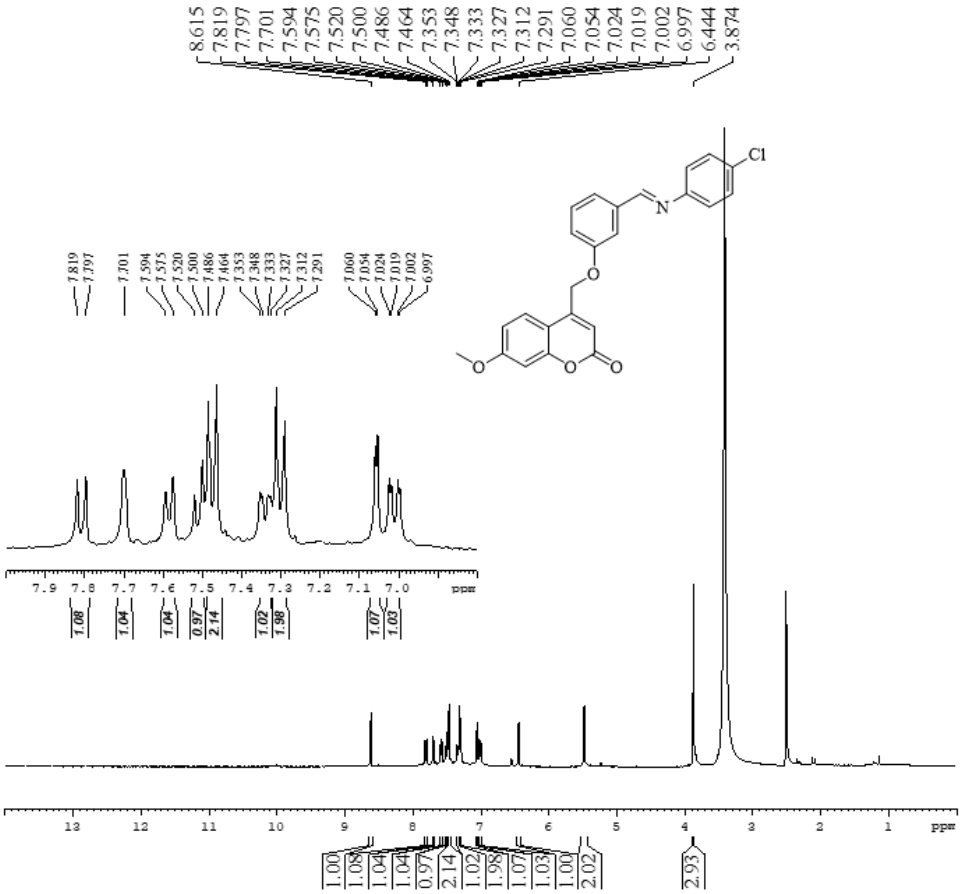
MS Zoomed Spectrum



HRMS of (*E*)-4-((5-(((4-chlorophenyl)imino)methyl)-2-methoxy phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13i)**



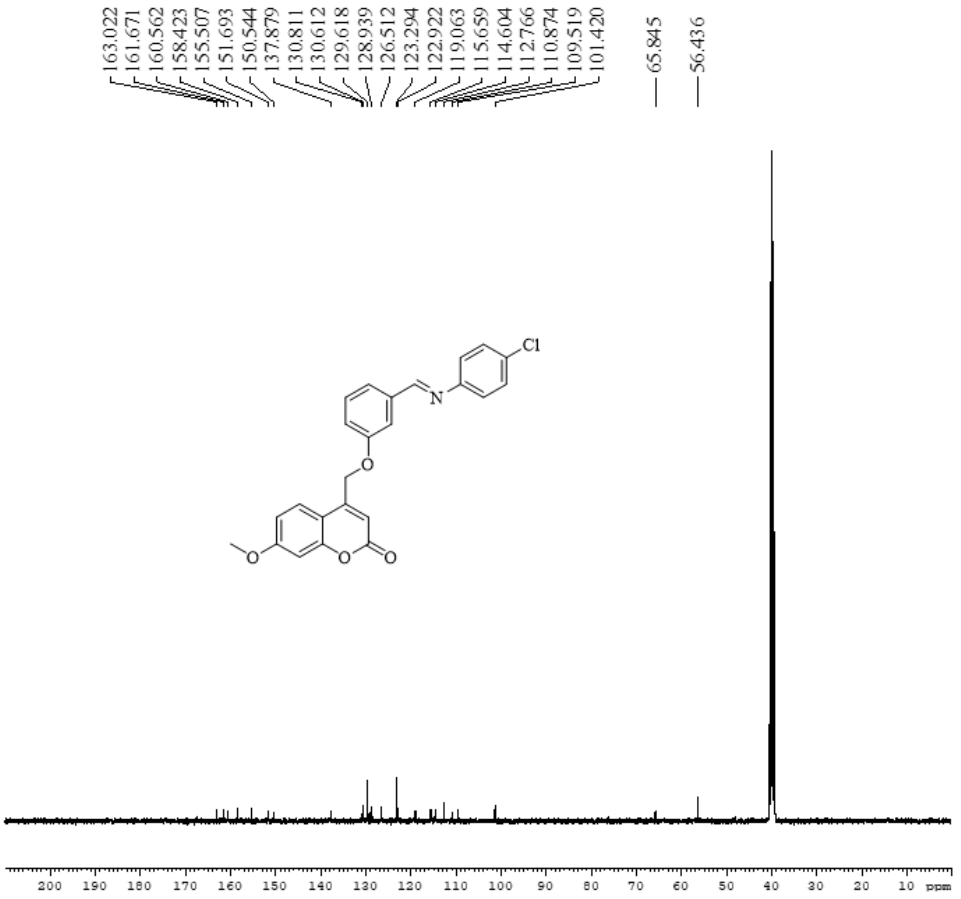
IR spectrum of (*E*)-4-((3-(((4-chlorophenyl)imino)methyl)phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13j)**




```
NAME          S2470MC-DMSO
EXPNO                    1
PROCNO                   1
Date_             20201015
Time                 11.12
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG               zg30
TD                   65536
SOLVENT               DMSO
NS                      16
DS                       2
SWH               8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9846387 sec
RG                     161
DW                  60.800 usec
DE                   6.50 usec
TE                  300.0 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   6.00 usec
PL1                 -6.00 dB
SFO1           400.1324710 MHz
SI                   32768
SF             400.1300000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

^{1}H NMR spectrum of (*E*)-4-((3-(((4-chlorophenyl)imino)methyl)phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one

(13j)




```
NAME          S2470MC-DMSO
EXPNO                    5
PROCNO                   1
Date_             20201018
Time                 16.23
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT               DMSO
NS                    1056
DS                       4
SWH              24038.461 Hz
FIDRES            0.366798 Hz
AQ                1.3631988 sec
RG                     203
DW                  20.800 usec
DE                   6.50 usec
TE                  300.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                  12.00 usec
PL1                 -1.00 dB
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz65
NUC2                    1H
PCPD2               80.00 usec
PL2                 -6.00 dB
PL12                19.50 dB
PL13                19.50 dB
SFO2           400.1316005 MHz
SI                   32768
SF             100.6127690 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

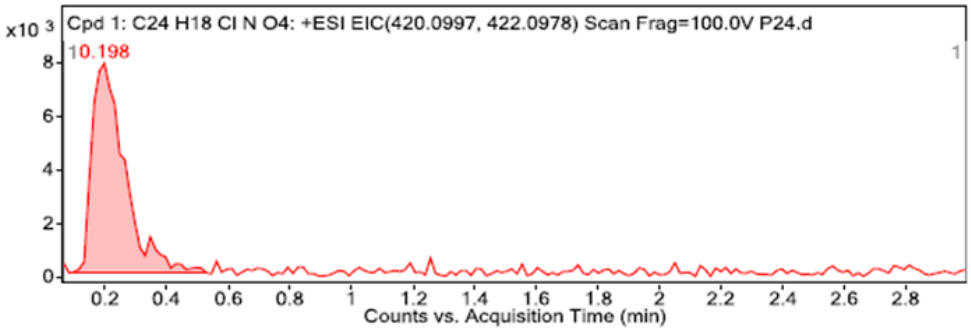
^{13}C NMR spectrum of (*E*)-4-((3-(((4-chlorophenyl)imino)methyl)phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one

(13j)

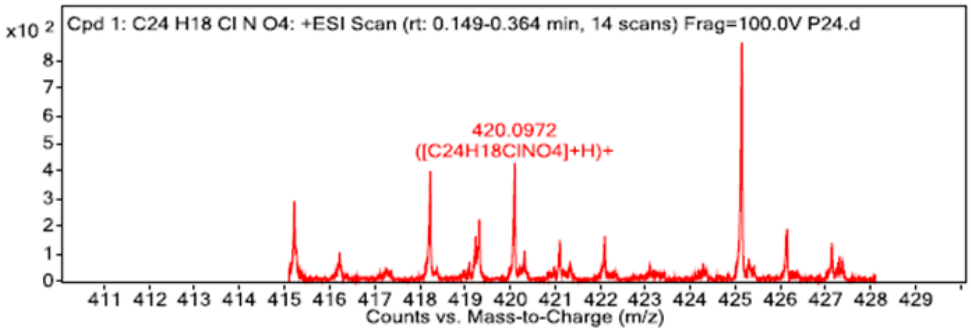
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C24 H18 Cl N O4	0.198	419.0908	429	C24 H18 Cl N O4	419.0924	-3.79

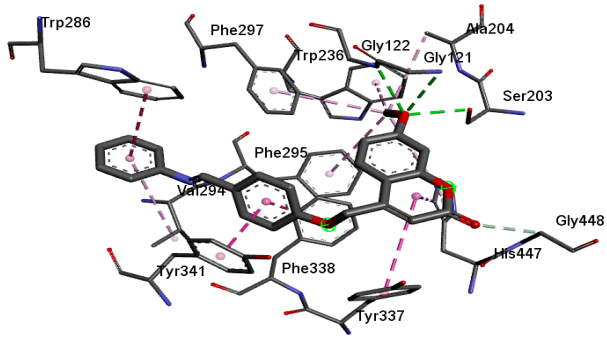
Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C24 H18 Cl N O4	420.0972	0.198	Find By Formula	419.0908



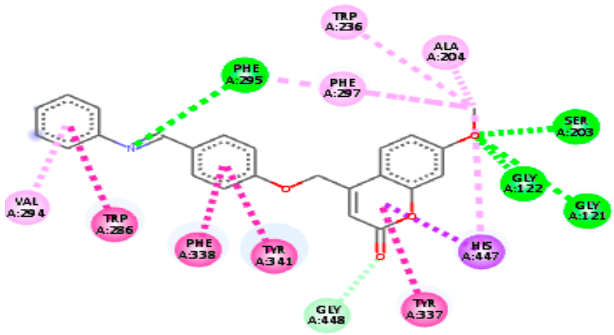
MS Zoomed Spectrum



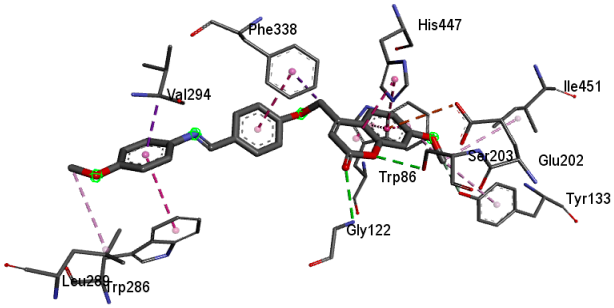
HRMS of (*E*)-4-((3-(((4-chlorophenyl)imino)methyl)phenoxy)methyl)-7-methoxy-2*H*-chromen-2-one **(13j)**



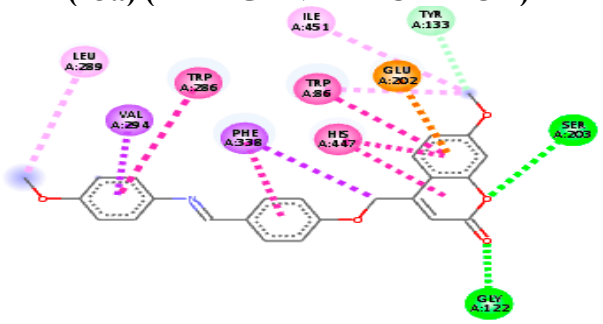
(13a) (3D LIGAND-RECEPTOR)



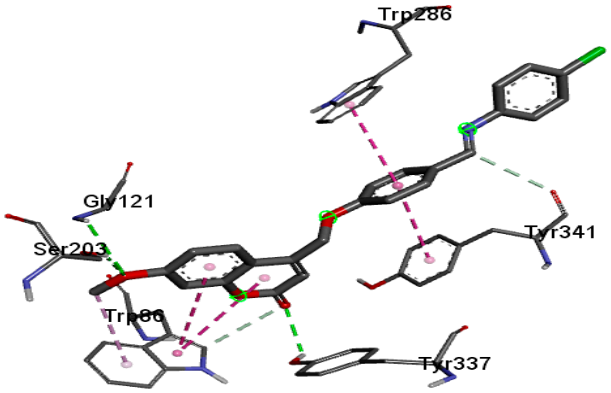
(13a) (2D LIGAND-RECEPTOR)



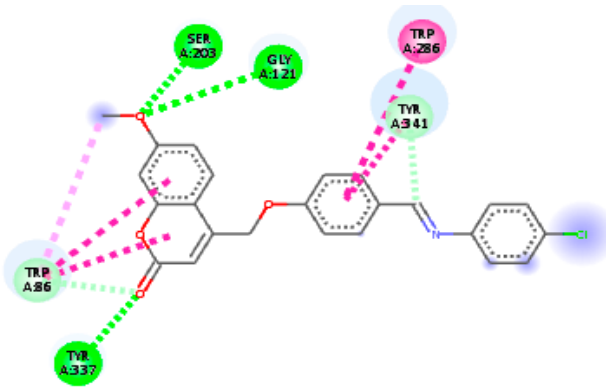
(13b) (3D LIGAND-RECEPTOR)



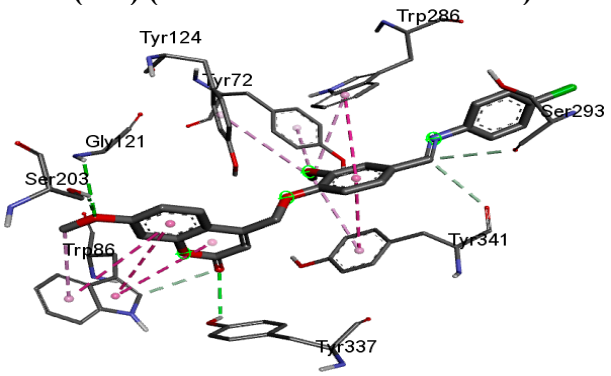
(13b) (2D LIGAND-RECEPTOR)



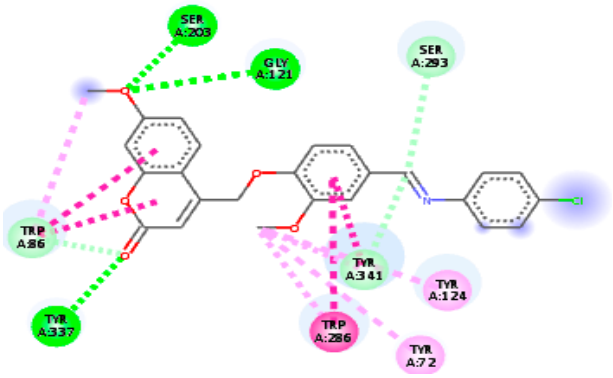
(13c) (3D LIGAND-RECEPTOR)



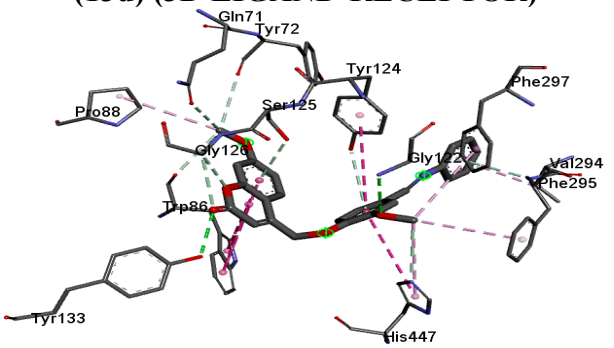
(13c) (2D LIGAND-RECEPTOR)



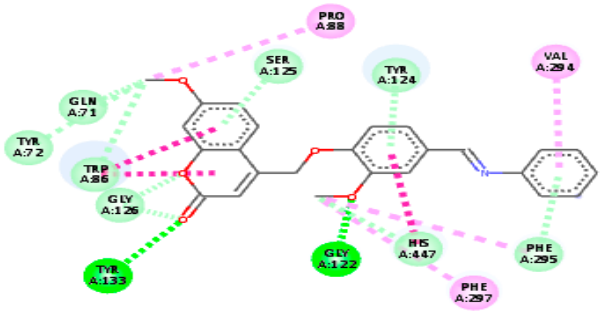
(13d) (3D LIGAND-RECEPTOR)



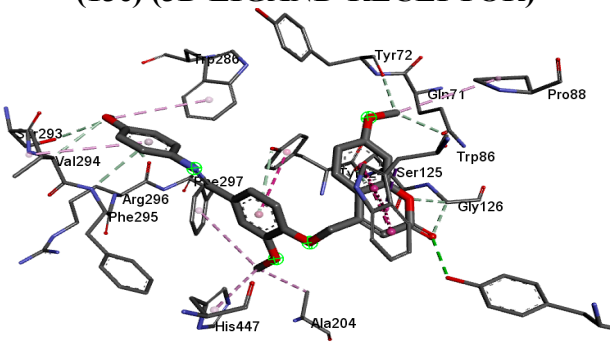
(13d) (2D LIGAND-RECEPTOR)



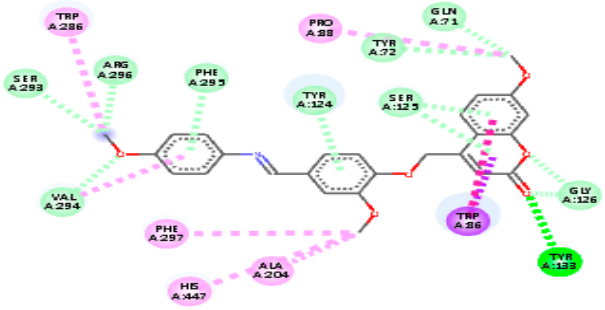
(13e) (3D LIGAND-RECEPTOR)



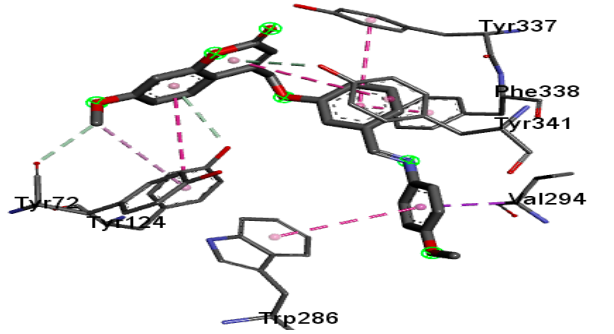
(13e) (2D LIGAND-RECEPTOR)



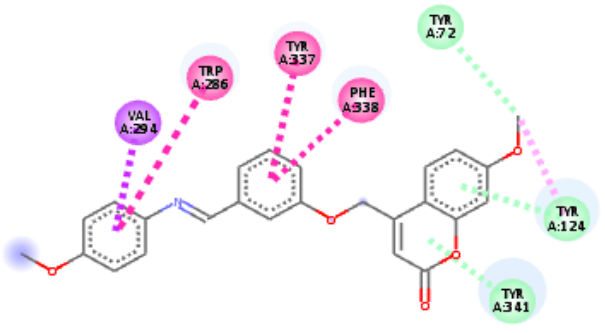
(13f) (3D LIGAND-RECEPTOR)



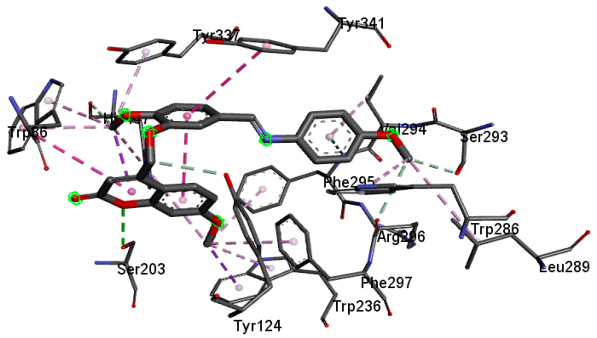
(13f) (2D LIGAND-RECEPTOR)



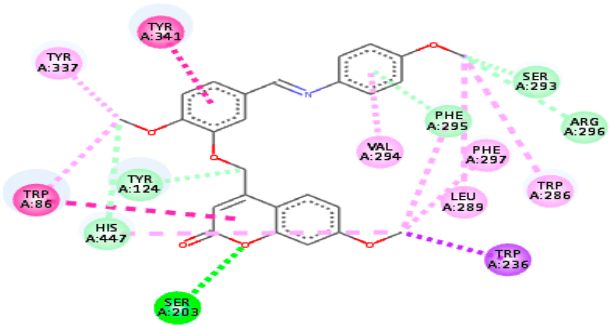
(13g) (3D LIGAND-RECEPTOR)



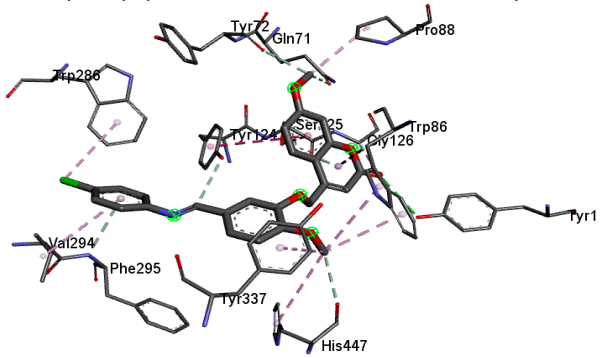
(13g) (2D LIGAND-RECEPTOR)



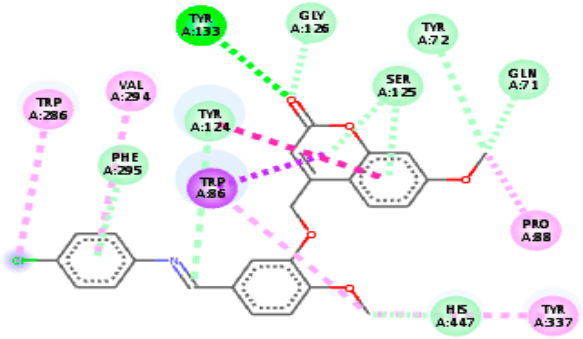
(13h) (3D LIGAND-RECEPTOR)



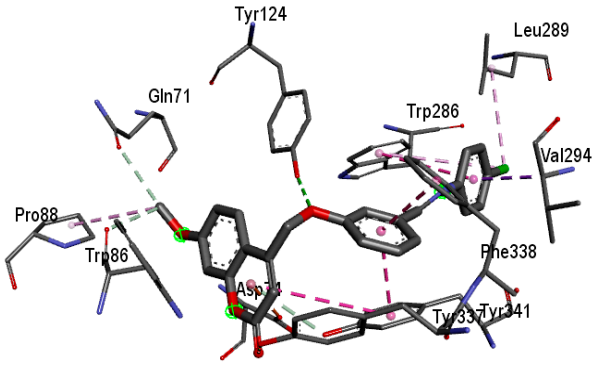
(13h) (2D LIGAND-RECEPTOR)



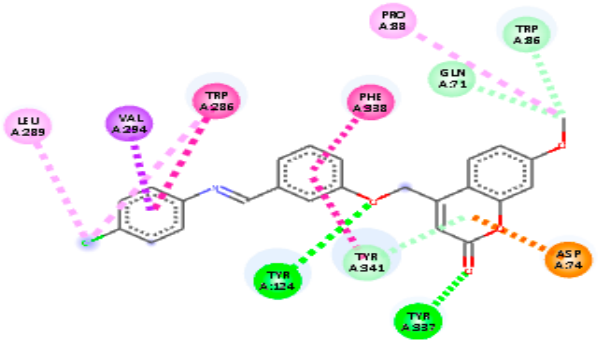
(13i) (3D LIGAND-RECEPTOR)



(13i) (2D LIGAND-RECEPTOR)



(13j) (3D LIGAND-RECEPTOR)



(13j) (2D LIGAND-RECEPTOR)

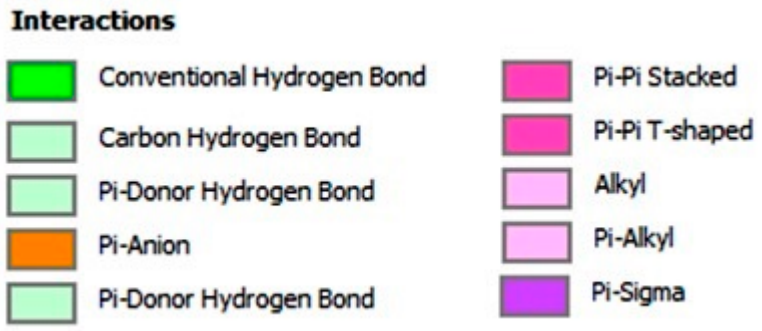
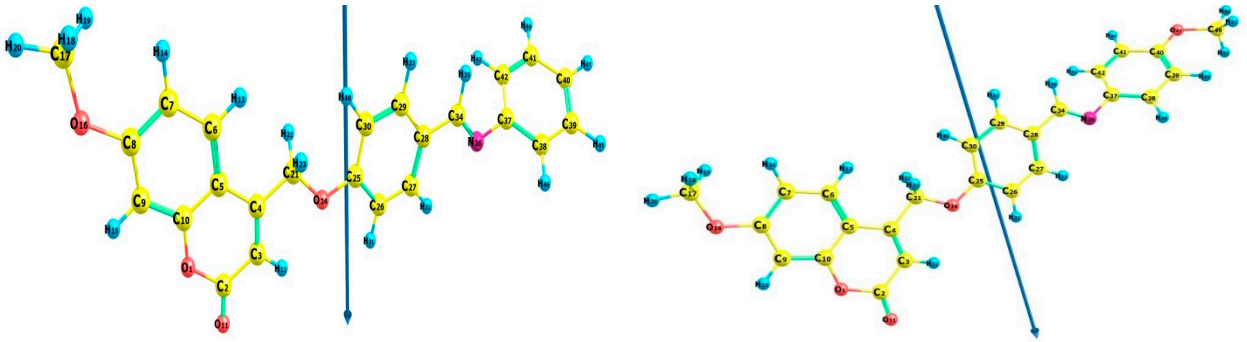
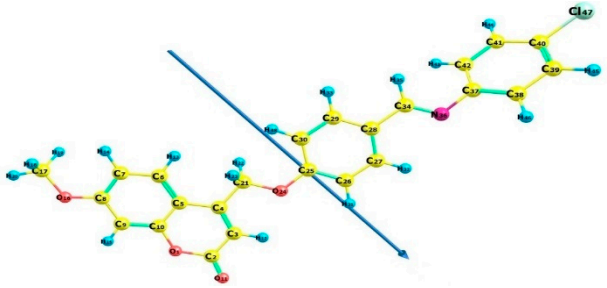


Figure S1. The proposed binding mode of newly synthesized hybrids (**13a-j)** docked in the active site of acetylcholinesterase (4EY7) protein; (2D and 3D ligand-receptor interactions).

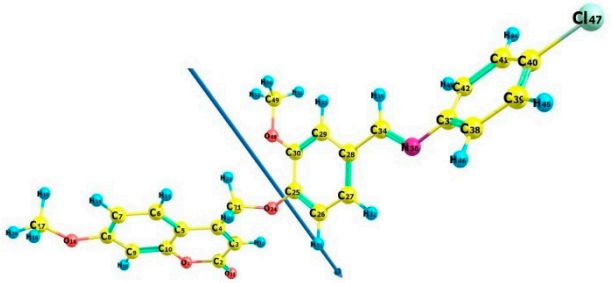


(13a)

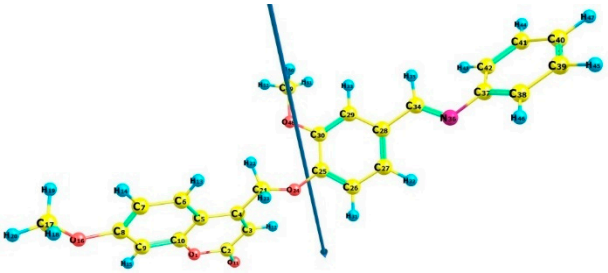
(13b)



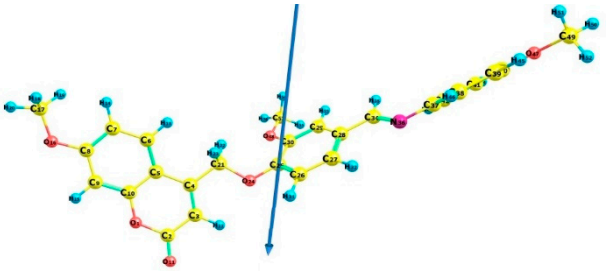
(13c)



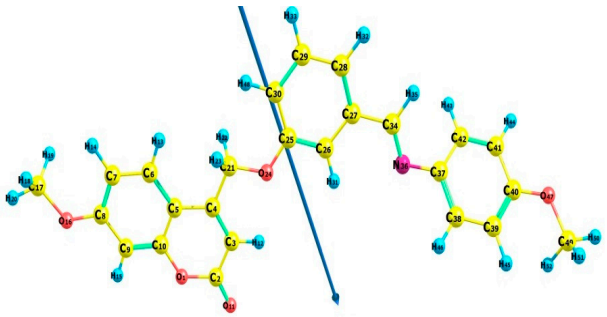
(13d)



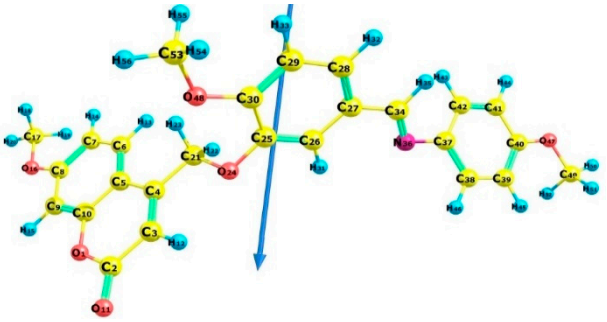
(13e)



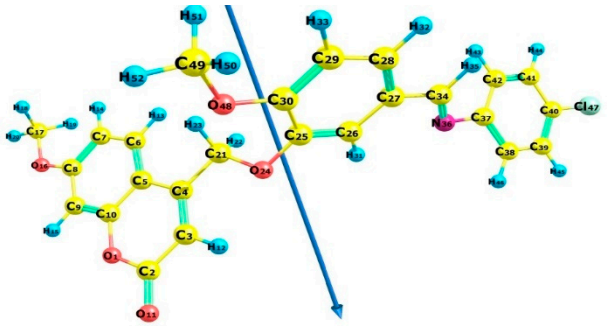
(13f)



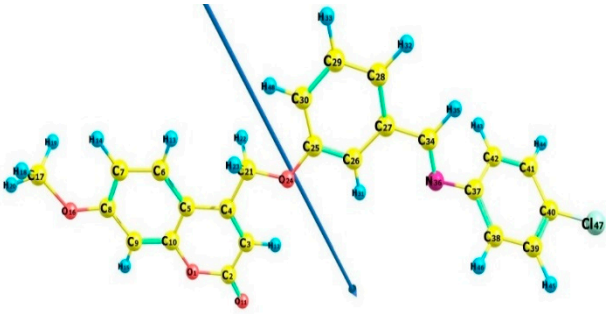
(13g)



(13h)

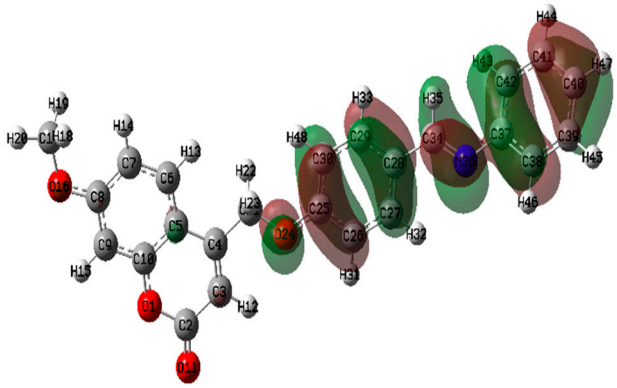


(13i)

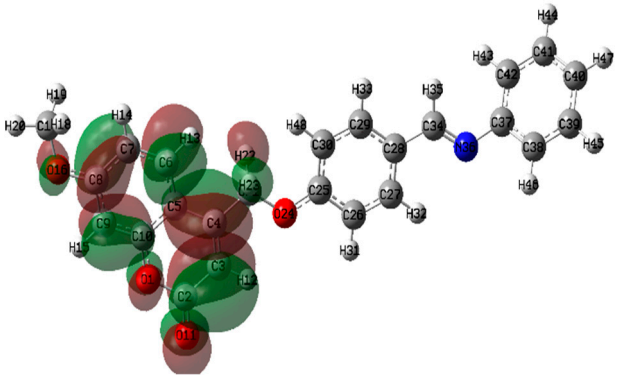


(13j)

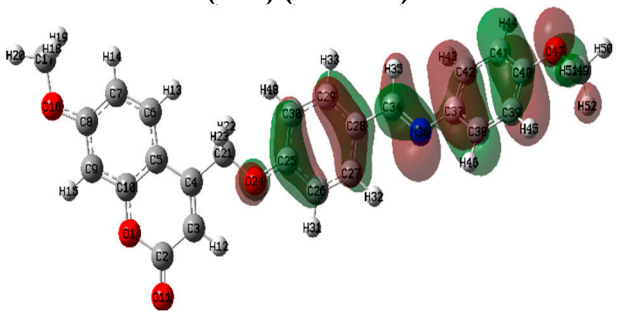
Figure S2. The optimized geometry, numbering system, vector of dipole moment of the synthesized compounds (**13a-j)** using wb97xd/6-311++g(d,p) level of calculation.



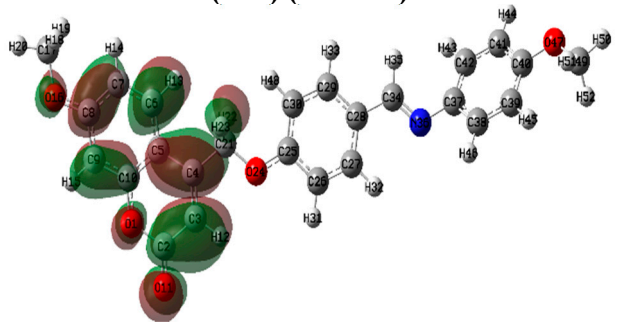
(13a) (HOMO)



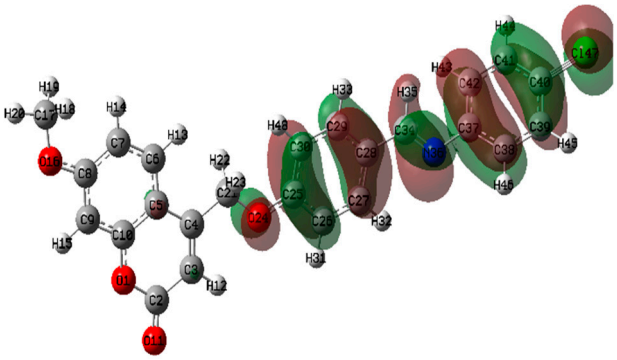
(13a) (LUMO)



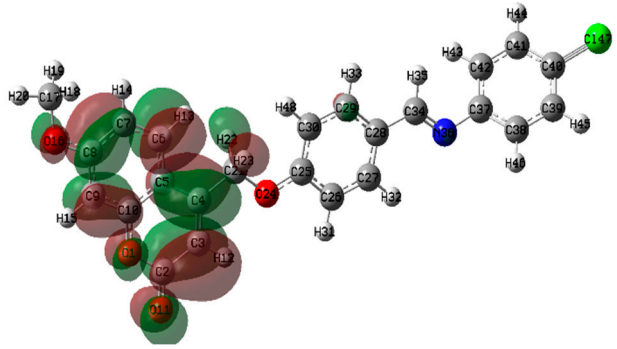
(13b) (HOMO)



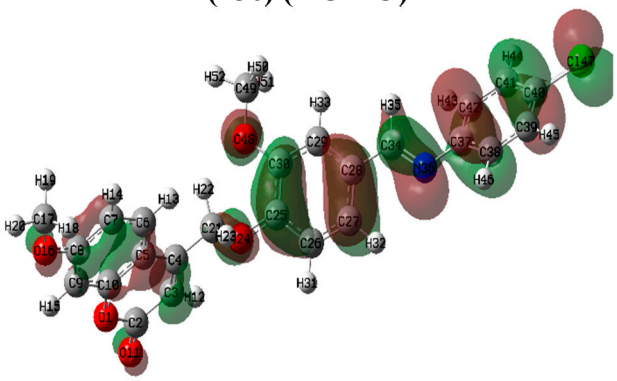
(13b) (LUMO)



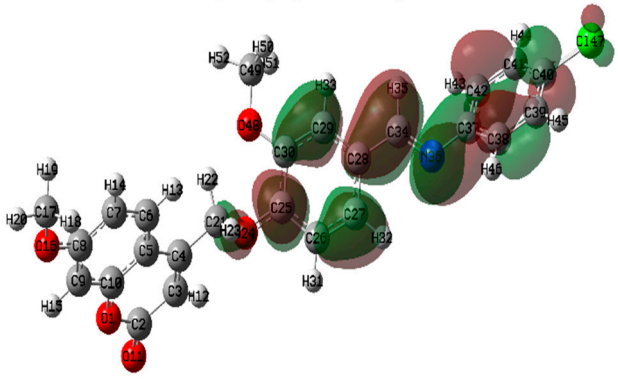
(13c) (HOMO)



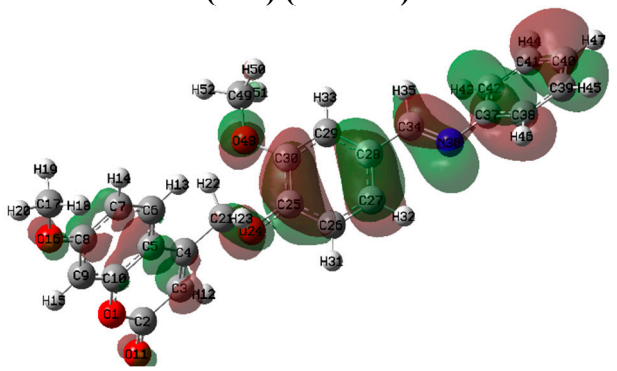
(13c) (LUMO)



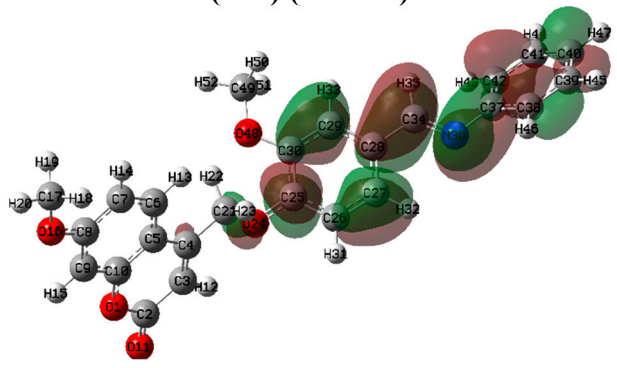
(13d) (HOMO)



(13d) (LUMO)



(13e) (HOMO)



(13e) (LUMO)

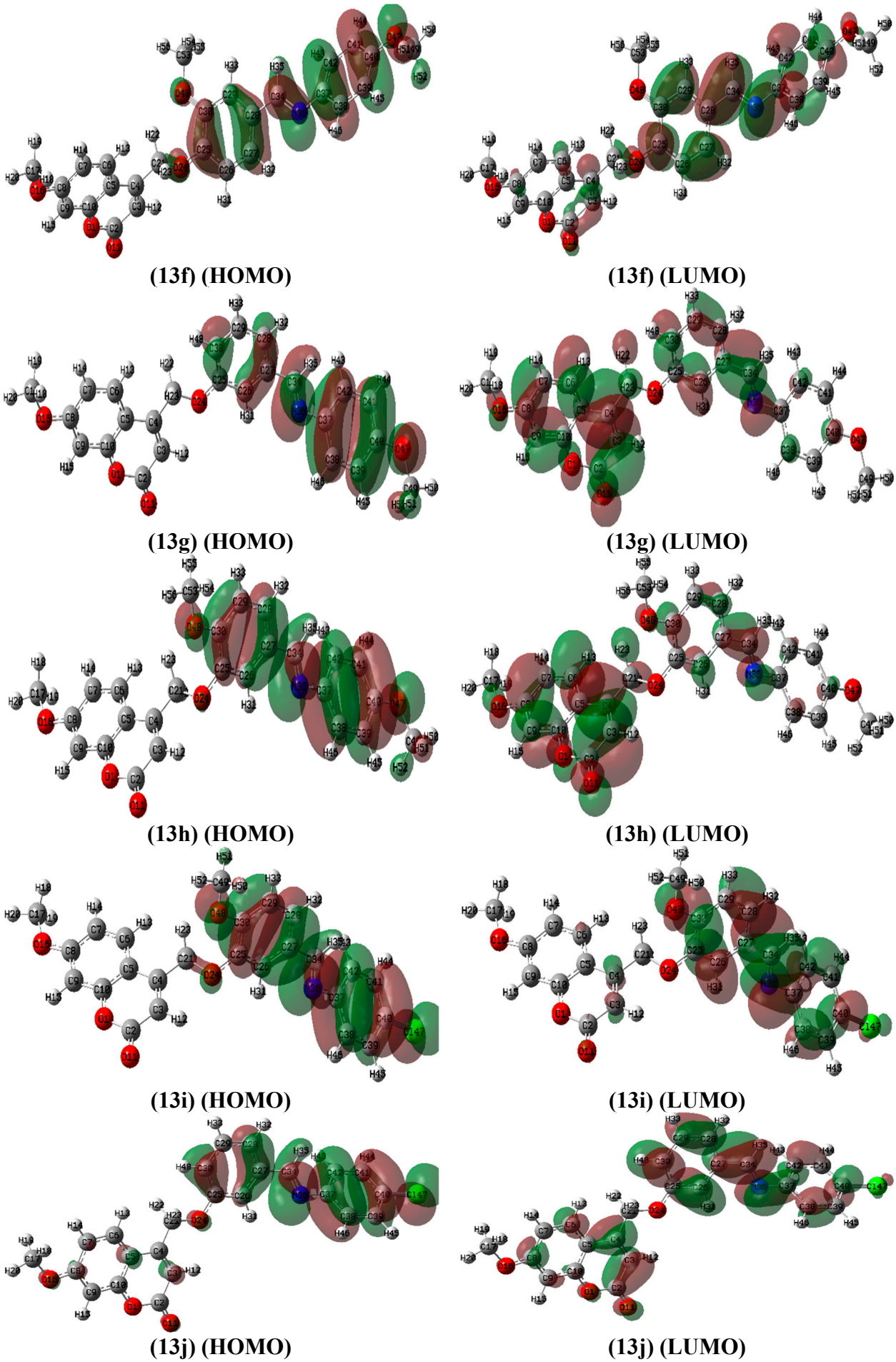


Figure S3. Frontier molecular orbitals of the synthesized compounds (**13a-j)** using wb97xd/6-311++g(d,p) level of calculation.

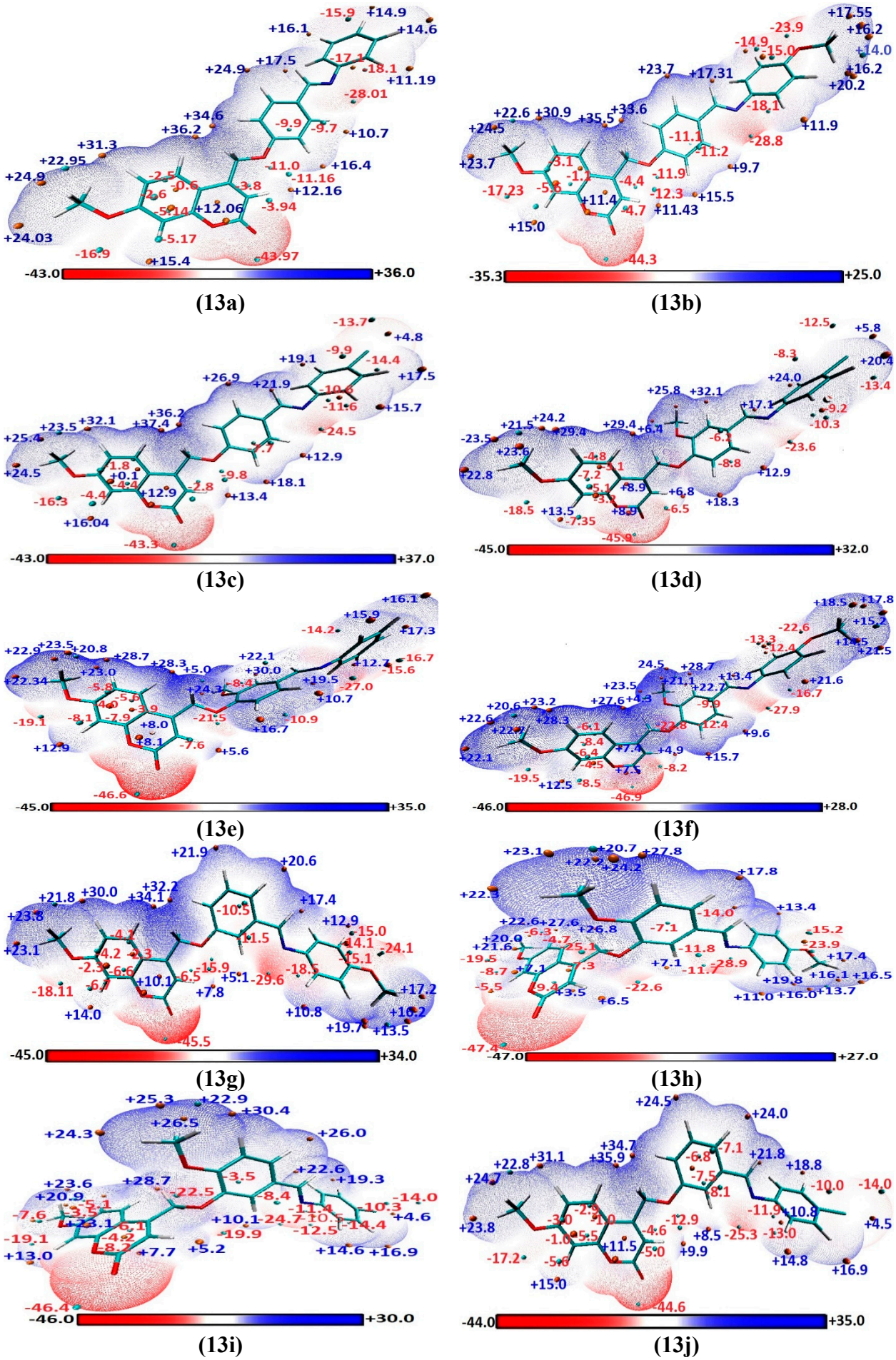


Figure S4. MEP surfaces of the synthesized compounds (**13a-j)** using wb97xd/6-311++g(d,p) level of calculation.

Table S1. The selected bond length (A°), bond angles and dihedral angles, (degree) of the newly synthesized compounds (**13a-j)** using wb97xd/6-311++g(d,p) level of level of theory.

	Exp. [6]	**13a**	**13b**	**13c**	**13d**	**13e**	**13f**	**13g**	**13h**	**13i**	**13j**
R(O1,C2)	1.383	1.380	1.380	1.380	1.381	1.381	1.381	1.381	1.382	1.382	1.381
R(O1,C10)	1.360	1.356	1.356	1.356	1.356	1.356	1.356	1.356	1.356	1.356	1.356
R(C2,C3)	1.450	1.457	1.457	1.458	1.456	1.456	1.456	1.458	1.456	1.456	1.458
R(C2,O11)	1.204	1.198	1.198	1.198	1.198	1.198	1.198	1.198	1.198	1.198	1.198
R(C4,C21)		1.501	1.501	1.501	1.499	1.499	1.499	1.502	1.499	1.499	1.502
R(C8,C9)	1.379	1.391	1.391	1.391	1.390	1.390	1.390	1.390	1.390	1.390	1.390
R(C8,O16)	1.388	1.349	1.349	1.348	1.350	1.350	1.350	1.349	1.350	1.350	1.349
R(C9,C10)	1.381	1.383	1.383	1.383	1.384	1.384	1.384	1.384	1.384	1.384	1.383
R(O16,C17)	1.363	1.414	1.414	1.414	1.413	1.413	1.413	1.413	1.413	1.413	1.414
R(C21,O24)		1.404	1.404	1.405	1.414	1.414	1.414	1.403	1.413	1.413	1.403
R(O24,C25)		1.357	1.358	1.356	1.365	1.365	1.366	1.361	1.369	1.367	1.360
R(C30,A48)		1.082	1.082	1.082	1.355	1.356	1.356	1.082	1.350	1.349	1.082
R(C34,N36)		1.270	1.270	1.271	1.270	1.269	1.270	1.269	1.270	1.271	1.269
R(N36,C37)		1.407	1.408	1.405	1.405	1.407	1.408	1.408	1.408	1.405	1.406
R(C40,A47)		1.084	1.358	1.749	1.749	1.084	1.357	1.357	1.358	1.749	1.749
A(C2,O1,C10)	122.1	122.5	122.5	122.5	122.5	122.5	122.5	122.5	122.5	122.5	122.5
A(O1,C2,C3)	117.1	116.5	116.6	116.6	116.5	116.5	116.6	116.6	116.5	116.5	116.5
A(O1,C2,O11)	117.4	117.8	117.8	117.8	117.7	117.7	117.7	117.8	117.6	117.6	117.8
A(C4,C5,C6)	125.0	125.0	125.0	124.9	124.9	124.9	124.9	124.9	124.9	124.9	124.9
A(C4,C5,C10)	117.4	117.6	117.7	117.6	117.7	117.7	117.7	117.7	117.7	117.7	117.6
A(C7,C8,O16)		124.2	124.2	124.2	124.2	124.2	124.2	124.2	124.2	124.2	124.2
A(C8,O16,C17)	119.1	118.8	118.8	118.8	118.7	118.7	118.7	118.7	118.7	118.7	118.7
A(C4,C21,O24)		109.8	109.9	109.9	109.7	109.7	109.7	109.9	110.1	110.0	109.8
A(C21,O24,C25)		118.6	118.5	118.5	116.0	115.9	115.9	118.5	114.5	114.8	118.6
A(O24,C25,C30)		124.5	124.4	124.4	121.2	121.2	121.2	124.2	119.8	119.9	124.2
A(C25,C26,C27)		120.1	120.1	120.1	120.9	120.9	120.9	120.0	120.6	120.6	120.0
A(C27,C28,C34)		121.5	121.5	121.5	121.5	121.5	121.6	120.0	119.7	119.8	120.1
A(C34,N36,C37)		119.1	119.3	119.1	119.2	119.1	119.6	119.7	119.3	119.2	119.2
A(N36,C37,C38)		118.3	118.4	118.4	118.2	118.2	118.1	118.0	118.5	118.4	118.3
A(C39,C40,C41)		119.5	119.5	120.9	120.9	119.6	119.5	119.5	119.5	120.9	121.0
D(C10,O1,C2,O11)	180.0	179.9	179.8	179.8	-179.9	180.0	-179.9	-179.9	179.6	179.6	-180.0
D(C2,C3,C4,C21)	179.1	-179.8	-179.5	-179.6	180.0	180.0	-180.0	179.9	179.5	179.5	-179.9
D(C5,C4,C21,O24)		179.8	179.3	-179.5	179.5	179.3	-179.9	179.0	-177.8	-177.6	178.8
D(C4,C5,C6,C7)	-179.1	-179.9	-179.8	179.9	-179.9	-179.8	179.9	180.0	-179.9	180.0	179.9
D(C4,C5,C10,C9)	179.6	179.9	179.9	-179.9	179.9	179.8	-179.9	-180.0	179.9	-179.9	-179.9
D(O16,C8,C9,C10)	178.6	-179.9	-179.8	-179.9	-179.9	-179.8	-180.0	179.9	-179.9	180.0	179.9
D(C7,C8,O16,C17)		0.3	0.0	0.4	-1.2	-1.4	-0.8	0.3	-0.3	0.1	0.4
D(C21,O24,C25,C26)		179.2	178.7	-179.9	115.1	114.8	115.0	176.5	-107.0	-108.0	177.9
D(C26,C27,C28,C34)		180.0	-180.0	-179.8	180.0	-179.9	179.8	180.0	180.0	179.9	-180.0
D(C27,C28,C34,N36)		-2.8	-3.9	-3.3	-1.1	-1.0	-0.6	179.9	179.5	179.5	179.8
D(C28,C34,N36,C37)		177.6	177.5	177.4	177.5	177.4	177.7	178.3	177.3	177.2	177.9
D(C34,N36,C37,C42)		-47.6	-42.2	-47.6	-44.7	-45.1	-38.5	-39.5	-41.8	-46.2	-46.8
D(N36,C37,C38,C39)		179.9	-179.7	179.9	-180.0	179.9	-179.6	-179.4	-179.8	179.6	180.0

Values are mean ± SD triplicate assays.

Table S2: Mean absolute errors computed for selected bond lengths (A^o) and angles (degree) of synthesized compounds (**13a-j)** verses **7-Acetoxy-coumarin** calculated at long-range corrections wb97xd/6-311++g(d,p) level of theory. The X-ray crystal structure data have been taken from ref. [1]

	13a	**13b**	**13c**	**13d**	**13e**	**13f**	**13g**	**13h**	**13i**	**13j**
R(O1,C2)	0.003	0.002	0.003	0.002	0.001	0.001	0.002	0.001	0.001	0.002
R(O1,C10)	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004
R(C2,C3)	0.007	0.007	0.008	0.006	0.006	0.006	0.008	0.006	0.006	0.008
R(C2,O11)	0.007	0.007	0.007	0.006	0.006	0.006	0.007	0.006	0.006	0.007
R(C8,C9)	0.012	0.012	0.012	0.011	0.011	0.011	0.011	0.011	0.011	0.011
R(C8,O16)	0.039	0.039	0.039	0.038	0.038	0.038	0.039	0.038	0.038	0.039
R(C9,C10)	0.002	0.002	0.002	0.003	0.003	0.003	0.002	0.003	0.003	0.002
R(O16,C17)	0.051	0.051	0.051	0.050	0.050	0.050	0.050	0.050	0.050	0.051
A(C2,O1,C10)	0.436	0.427	0.434	0.385	0.389	0.375	0.423	0.402	0.414	0.444
A(O1,C2,C3)	0.562	0.551	0.549	0.554	0.557	0.548	0.540	0.555	0.561	0.555
A(O1,C2,O11)	0.450	0.430	0.462	0.306	0.289	0.273	0.370	0.231	0.263	0.395
A(C4,C5,C6)	0.014	0.059	0.069	0.124	0.140	0.132	0.082	0.142	0.123	0.068
A(C4,C5,C10)	0.250	0.277	0.271	0.301	0.308	0.313	0.293	0.317	0.301	0.272
A(C8,O16,C17)	0.337	0.331	0.325	0.398	0.374	0.433	0.407	0.410	0.392	0.388
D(C10,O1,C2,O11)	0.037	0.137	0.148	0.042	0.025	0.040	0.035	0.315	0.352	0.004
D(C2,C3,C4,C21)	0.697	0.422	0.545	0.907	0.955	0.904	0.819	0.415	0.468	0.855
D(C4,C5,C6,C7)	0.778	0.736	0.843	0.812	0.718	0.841	0.911	0.786	0.890	0.864
D(C4,C5,C10,C9)	0.333	0.322	0.338	0.341	0.250	0.390	0.417	0.370	0.359	0.362
D(O16,C8,C9,C10)	1.267	1.200	1.314	1.266	1.187	1.353	1.281	1.314	1.354	1.267

Table S3. Values of the Fukui functions and dual descriptor of compounds **(13a-e)** by using wb97xd/6-311++g(d,p) level of theory

	(13a)			(13b)			(13c)			(13d)			(13e)		
Atom	**f(-)**	**f(+)**	**Δf**	**f(-)**	**f(+)**	**Δf**	**f(-)**	**f(+)**	**Δf**	**f(-)**	**f(+)**	**Δf**	**f(-)**	**f(+)**	**Δf**
O1	0.000	**0.021**	**0.021**	0.000	**0.021**	**0.021**	0.000	0.021	0.020	0.001	0.000	-0.001	0.001	0.000	-0.001
C2	0.000	**0.084**	**0.084**	0.000	**0.084**	**0.084**	0.000	0.084	0.083	0.001	0.001	0.000	0.001	0.001	0.001
C3	0.004	**0.199**	**0.195**	0.000	**0.198**	**0.198**	0.003	0.198	0.194	0.011	0.007	-0.003	0.007	0.009	0.002
C4	0.001	**0.209**	**0.208**	0.000	**0.209**	**0.209**	0.001	0.207	0.206	0.016	-0.003	-0.019	0.018	0.000	-0.017
C6	0.001	**0.166**	**0.165**	0.000	**0.167**	**0.167**	0.001	0.164	0.163	0.004	-0.004	-0.008	0.003	-0.003	-0.006
C8	0.003	**0.082**	**0.080**	0.000	**0.083**	**0.083**	0.003	0.081	0.078	0.010	-0.001	-0.011	0.008	-0.001	-0.008
C9	0.001	**0.052**	**0.051**	0.000	**0.052**	**0.052**	0.001	0.051	0.050	0.004	0.001	-0.003	0.003	0.002	-0.002
C10	0.001	**0.035**	**0.034**	0.000	**0.035**	**0.035**	0.001	0.035	0.034	0.005	0.002	-0.002	0.004	0.003	-0.001
O11	0.002	0.065	0.063	0.000	**0.065**	**0.065**	0.002	0.065	0.063	0.007	0.000	-0.007	0.006	0.001	-0.005
O16	0.002	**0.011**	**0.009**	0.000	**0.011**	**0.011**	0.002	0.011	0.009	0.009	0.000	-0.009	0.007	0.000	-0.007
C21	0.001	-0.039	-0.039	0.000	-0.038	-0.039	0.001	-0.040	-0.041	-0.001	0.004	0.005	-0.003	0.002	0.004
O24	**0.051**	0.001	**-0.050**	**0.021**	0.001	**-0.019**	0.043	0.001	-0.042	0.029	0.006	-0.023	0.033	0.006	-0.027
C25	**0.073**	0.004	**-0.069**	**0.036**	0.004	**-0.033**	0.061	0.004	-0.057	0.093	0.112	0.019	0.109	0.117	0.009
C26	**0.027**	0.000	**-0.027**	**0.009**	0.000	**-0.009**	0.022	0.000	-0.022	0.010	0.010	0.000	0.010	0.013	0.004
C27	**0.008**	0.001	**-0.008**	**0.011**	0.001	**-0.010**	0.008	0.001	-0.008	0.073	0.085	0.012	0.086	0.089	0.003
C28	**0.096**	0.000	**-0.096**	**0.047**	0.000	**-0.047**	0.083	0.001	-0.082	0.068	0.082	0.014	0.077	0.087	0.010
C29	**0.037**	0.002	**-0.035**	**0.025**	0.002	**-0.023**	0.031	0.004	-0.027	-0.008	0.075	0.083	-0.010	0.073	0.083
C30	**0.040**	0.003	**-0.038**	**0.015**	0.003	**-0.013**	0.034	0.002	-0.031	0.042	0.023	-0.019	0.052	0.025	-0.027
C34	**0.021**	0.002	**-0.020**	**0.052**	0.001	**-0.051**	**0.021**	0.005	**-0.016**	0.027	**0.238**	**0.211**	0.029	0.229	0.200
N36	**0.141**	0.001	**-0.141**	**0.103**	0.000	**-0.103**	**0.128**	0.002	**-0.126**	0.104	**0.164**	**0.060**	0.114	0.168	0.053
C37	**0.129**	0.000	**-0.129**	**0.144**	0.000	**-0.144**	**0.125**	0.000	**-0.125**	**0.092**	0.051	**-0.041**	0.093	0.043	-0.050
C38	**0.089**	0.000	**-0.089**	**0.092**	0.000	**-0.092**	**0.078**	0.000	**-0.077**	**0.060**	0.016	**-0.045**	0.067	0.017	-0.050
C39	**0.016**	0.000	**-0.016**	**0.055**	0.000	**-0.055**	**0.023**	0.000	**-0.024**	**0.018**	0.001	**-0.017**	0.012	0.006	-0.007
C40	**0.138**	0.000	**-0.138**	**0.133**	0.000	**-0.133**	**0.128**	0.001	**-0.128**	**0.101**	0.052	**-0.049**	0.107	0.050	-0.058
C41	**0.032**	0.000	**-0.032**	**0.078**	0.000	**-0.078**	**0.039**	0.000	**-0.039**	**0.034**	0.017	**-0.017**	0.029	0.007	-0.022
C42	**0.058**	0.000	**-0.058**	**0.038**	0.000	**-0.038**	**0.057**	0.000	**-0.056**	**0.050**	0.032	**-0.018**	0.052	0.029	-0.023
A47	0.001	0	-0.001	0.1063	0	-0.1063	0.0796	0.0001	-0.0795	0.0622	0.0066	-0.0556	0.0008	0.0007	-0.0001
A48	0.0005	0.0001	-0.0004	0.0002	0.0003	0.0001	0.0004	0.0001	-0.0003	0.0333	0.0006	-0.0327	0.0402	0.0006	-0.0396

A = H, O or Cl *which different atom in derivatives series; Values are mean ± SD triplicate assays.*

Table S4. Values of the Fukui functions and dual descriptor of compounds **(13f-j)** by using wb97xd/6-311++g(d,p) level of theory.

	(13f)			(13g)			(13h)			(13i)			(13j)		
Atom	**f(-)**	**f(+)**	**Δf**	**f(-)**	**f(+)**	**Δf**	**f(-)**	**f(+)**	**Δf**	**f(-)**	**f(+)**	**Δf**	**f(-)**	**f(+)**	**Δf**
O1	0.000	0.001	0.001	0.000	0.016	0.016	0.000	0.017	0.017	0.000	0.001	0.001	0.000	0.004	0.003
C2	0.000	0.005	0.005	0.000	0.063	0.063	0.000	0.073	0.073	0.001	0.003	0.002	0.000	0.013	0.013
C3	0.000	0.017	0.017	0.000	0.153	0.153	-0.001	0.163	0.164	-0.001	0.005	0.007	0.008	0.036	0.027
C4	0.001	0.009	0.008	0.000	0.162	0.162	0.000	0.183	0.183	0.000	-0.001	-0.001	0.002	0.038	0.037
C6	0.001	0.004	0.004	0.000	0.121	0.121	0.000	0.152	0.152	0.001	0.009	0.008	0.001	0.023	0.021
C8	0.000	0.002	0.002	0.000	0.062	0.062	0.000	0.073	0.073	0.000	0.002	0.002	0.005	0.012	0.008
C9	0.000	0.004	0.004	0.000	0.038	0.038	0.000	0.048	0.048	0.000	0.001	0.001	0.002	0.007	0.005
C10	0.000	0.004	0.004	0.000	0.028	0.028	0.000	0.029	0.029	0.000	-0.004	-0.003	0.002	0.007	0.005
O11	0.000	0.004	0.004	0.000	0.049	0.049	0.000	0.056	0.056	0.000	0.002	0.002	0.004	0.011	0.007
O16	0.000	0.001	0.000	0.000	0.009	0.009	0.000	0.010	0.010	0.000	0.000	0.000	0.004	0.002	-0.002
C21	0.007	-0.001	-0.008	0.000	-0.040	-0.040	0.002	-0.036	-0.039	0.005	0.013	0.008	0.000	-0.017	-0.017
O24	0.014	0.006	-0.008	0.001	0.002	0.001	0.002	0.001	-0.002	0.007	0.001	-0.006	0.006	0.001	-0.005
C25	0.051	0.116	0.065	-0.001	0.003	0.005	0.011	0.005	-0.006	0.029	0.004	-0.025	0.005	0.007	0.003
C26	0.003	0.015	0.012	-0.003	0.031	0.034	0.006	0.021	0.015	0.007	0.087	0.080	-0.017	0.098	0.116
C27	0.038	0.083	0.045	0.023	0.026	0.003	0.046	0.009	-0.036	0.083	0.074	-0.009	0.031	0.078	0.047
C28	0.042	0.087	0.044	0.028	0.007	-0.021	0.030	0.004	-0.026	0.042	0.069	0.027	0.039	0.032	-0.007
C29	0.007	0.068	0.062	0.003	0.014	0.010	0.014	-0.002	-0.016	0.031	0.018	-0.013	0.003	0.037	0.034
C30	0.018	0.023	0.004	0.029	0.042	0.013	0.042	0.030	-0.012	0.074	0.115	0.041	0.045	0.116	0.072
C34	0.055	0.215	0.160	0.079	0.055	-0.024	0.057	0.032	-0.025	0.035	0.235	0.200	0.050	0.197	0.147
N36	0.096	0.162	0.066	0.094	0.040	-0.053	0.103	0.024	-0.079	0.125	0.157	0.032	0.126	0.137	0.011
C37	0.135	0.041	-0.095	0.159	0.005	-0.154	0.132	0.005	-0.128	0.105	0.051	-0.054	0.151	0.036	-0.115
C38	0.083	0.023	-0.059	0.091	0.008	-0.083	0.088	0.007	-0.081	0.071	0.016	-0.055	0.084	0.015	-0.068
C39	0.053	-0.002	-0.055	0.065	-0.001	-0.065	0.053	0.000	-0.053	0.022	-0.001	-0.023	0.034	-0.004	-0.037
C40	0.128	0.043	-0.085	0.145	0.009	-0.136	0.130	0.006	-0.124	0.120	0.051	-0.069	0.159	0.039	-0.120
C41	0.078	0.009	-0.069	0.090	0.002	-0.088	0.079	0.002	-0.077	0.038	0.019	-0.019	0.050	0.012	-0.039
C42	0.047	0.022	-0.025	0.042	0.004	-0.038	0.044	0.000	-0.044	0.060	0.025	-0.035	0.068	0.018	-0.049
A47	0.102	0.0055	-0.0965	0.1224	0.0012	-0.1212	0.1034	0.0007	-0.1027	0.0731	0.0062	-0.0669	0.1083	0.0045	-0.1038
A48	0.0109	0.0007	-0.0102	0.0002	0.0007	0.0005	0.0249	0.0032	-0.0217	0.0532	0.016	-0.0372	0.0003	0.0016	0.0013

A = H, O or Cl *which different atom in derivatives series; Values are mean ± SD triplicate assays.*

Table S5. Values of the condensed local softnesses (Hartree*e) of compounds **(13a-j)** by using wb97xd/6-311++g(d,p) level of theory from CDFT point of view.

Atoms	13a		13b		13c		13d		13e		13f		13g		13h		13i		13j	
	s+/s-	s-/s+	s+/s-	s-/s+	s+/s-	s-/s+	s+/s-	s-/s+	s+/s-	s-/s+	s+/s-	s-/s+	s+/s-	s-/s+	s+/s-	s-/s+	s+/s-	s-/s+	s+/s-	s-/s+
O1	0.5	2.0	0.1	7.1	0.2	5.9	0.0	-51.1	1.1	0.9	0.8	1.3	0.6	1.8	0.1	7.3	0.2	4.5	2.7	0.4
C2	0.2	5.0	0.0	23.9	0.1	19.0	0.0	26.6	1.0	1.0	0.7	1.5	0.2	4.4	0.0	29.1	0.1	15.7	4.2	0.2
C3	0.0	31.6	0.0	1993.5	0.0	186.6	0.0	-35.7	1.2	0.8	0.4	2.8	-1.2	-0.8	0.0	-144.2	0.0	-163.1	225.3	0.0
C8	0.5	2.1	0.1	9.4	0.1	7.7	0.1	9.8	1.1	0.9	0.8	1.3	0.6	1.6	0.1	9.9	0.2	5.8	5.1	0.2
C9	0.5	2.0	0.1	7.2	0.2	6.0	0.1	8.3	1.1	0.9	0.8	1.3	0.6	1.7	0.1	7.7	0.2	4.7	3.2	0.3
C10	0.6	1.7	0.1	8.2	0.2	6.6	0.1	6.9	1.1	0.9	0.8	1.3	0.5	2.1	0.1	10.2	0.2	5.7	9.1	0.1
O11	0.4	2.6	0.1	10.6	0.1	8.5	0.1	10.7	1.1	0.9	0.7	1.3	0.3	3.5	0.1	11.0	0.2	6.4	5.8	0.2
O16	0.6	1.6	0.2	5.2	0.2	4.3	0.1	18.6	1.1	0.9	0.8	1.2	0.7	1.5	0.2	5.3	0.3	3.4	7.3	0.1
C21	0.6	1.7	0.2	4.2	0.3	3.0	0.1	14.4	1.0	1.0	0.6	1.7	0.4	2.5	0.1	10.5	0.2	4.4	0.9	1.2
O24	2.1	0.5	-2.4	-0.4	-3.3	-0.3	-1.6	-0.6	1.8	0.6	1.0	1.0	0.7	1.5	-2.6	-0.4	12.9	0.1	0.5	1.8
C25	1.0	1.0	-3.1	-0.3	-4.0	-0.3	-2.0	-0.5	1.1	0.9	0.7	1.5	0.5	2.0	-1.7	-0.6	33.9	0.0	0.1	7.4
C26	1.2	0.8	20.1	0.0	25.1	0.0	2.6	0.4	0.8	1.2	0.6	1.8	0.3	3.6	7.4	0.1	1.0	1.0	0.1	15.5
C27	0.7	1.5	1.6	0.6	2.1	0.5	5.8	0.2	1.2	0.8	0.6	1.7	0.0	-23.0	0.9	1.1	1.8	0.5	0.3	3.3
C28	1.1	0.9	0.5	2.2	1.7	0.6	-0.3	-3.1	1.4	0.7	0.2	4.2	0.6	1.6	2.3	0.4	1.8	0.6	0.8	1.3
C29	0.9	1.1	4.5	0.2	5.5	0.2	53.7	0.0	0.4	2.4	0.4	2.6	0.4	2.3	2.3	0.4	1.7	0.6	0.3	3.3
C30	1.3	0.8	-13.8	-0.1	-19.8	-0.1	0.3	3.6	1.4	0.7	0.6	1.5	0.5	1.9	-7.6	-0.1	2.7	0.4	0.3	3.8
C34	0.5	2.2	-27.5	0.0	-60.1	0.0	2.3	0.4	0.3	3.9	0.5	2.2	0.6	1.7	-48.5	0.0	0.9	1.1	0.1	7.5
N36	0.9	1.1	3.6	0.3	5.2	0.2	1.0	1.0	0.7	1.5	0.4	2.3	0.4	2.3	8.5	0.1	1.9	0.5	0.2	4.1
C37	9.6	0.1	-22.3	0.0	-16.1	-0.1	1.8	0.5	4.5	0.2	22.7	0.0	67.7	0.0	-16.4	-0.1	1321.0	0.0	3.5	0.3
C38	2.6	0.4	18.7	0.1	20.1	0.0	42.8	0.0	1.6	0.6	2.0	0.5	2.3	0.4	58.7	0.0	5.7	0.2	0.7	1.4
C39	1.5	0.7	9.5	0.1	6.6	0.2	1.8	0.5	1.1	0.9	1.9	0.5	2.3	0.4	10.9	0.1	2.9	0.3	0.6	1.6
C40	2.1	0.5	9.6	0.1	9.7	0.1	-0.1	-7.3	1.4	0.7	1.7	0.6	2.0	0.5	9.6	0.1	3.6	0.3	0.8	1.3
C41	1.8	0.5	12.6	0.1	9.3	0.1	2.0	0.5	1.2	0.8	2.4	0.4	2.8	0.4	10.8	0.1	3.4	0.3	0.8	1.3
C42	2.5	0.4	29.7	0.0	28.1	0.0	36.4	0.0	1.6	0.6	1.8	0.6	2.1	0.5	33.4	0.0	5.1	0.2	0.8	1.3
A47	1.5	0.7	15.4	0.1	8.0	0.1	-2.2	-0.5	1.1	0.9	3.4	0.3	4.1	0.2	14.1	0.1	3.8	0.3	0.9	1.1

A48	1.2	0.9	-10.4	-0.1	-13.7	-0.1	-1.7	-0.6	2.1	0.5	1.0	1.0	0.5	1.9	-2.3	-0.4	23.8	0.0	0.2	5.5

Table S6. Values of the condensed local electrophilicity (ElP)/nucleophilicity (NuP) index (e*eV) of compounds **(13a-j)** by using wb97xd/6-311++g(d,p) level of theory from CDFT point of view.

Atoms	**13a**		**13b**		**13c**		**13d**		**13e**		**13f**		**13g**		**13h**		**13i**		**13j**	
	ElP	**NuP**	**ElP**	**NuP**	**ElP**	**NuP**	**ElP**	**NuP**	**ElP**	**NuP**	**ElP**	**NuP**	**ElP**	**NuP**	**ElP**	**NuP**	**ElP**	**NuP**	**ElP**	**NuP**
O1	-0.01	-0.01	-0.01	-0.05	-0.01	-0.03	0.00	-0.04	-0.01	-0.01	-0.01	-0.01	0.00	-0.01	0.00	-0.05	-0.01	-0.03	-0.02	-0.01
C2	0.00	-0.02	0.00	-0.10	0.00	-0.07	0.00	-0.06	-0.01	0.00	0.00	-0.01	0.00	-0.01	0.00	-0.10	0.00	-0.05	-0.02	0.00
C3	0.00	-0.02	0.00	-0.15	0.00	-0.10	0.00	-0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.15	0.00	-0.06	-0.08	0.00
C8	-0.01	-0.02	-0.01	-0.08	-0.01	-0.05	0.00	-0.05	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.09	-0.01	-0.04	-0.06	-0.01
C9	-0.01	-0.02	-0.01	-0.06	-0.01	-0.04	0.00	-0.04	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.07	-0.01	-0.03	-0.03	-0.01
C10	0.00	-0.01	0.00	-0.03	0.00	-0.02	0.00	-0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.03	0.00	-0.01	-0.03	0.00
O11	-0.01	-0.03	-0.01	-0.15	-0.01	-0.10	0.00	-0.10	-0.02	-0.01	-0.01	-0.02	0.00	-0.02	-0.01	-0.16	-0.01	-0.07	-0.09	-0.01
O16	-0.01	-0.01	-0.01	-0.04	-0.01	-0.03	0.00	-0.03	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.04	-0.01	-0.02	-0.06	-0.01
C21	-0.01	-0.01	0.00	-0.02	-0.01	-0.01	0.00	-0.01	-0.01	-0.01	0.00	-0.01	0.00	-0.01	0.00	-0.02	0.00	-0.01	0.00	0.00
O24	-0.04	-0.02	-0.03	0.02	-0.04	0.01	0.00	0.02	-0.04	-0.02	-0.02	-0.03	-0.01	-0.02	-0.01	0.00	-0.01	0.00	-0.01	-0.01
C25	-0.05	-0.05	-0.04	0.02	-0.06	0.01	-0.01	0.02	-0.08	-0.07	-0.05	-0.09	-0.02	-0.04	-0.02	0.02	-0.03	0.00	-0.01	-0.02
C26	-0.03	-0.03	-0.02	0.00	-0.03	0.00	0.00	0.00	-0.03	-0.03	-0.02	-0.05	-0.02	-0.08	-0.01	0.00	-0.02	-0.02	0.00	-0.05
C27	-0.03	-0.04	-0.02	-0.02	-0.03	-0.01	0.00	0.00	-0.07	-0.05	-0.03	-0.07	0.00	-0.06	-0.01	-0.01	-0.04	-0.02	-0.01	-0.03
C28	-0.03	-0.03	-0.01	-0.02	-0.03	-0.01	0.00	-0.02	-0.05	-0.03	-0.01	-0.05	-0.02	-0.05	-0.03	-0.02	-0.04	-0.02	-0.03	-0.03
C29	-0.04	-0.04	-0.03	-0.01	-0.04	-0.01	0.00	0.00	-0.02	-0.04	-0.02	-0.06	-0.02	-0.07	-0.02	-0.01	-0.03	-0.02	-0.02	-0.04
C30	-0.04	-0.03	-0.02	0.00	-0.04	0.00	0.00	-0.01	-0.05	-0.03	-0.02	-0.04	-0.04	-0.10	-0.04	0.01	-0.05	-0.02	-0.02	-0.06
C34	-0.04	-0.09	-0.05	0.00	-0.05	0.00	0.00	-0.01	-0.03	-0.11	-0.05	-0.15	-0.06	-0.14	-0.05	0.00	-0.04	-0.04	-0.02	-0.09
N36	-0.08	-0.08	-0.05	-0.02	-0.08	-0.01	0.00	-0.02	-0.07	-0.10	-0.04	-0.14	-0.04	-0.13	-0.04	-0.01	-0.07	-0.03	-0.03	-0.08
C37	-0.05	0.00	-0.08	0.00	-0.06	0.00	-0.01	-0.03	-0.03	-0.01	-0.07	0.00	-0.09	0.00	-0.07	0.01	-0.04	0.00	-0.02	0.00
C38	-0.06	-0.02	-0.06	0.00	-0.06	0.00	-0.01	0.00	-0.05	-0.03	-0.06	-0.04	-0.07	-0.04	-0.06	0.00	-0.05	-0.01	-0.02	-0.02
C39	-0.04	-0.02	-0.05	-0.01	-0.04	0.00	-0.01	-0.02	-0.03	-0.03	-0.05	-0.03	-0.05	-0.03	-0.04	-0.01	-0.03	-0.01	-0.02	-0.02
C40	-0.09	-0.04	-0.08	-0.01	-0.08	-0.01	0.00	-0.06	-0.08	-0.05	-0.07	-0.06	-0.08	-0.05	-0.07	-0.01	-0.06	-0.02	-0.03	-0.03
C41	-0.04	-0.02	-0.06	-0.01	-0.04	0.00	-0.01	-0.02	-0.04	-0.03	-0.06	-0.03	-0.07	-0.03	-0.05	-0.01	-0.04	-0.01	-0.02	-0.02

C42	-0.05	-0.02	-0.04	0.00	-0.05	0.00	-0.01	0.00	-0.04	-0.02	-0.04	-0.03	-0.04	-0.03	-0.04	0.00	-0.04	-0.01	-0.02	-0.02
A47	-0.04	-0.03	-0.08	-0.01	-0.14	-0.01	-0.05	0.17	-0.04	-0.03	-0.07	-0.03	-0.08	-0.03	-0.07	-0.01	-0.12	-0.03	-0.07	-0.05
A48	-0.02	-0.02	-0.02	0.00	-0.02	0.00	0.00	0.00	-0.04	-0.02	-0.02	-0.02	-0.02	-0.05	-0.03	0.02	-0.05	0.00	-0.01	-0.03

Values are mean ± SD triplicate assays

References

1. Z. Yang, D. Zhang, J. Ren, M. Yang, and S. Li. Acetylcholinesterase inhibitory activity of the total alkaloid from traditional Chinese herbal medicine for treating Alzheimer's disease. Medicinal Chemistry Research. 21(6) (2012) 734-738. https://doi.org/10.1007/s00044-011-9582-8.
2. A.H. Hasan, S. Shakya, F.H.S. Hussain, S. Murugesan, S. Chander, M.R.F. Pratama, S. Jamil, B. Das, S. Biswas, and J. Jamalis. Design, synthesis, anti-acetylcholinesterase evaluation and molecular modelling studies of novel coumarin-chalcone hybrids. Journal of Biomolecular Structure and Dynamics. (2023) 1-13. https://doi.org/10.1080/07391102.2022.2162583.
3. A.H. Hasan, S. Murugesan, S.I. Amran, S. Chander, M.M. Alanazi, T.B. Hadda, S. Shakya, M.R.F. Pratama, B. Das, S. Biswas, and J. Jamalis. Novel thiophene Chalcones-Coumarin as acetylcholinesterase inhibitors: Design, synthesis, biological evaluation, molecular docking, ADMET prediction and molecular dynamics simulation. Bioorganic Chemistry. 119 (2022) 105572. https://doi.org/10.1016/j.bioorg.2021.105572.
4. A. Abdalla Ali, S.A. Mhamad, A.H. Hasan, I. Ahmad, S.A. Abdullah, S. Jamil, H. Patel, S. Murugesan, and J. Jamalis. Synthesis, biological evaluation and molecular modeling studies of modulated benzyloxychalcones as potential acetylcholinesterase inhibitors. Journal of Biomolecular Structure and Dynamics. (2023) 1-12. https://doi.org/10.1080/07391102.2023.2220032.
5. H.A. Hasan, S.M.F. Yusof, A.N. Kamarudin, S. Murugesan, S. Shakya, and J. Jamalis. Synthesis, Anti-acetylcholinesterase Evaluation, Molecular Docking and Molecular Dynamics Simulation of Novel Psoralen Derivatives. Current Organic Synthesis. 20 (2023) 1-17. http://dx.doi.org/10.2174/1570179420666230328121554.
6. K. Gnanaguru, N. Ramasubbu, K. Venkatesan, and V. Ramamurthy. A study on the photochemical dimerization of coumarins in the solid state. The Journal of Organic Chemistry. 50(13) (1985) 2337-2346. https://doi.org/10.1021/jo00213a027.