Supplementary Information

Synthesis of 3-(4-fluorophenyl)-1-isopropyl-1*H*-indole (2)

2-chloro-4'fluoroacetophenone and *N*-isopropylaniline was dissolved in minimum amount of freshly distilled DMF. The contents were heated to about 100 ºC for about 10-11 hours. The progress of the reaction was monitored by TLC. After completion of reaction, the reaction mixture was cooled to room temperature and then poured to crushed ice with constant stirring. The separated solid was filtered and recrystallized in ethanol to get pure 1-(4-fluorophenyl)-2-(isopropyl(phenyl)amino)ethanone (**1**) [Yield: 78% MP: 78-80 ºC]. Further, compound **1** (1 mol) and $ZnCl_2$ (0.43 mol) was dissolved in the minimum amount of boiling ethyl alcohol and the contents were refluxed for 3-5 h. The progress of the reaction was monitored by TLC. After completion of reaction, the reaction mixture was cooled to room temperature and then poured into excess of cold dilute hydrochloric acid with constant stirring. The separated solid was filtered and recrystallized in ethanol to get pure 3-(4-fluorophenyl)-1-isopropyl-1*H*-indole (**2**). [Yield: 80% MP: 94-96 ºC].

Synthesis of (*E*)-3-(3-(4-fluorophenyl)-1-isopropyl-1*H*-indol-2-yl)acrylaldehyde (3).

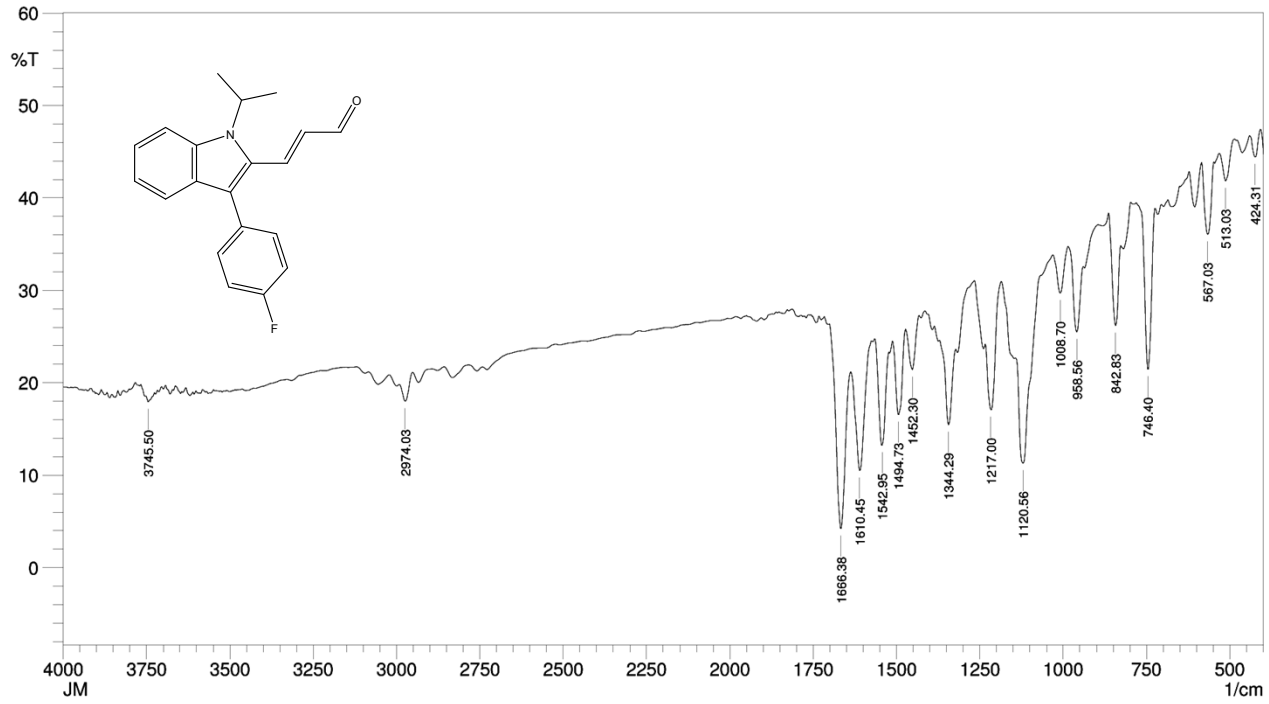
A solution of $POCl_3$ (2.5 equiv) in CH_3CN was cooled to -5 ºC. Crude 3-(*N*-Methyl-*N*-phenylamino)acrolein (MPAA) (2.1 equiv) in CH_3CN was added over a period of 45 min, while maintaining an internal temperature of 5-7 ºC. The mixture was stirred at 5-7 ºC for 10 min followed by the addition of 3-(4-fluorophenyl)-1-isopropyl-1*H*-indole (**2**) (1 equiv) over a period of 10 min and then heated to reflux (83 ºC) for 3 h. The reaction mixture was cooled to 22 ºC and water was slowly added over 15 min. The mixture was stirred at 35-50 ºC for 0.5 h and then heated to 50-55 ºC for 1.5 h. After the solution was cooled to 22 ºC and stirred for 15 min, the separated solid was collected by vacuum filtration, washed with water and vacuum dried for 6 h. Toluene (2.5 mL) and cellulose (0.18 g) were added to the dry solid, and the solution was heated to 50-55 ºC for 1.5 h.

The slurry was cooled to 22 ºC, filtered and washed with toluene. The combined toluene fractions were concentrated in *vacuo* to give a crude oil. The oil was dissolved in 95% EtOH and concentrated *in vacuo*. This operation was repeated. The oil was once again dissolved in 95% EtOH (700 mL) and warmed to 78 ºC for 15 min, followed by slow cooling to room temperature and then to 0 ºC (over 1 h). The solids were collected by suction fitration, washed with cold (0 ºC) 95% EtOH (3 x 15 mL), and dried to a constant weight to give **3** (0.276 g, 75%). Purification was also achieved by column chromatography utilizing Et-OAc/hexane as the solvent on SiO_2: mp 129-130 ºC.

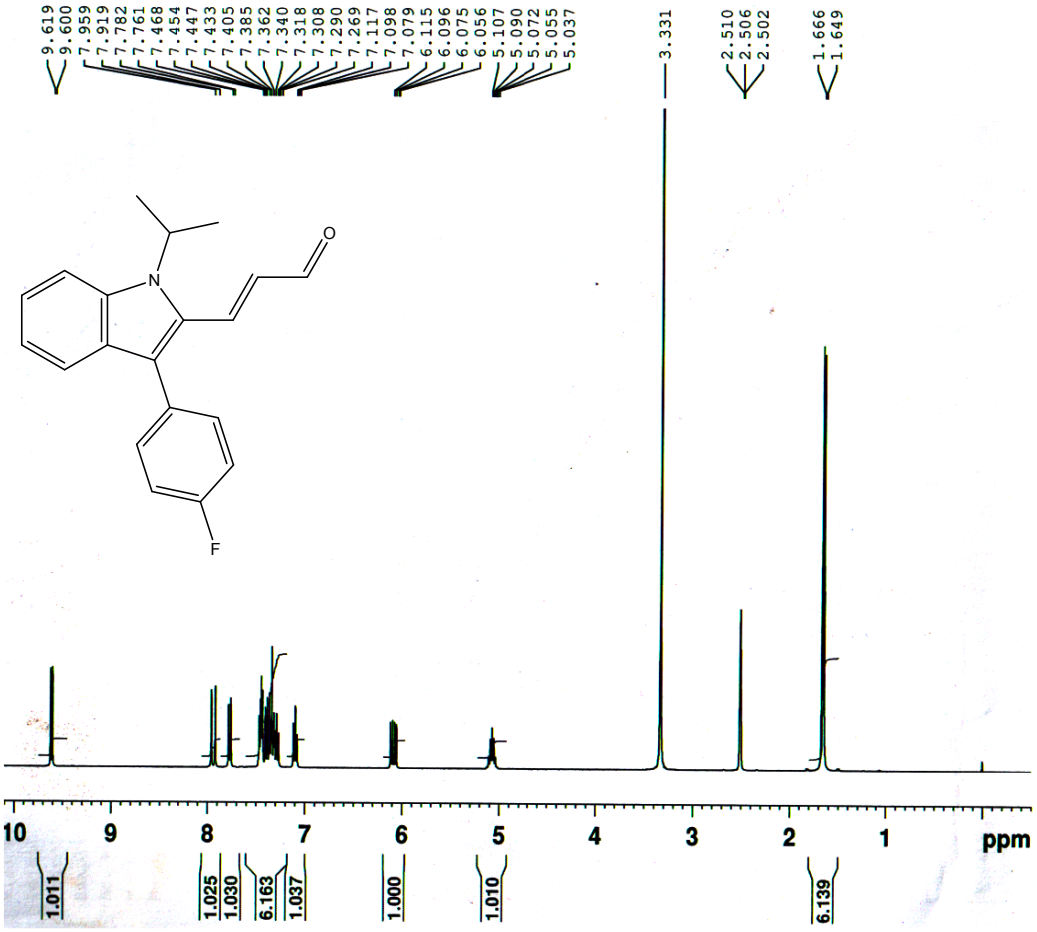
(*E*)-3-(3-(4-fluorophenyl)-1-isopropyl-1*H*-indol-2-yl)acrylaldehyde (3)

^{1}H NMR (400 MHz, DMSO-d6), δ): 1.657 (d, 6H, J = 6.8 Hz, isopropyl $(CH_3)_2$), 5.107 (m, 1H, isopropyl-CH), 6.115 (dd, 1H, J = 16, 7.6 Hz, H_β), 7.709-7.782 (m, 8H, Ar-H,), 7.959 (d, 1H, J = 16Hz, H_γ), 9.619 (d, 1H, J = 7.6Hz, CHO); ^{13}C NMR (100 MHz, DMSO-d6) δ ppm 21.37, 47.39, 112.60, 115.83 ($^2J_{C\text{-}F}$ = 21 Hz), 119.75, 119.95, 120.41, 124.13, 127.71, 130.14, 130.28, 131.96 ($^3J_{C\text{-}F}$ = 8 Hz), 136.45, 141.09, 161.41 ($^1J_{C\text{-}F}$ = 242 Hz), 194.02; LC-MS (*m/z*): 308.2 $[M+H]^+$, 309.2 $[M+2H]^+$, 310.2 $[M+3H]^+$; LC-MS purity: 99.97%, t_R-1.73 min; Anal. Calcd. for $C_{20}H_{18}FNO$ (307.36): C, 78.15%; H, 5.90%; N, 4.56%; Found: C, 78.09%; H, 5.86%; N, 4.48%.

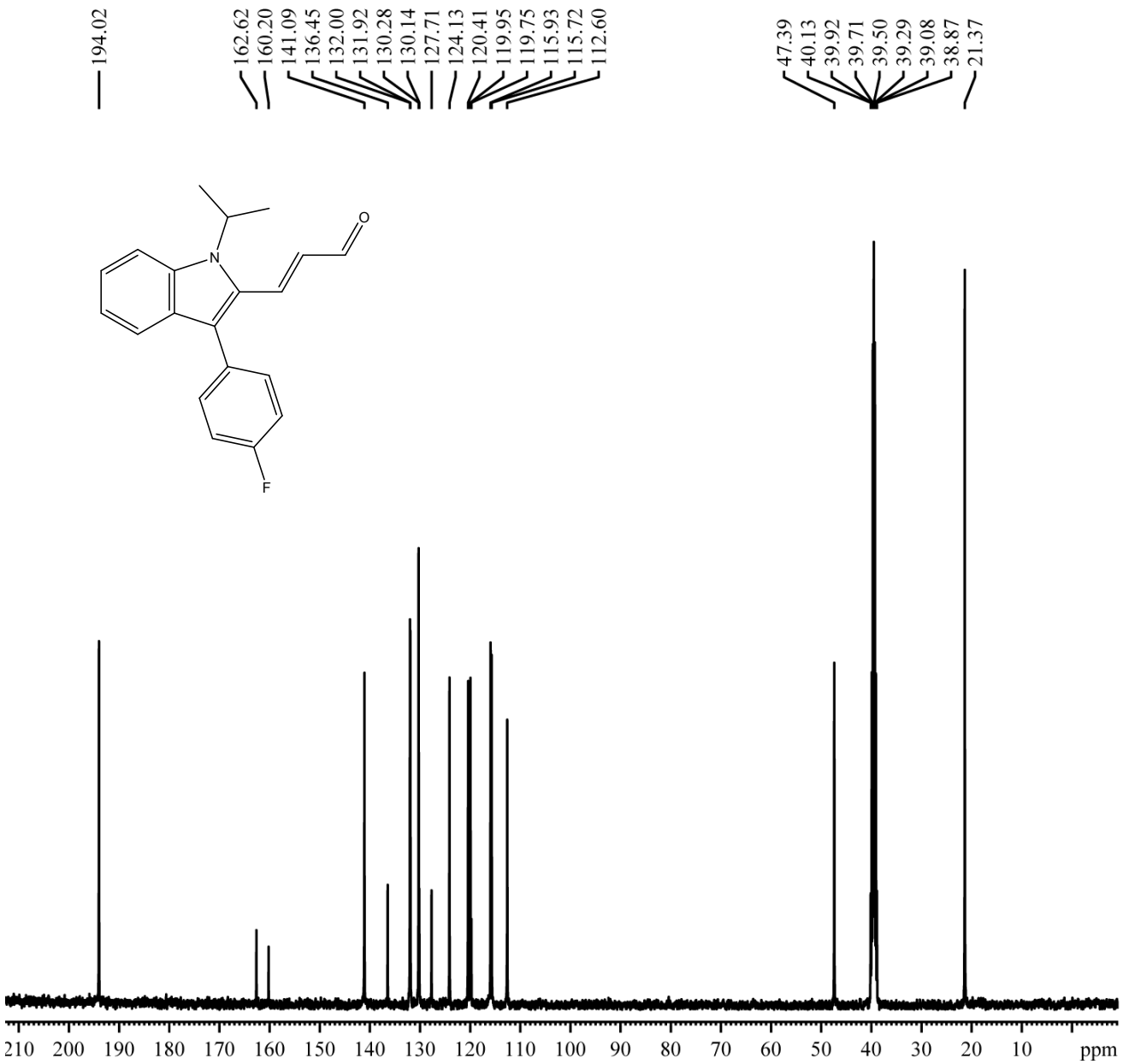
IR spectrum of 3



^{1}H NMR spectrum of 3

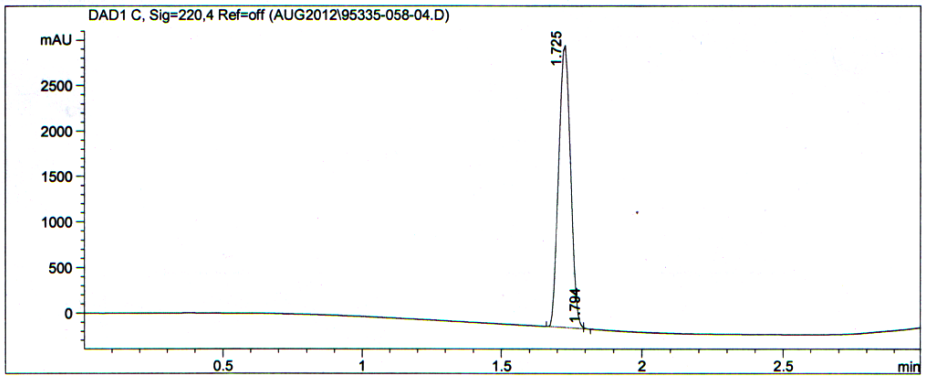


^{13}C NMR spectrum of 3

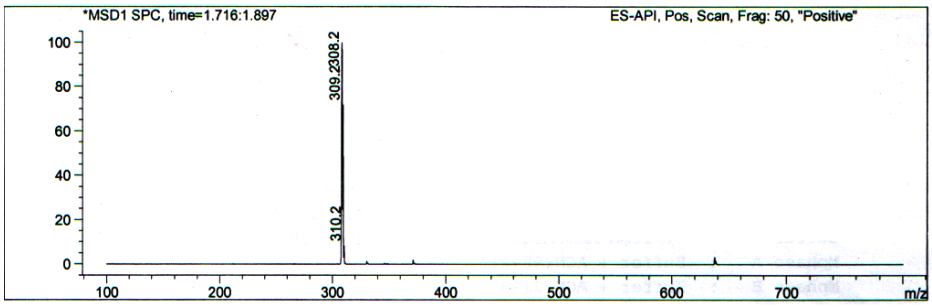


LCMS spectrum of 3

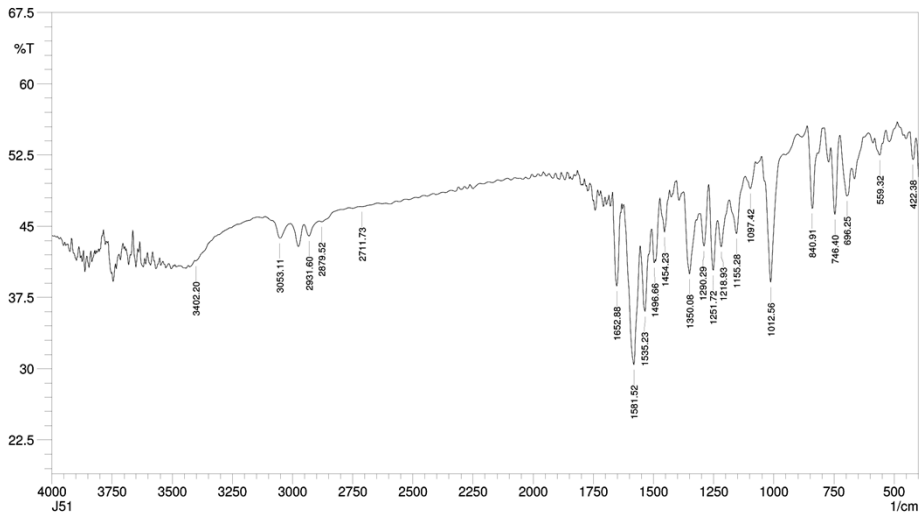
```
Method info  : Column       : Zorbax SB C18 (30 x 2.1 mm; 3.5 u)
               Buffer         : 10mM Ammonium Formate in Water pH 4.5
               Mphase A    :  Buffer + ACN(98+2)
               Mphase B    :  Buffer + ACN(2+98)
               Flow           :  1.5ml/min
               Time (min.)  :   0       1.5       2.2         2 .6      3.0
                % B            :   6     100       100           6          6
```



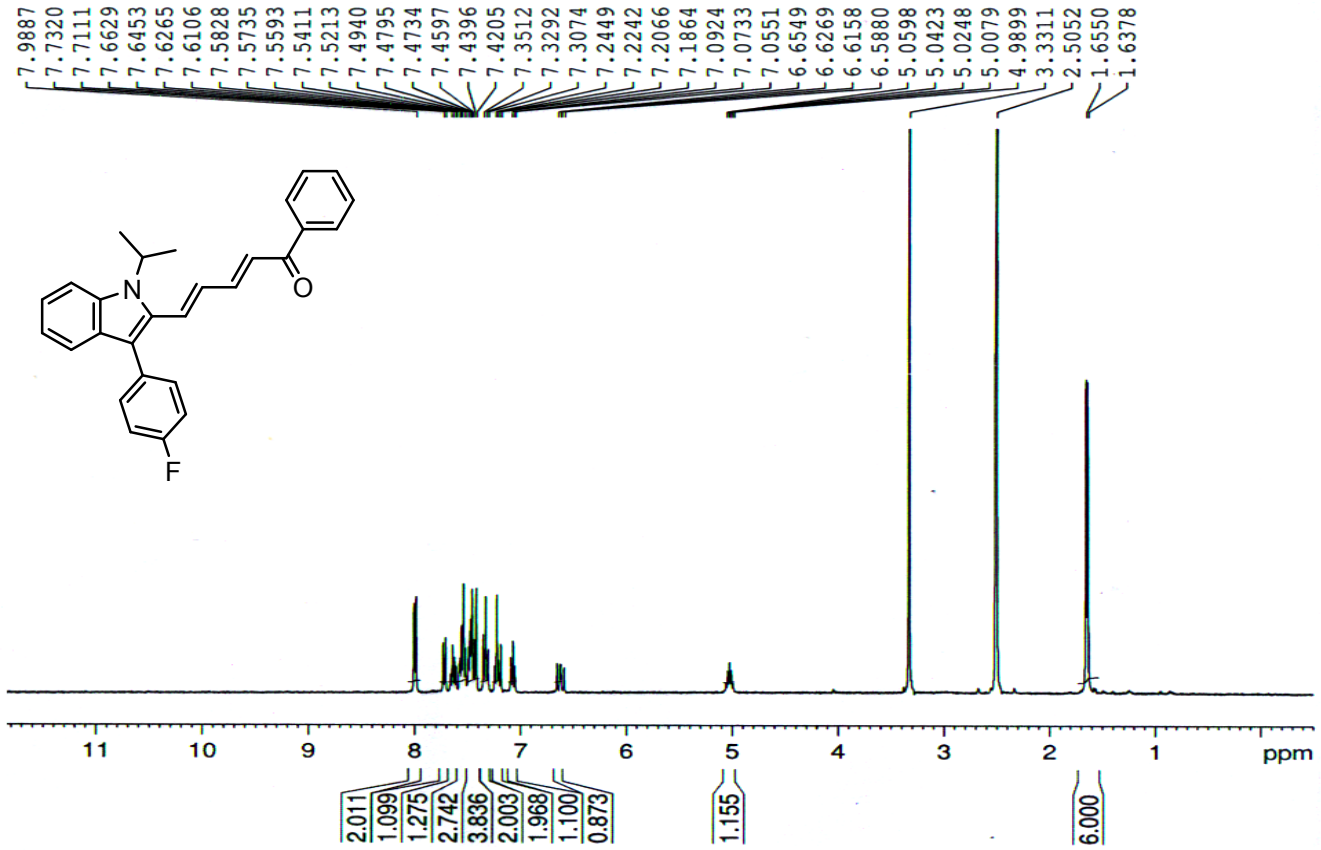
Peak No	RT min	Area	Area %
1	1.725	9.238e+003	99.974
2	1.794	2.393e+000	0.026



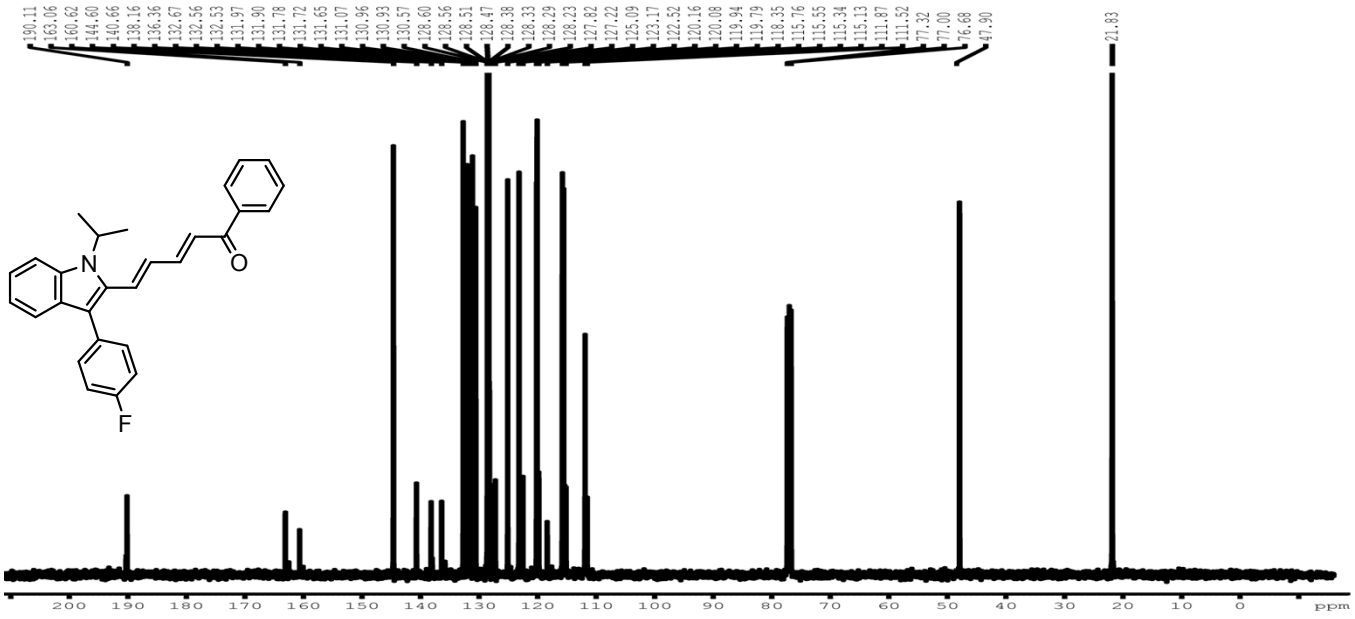
IR spectrum of 5a



^{1}H NMR spectrum of 5a

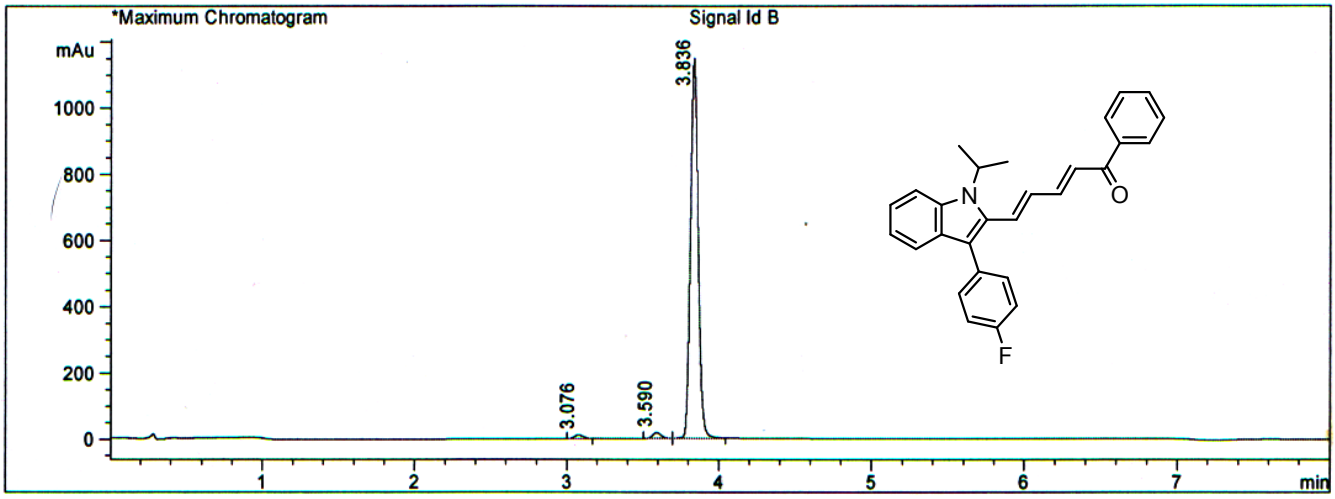


^{13}C NMR spectrum of 5a

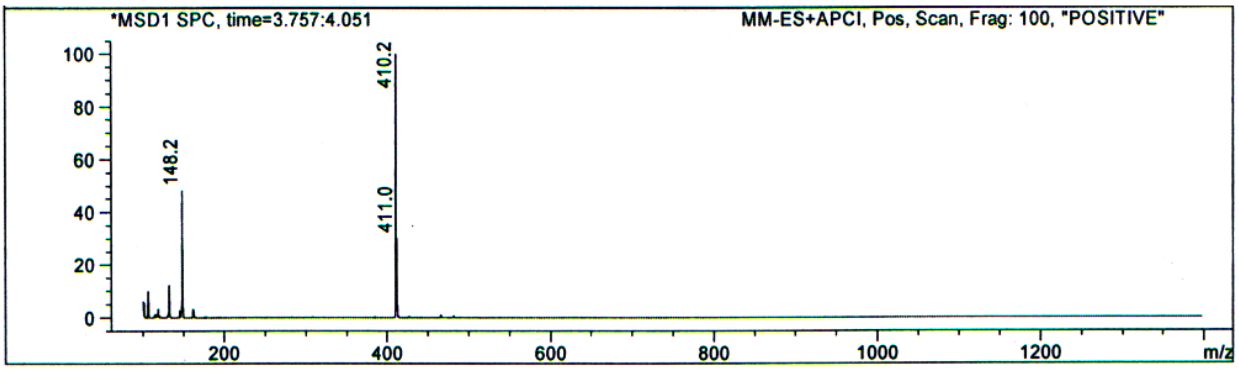


LCMS spectrum of 5a

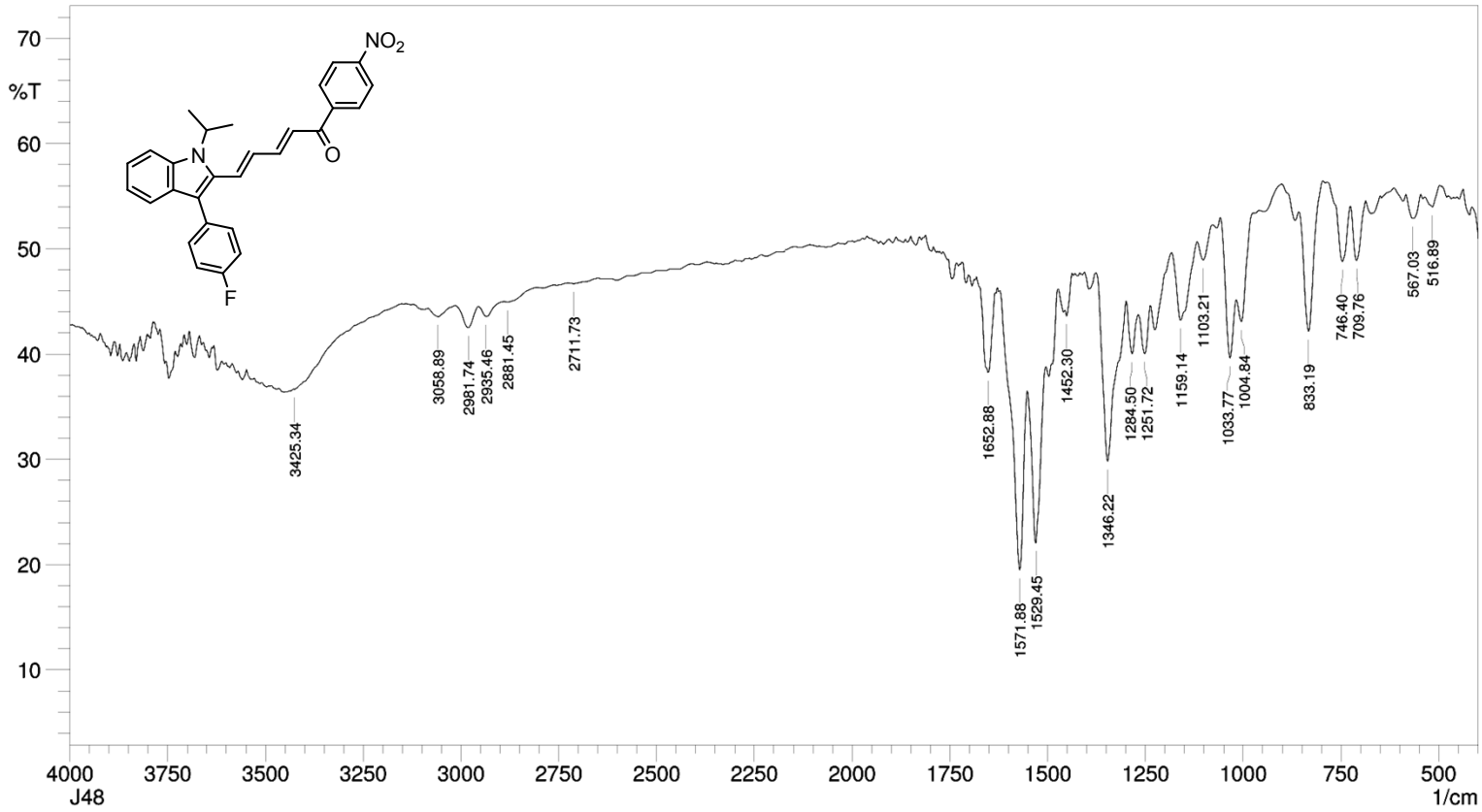
```
Method info  : A-0.1% HCOOH IN WATER ;B-ACN  Flow = 1.5ml/min,
               Column-Zorbax Extend  C18 (50X4.6mm-5µm, ) ,
              Time (min.):  0--3      3--6       6--7     7--8.0
               % B :        40-95     95       95-40      40
```



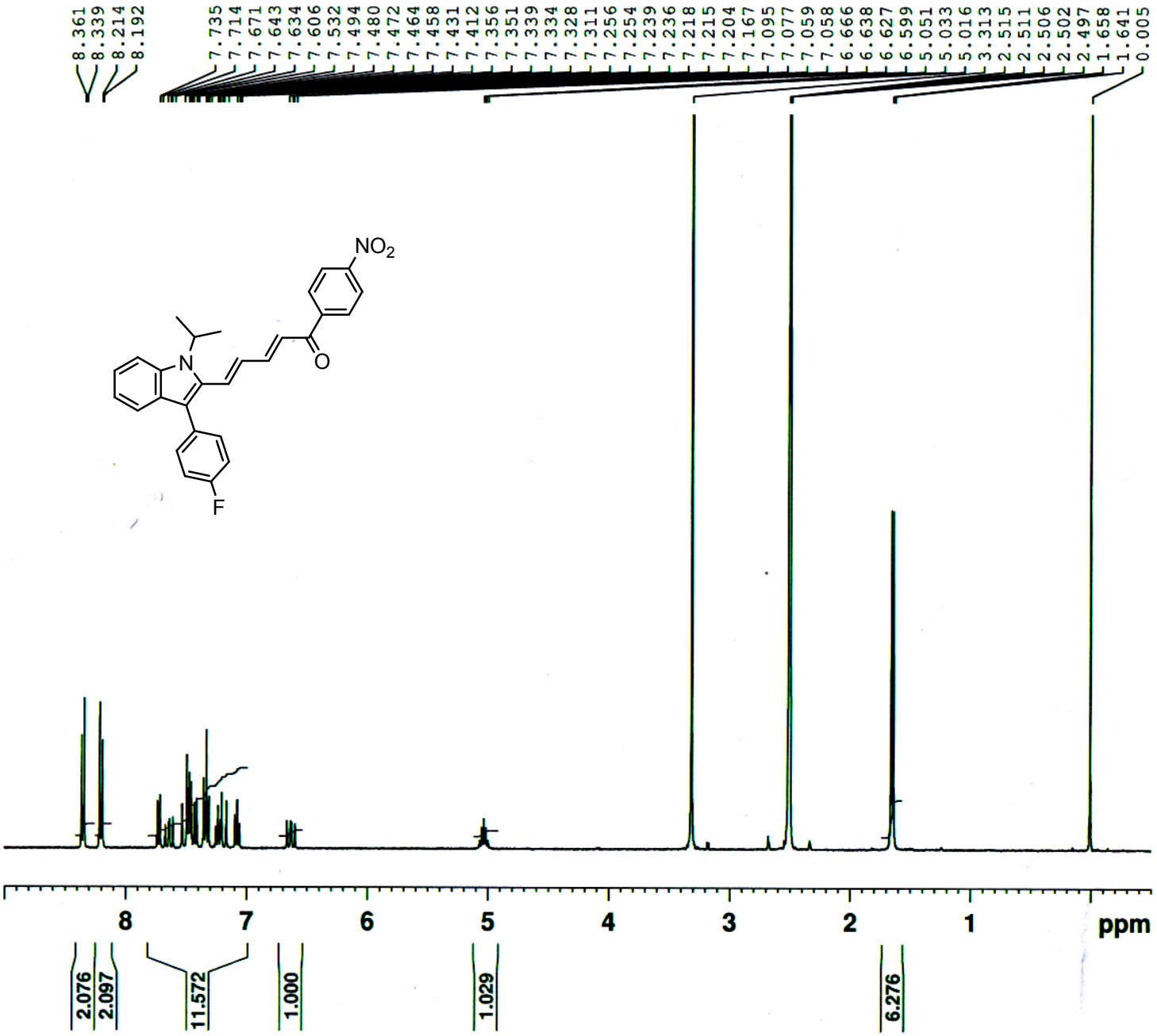
Peak No	RT min	Area	Area %
1	3.076	52.379	1.237
2	3.590	72.724	1.718
3	3.836	4108.868	97.045



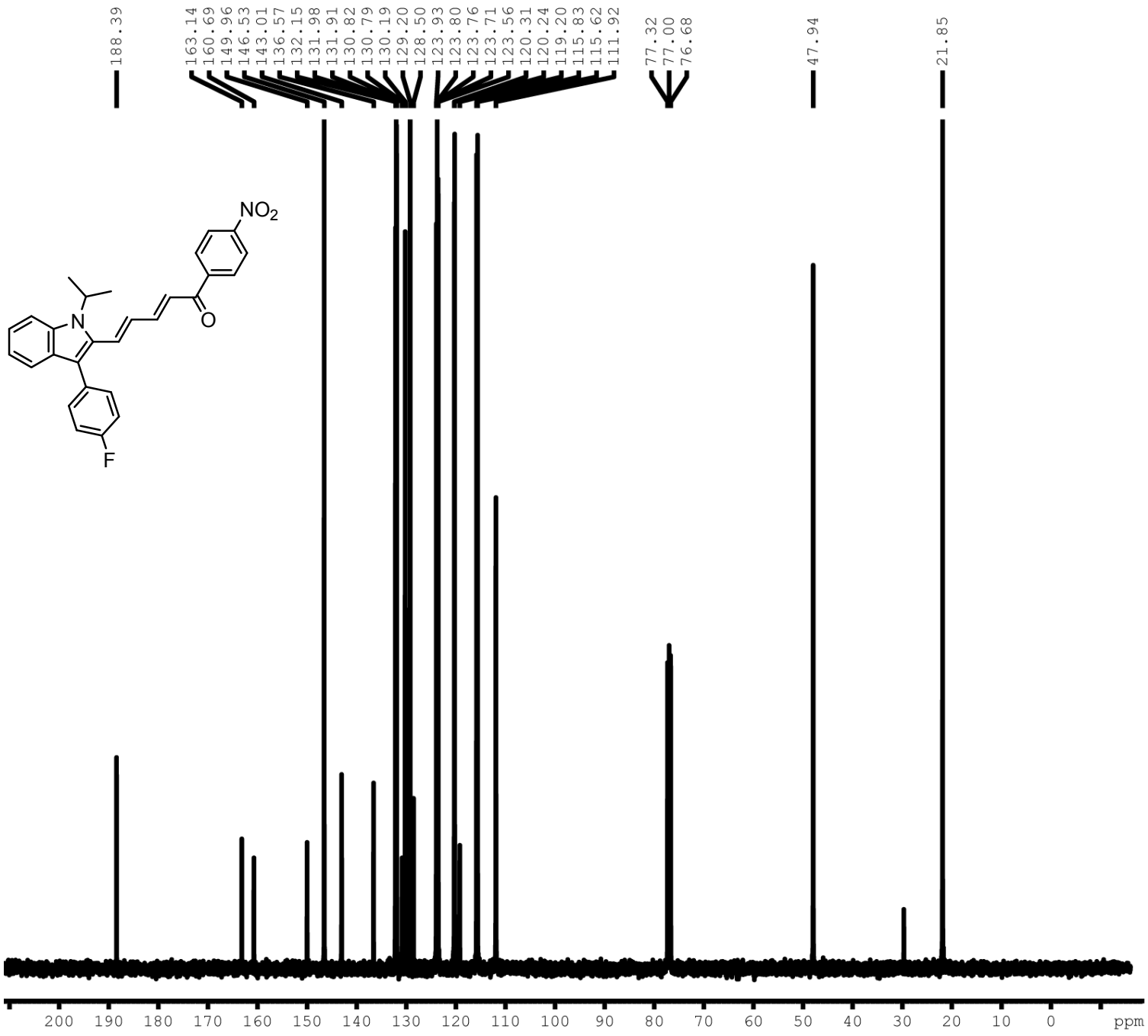
FTIR spectrum of 5b



^{1}H NMR spectrum of 5b



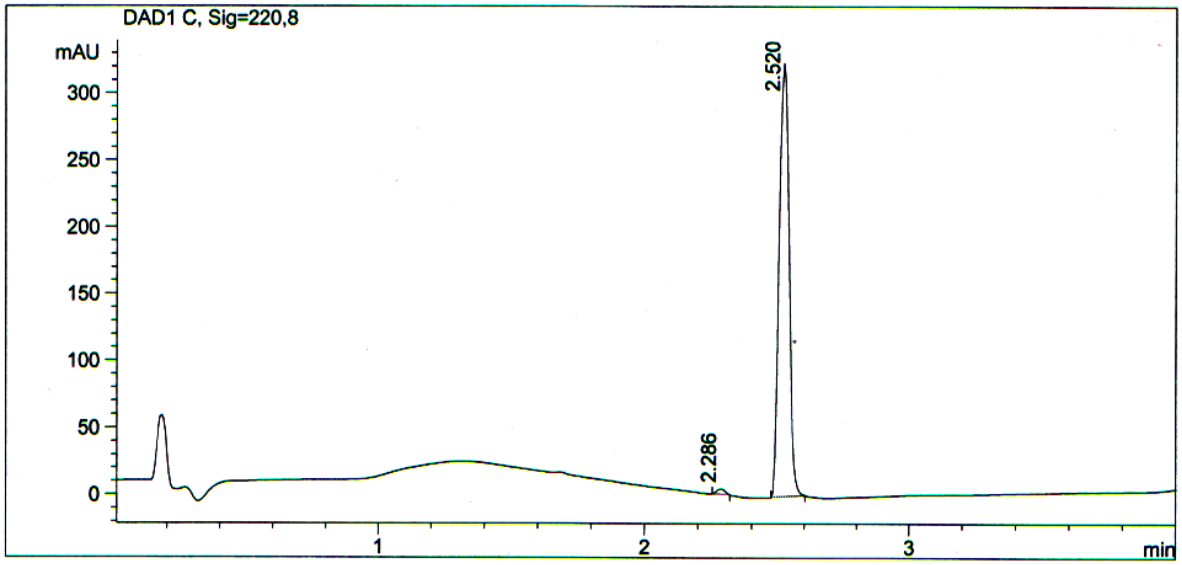
^{13}C NMR spectrum of 5b



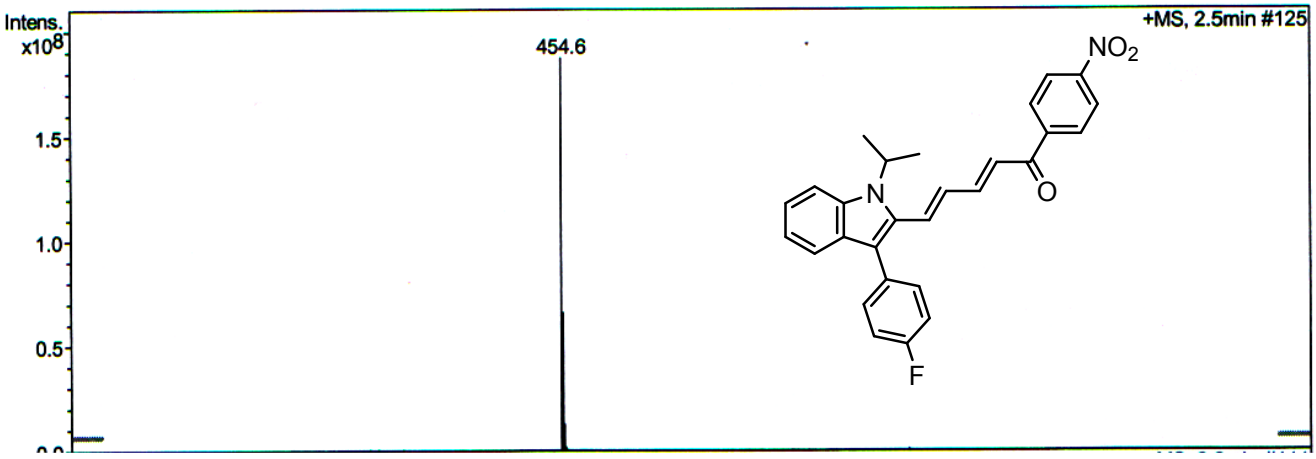
LCMS Spectrum of 5b

Method info : MOBILE PHASE- A:-10mM Ammonium Hydrogen Carbonate
MOBILE PHASE- B:- ACN
Flow :-1.0ml/min
Column:Xbridge C18 (50X2.1mm) 2.5µm

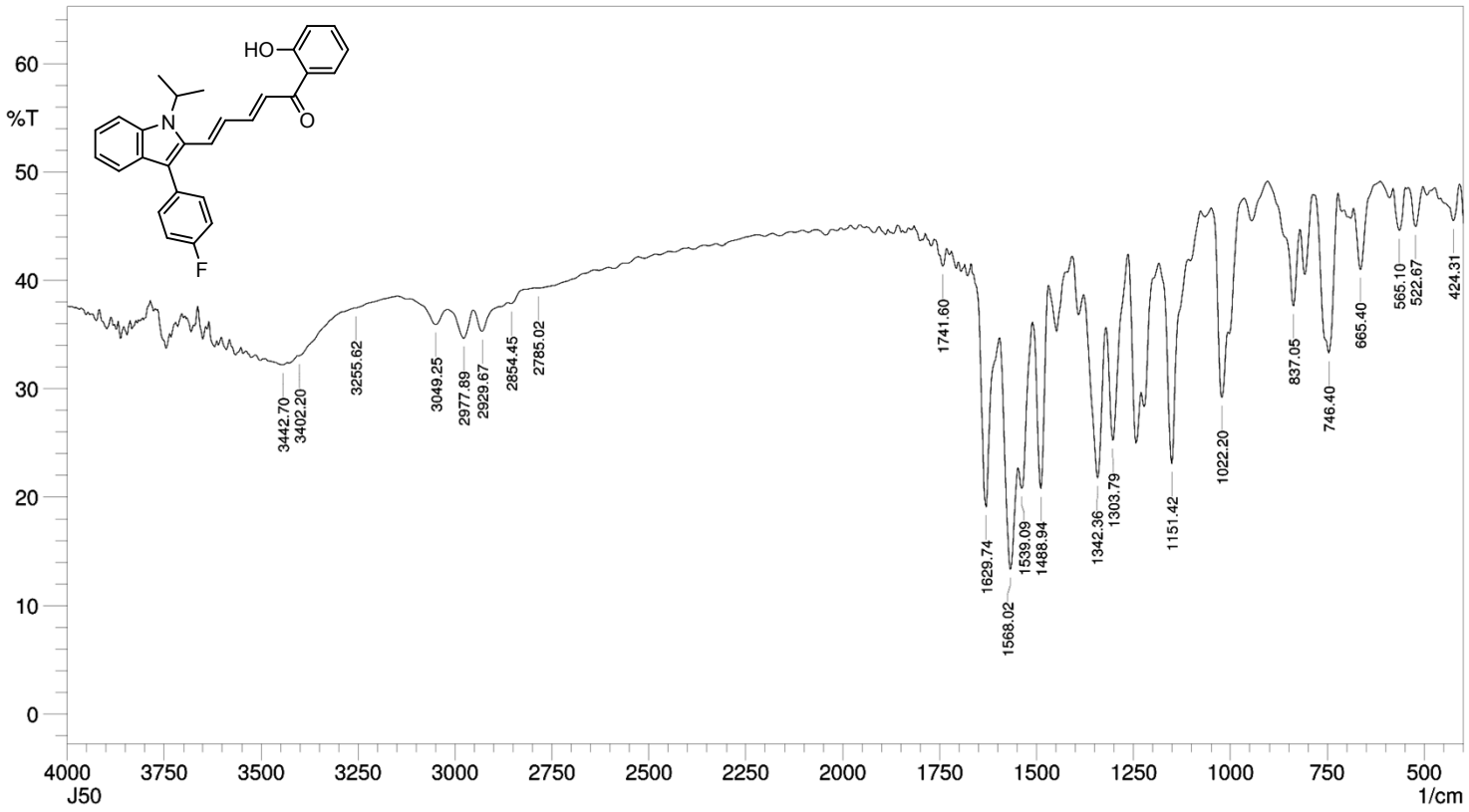
Time	%B	%A
0	0	100.0
1.7	100	0
3.2	100	0



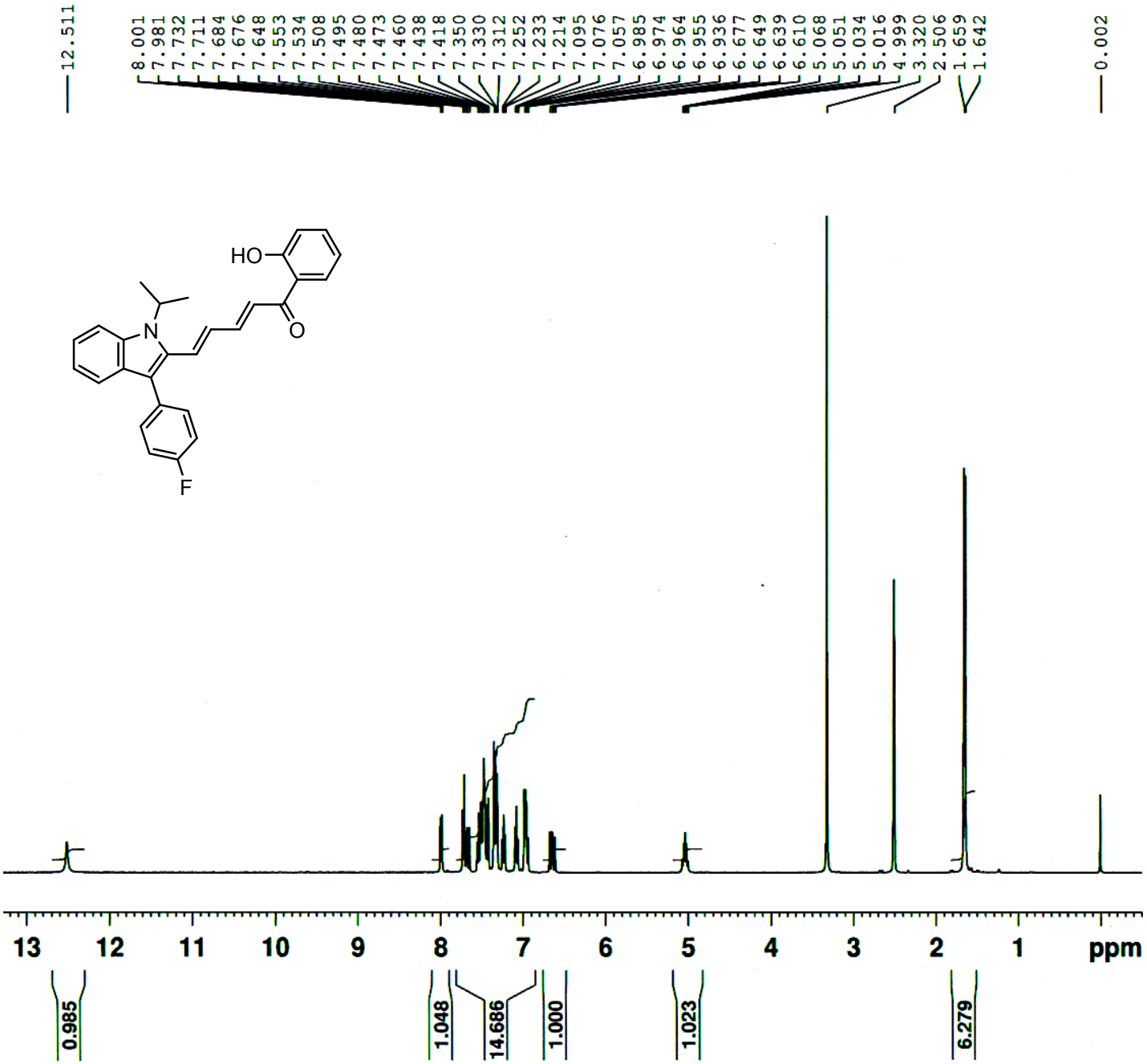
Peak No	RT min	Area	Area %
1	2.286	9.210	1.074
2	2.520	848.436	98.926



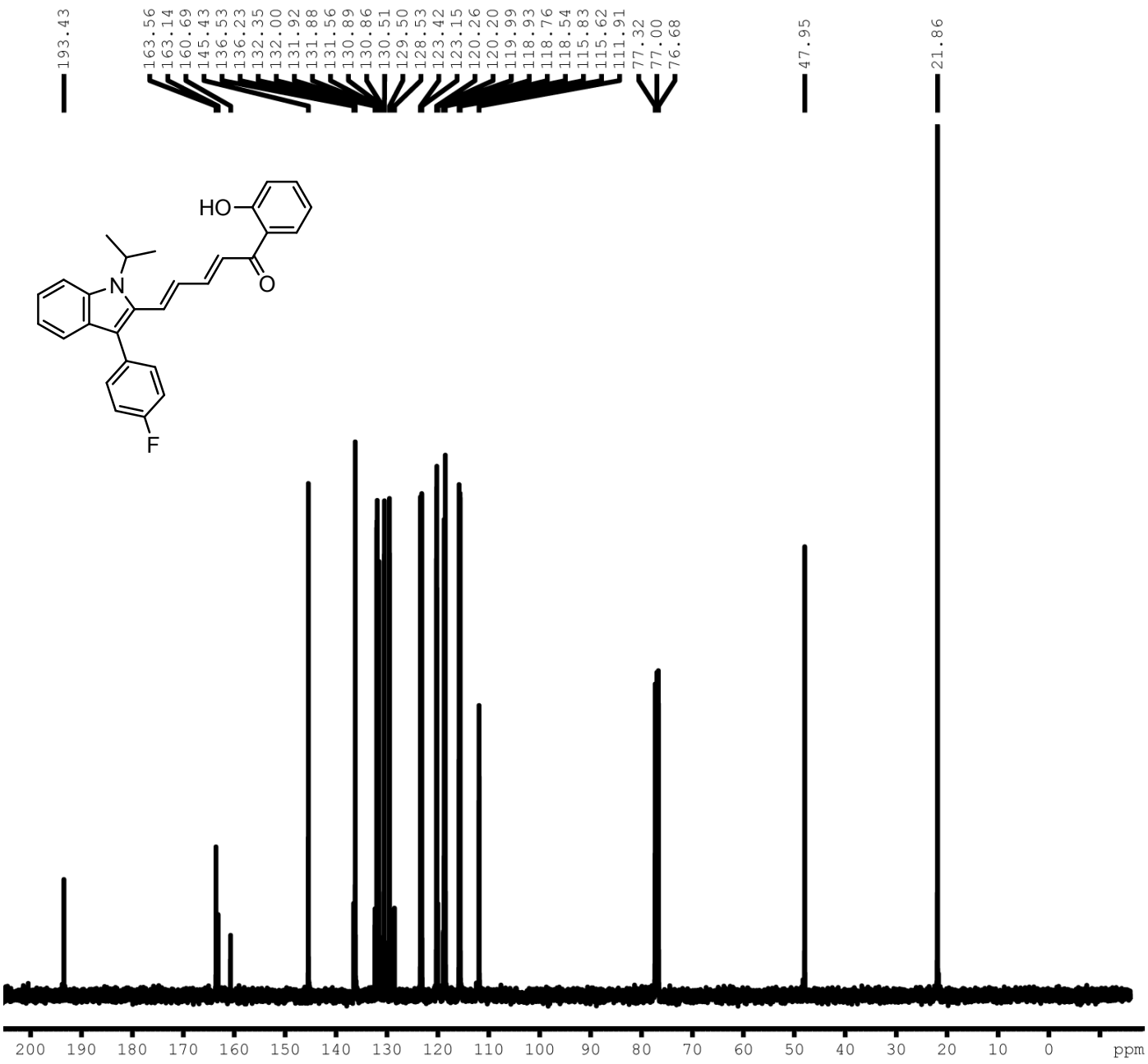
FTIR Spectrum of 5c



^{1}H NMR spectrum of 5c

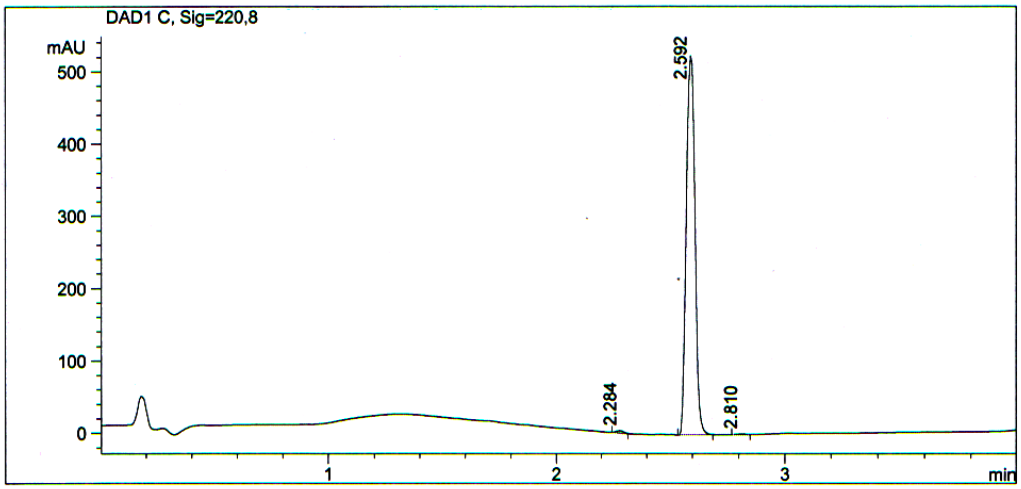


^{13}C NMR spectrum of 5c

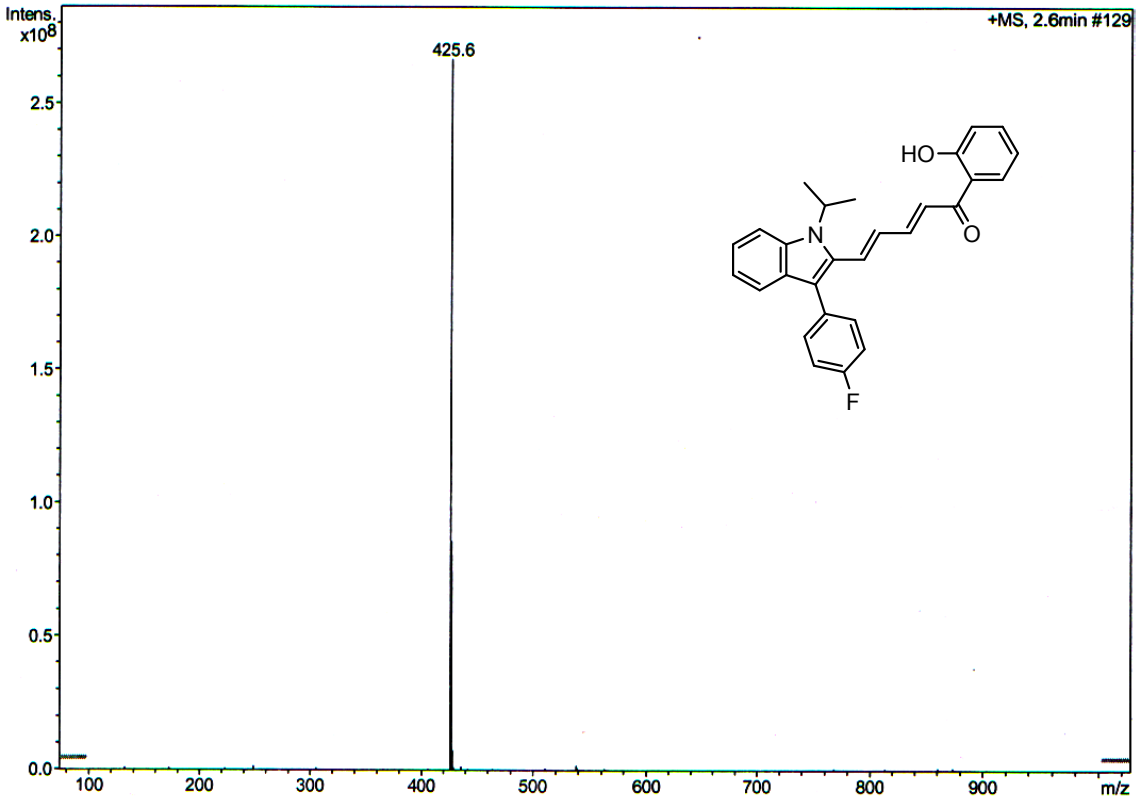


LCMS spectrum of 5c

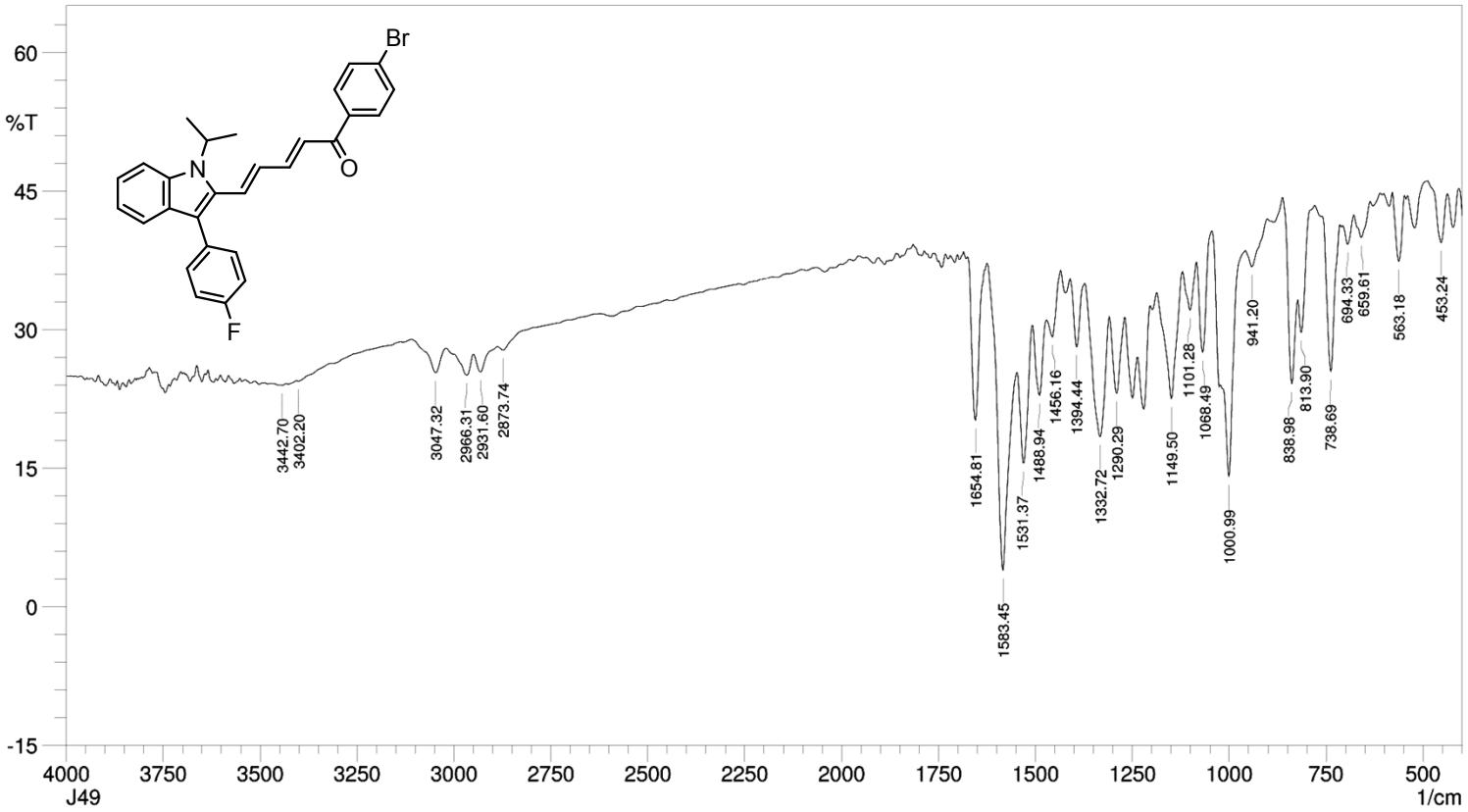
```
Method info  :   MOBILE PHASE- A:-10mM Ammonium Hydrogen Carbonate
                 MOBILE PHASE- B:- ACN
                 Flow :-1.0ml/min
                 Column:Xbridge C18  (50X2.1mm) 2.5µm
                 Time      %B            %A
                  0            0          100.0
                 1.7         100          0
                 3.2         100          0
```



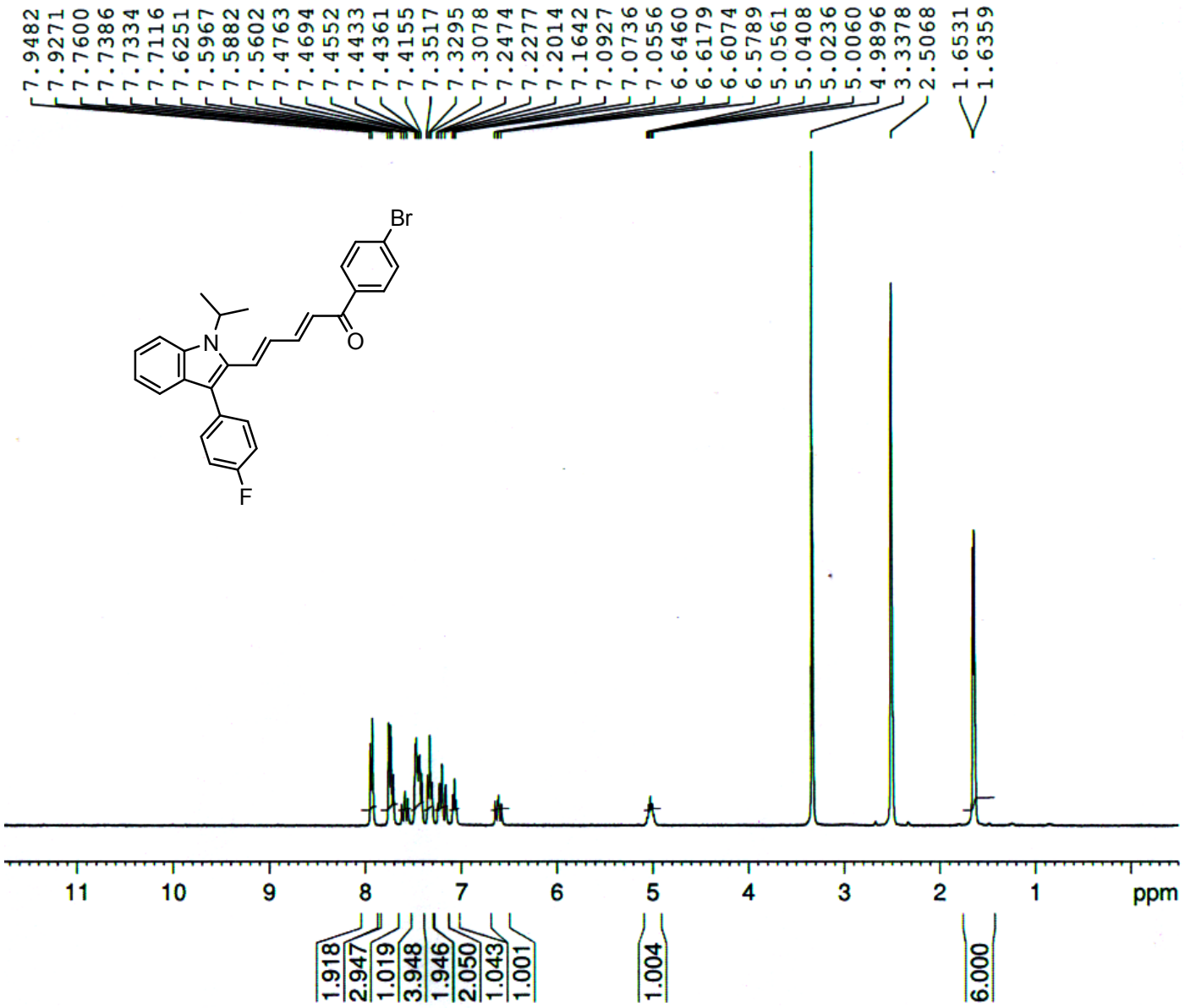
Peak No	RT min	Area	Area %
1	2.284	8.602	0.620
2	2.592	1373.523	99.010
3	2.810	5.129	0.370



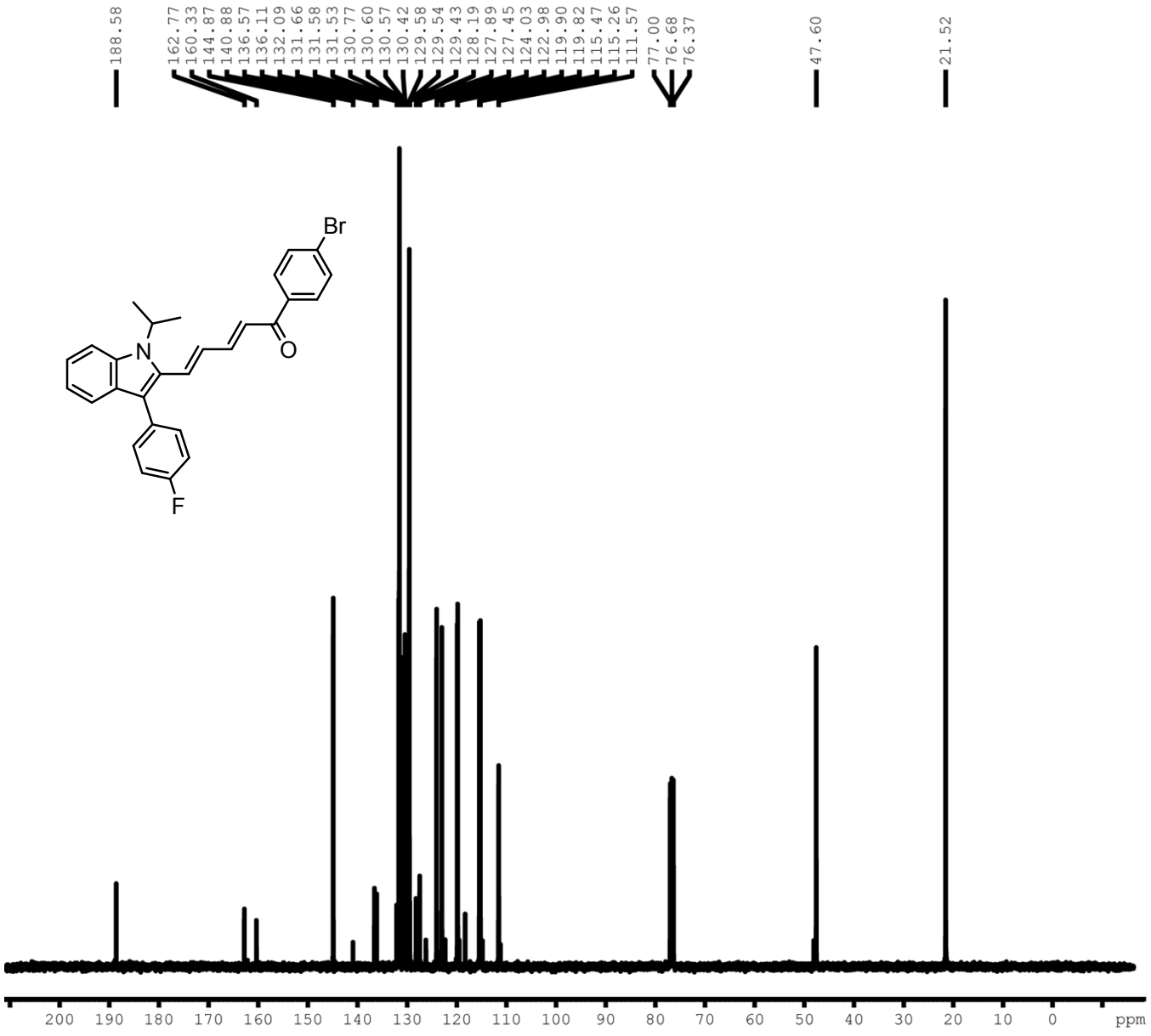
FTIR spectrum of 5d



^{1}H NMR spectrum of 5d

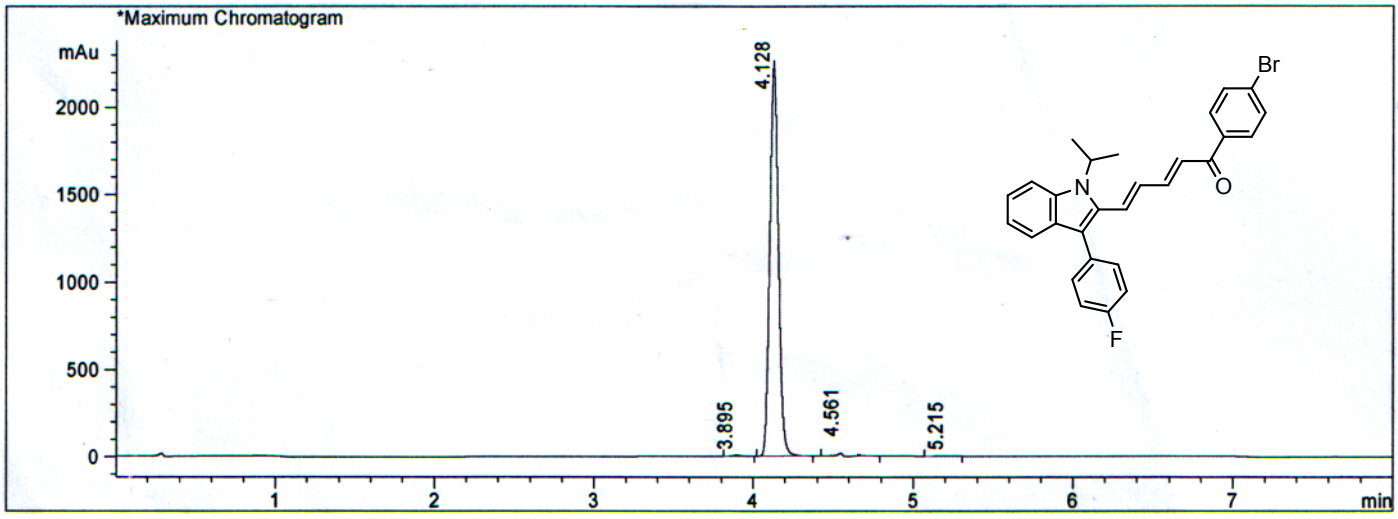


^{13}C NMR spectrum of 5d

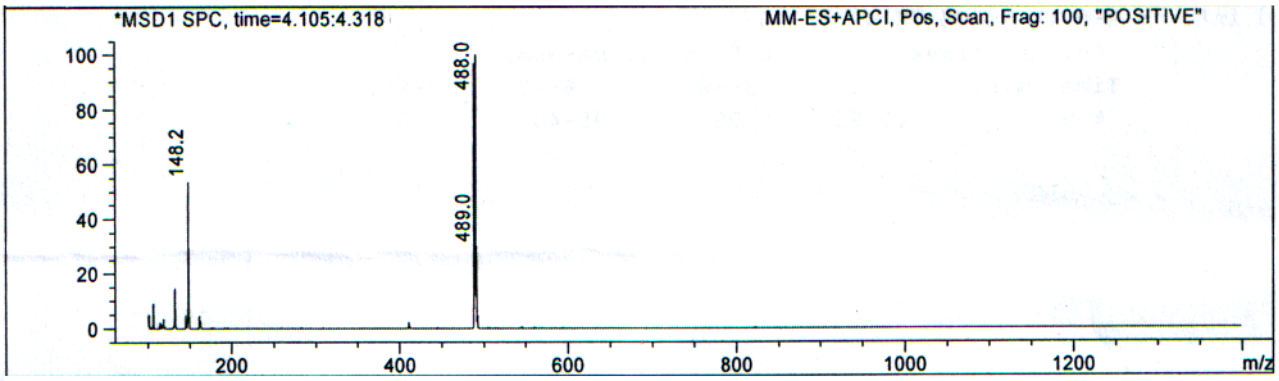


LCMS spectrum of 5d

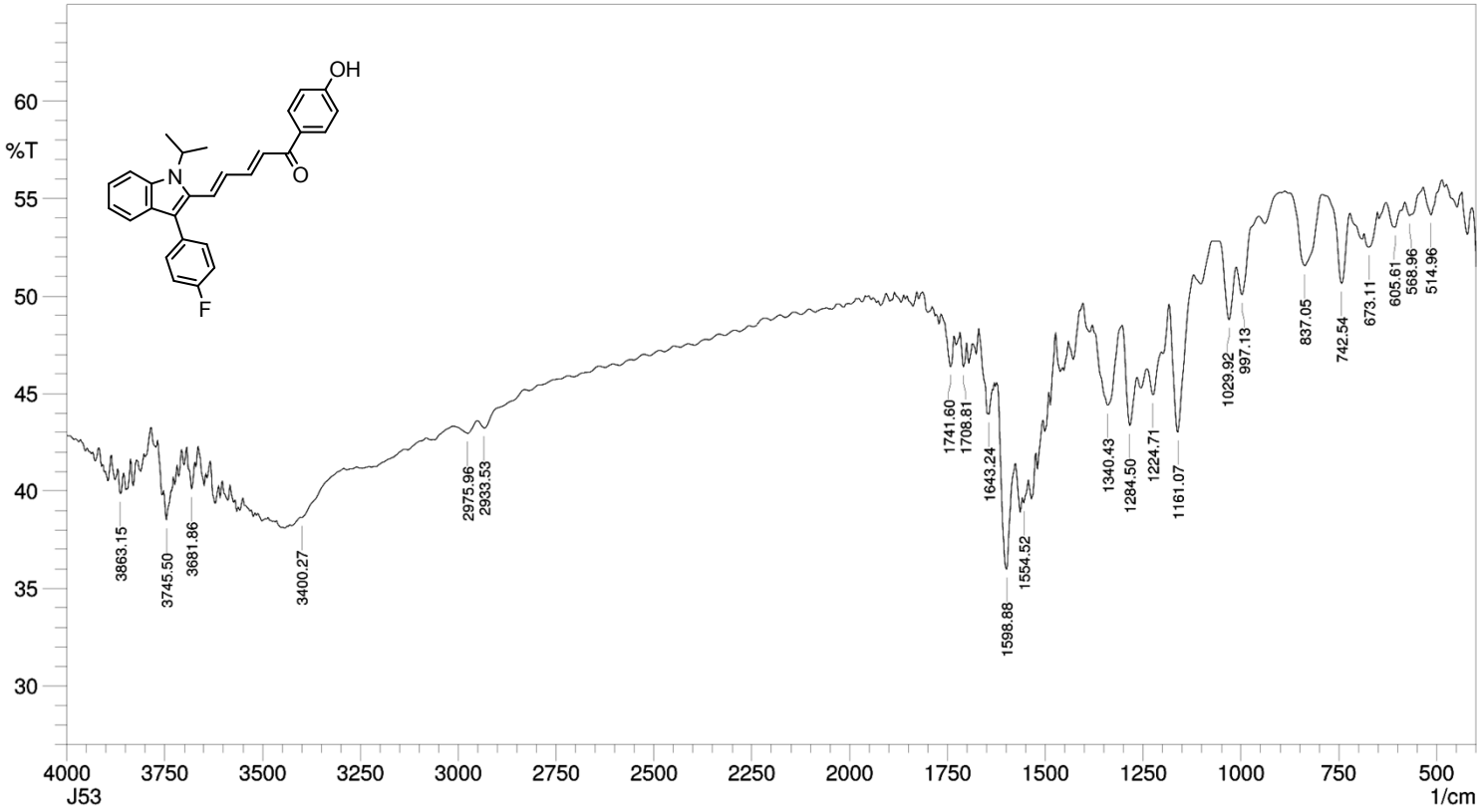
```
Method info  : A-0.1% HCOOH IN WATER ;B-ACN  Flow = 1.5ml/min,
               Column-Zorbax Extend  C18 (50X4.6mm-5µm, ) ,
              Time (min.):  0--3      3--6        6--7     7--8.0
               % B :        40-95     95       95-40       40
```



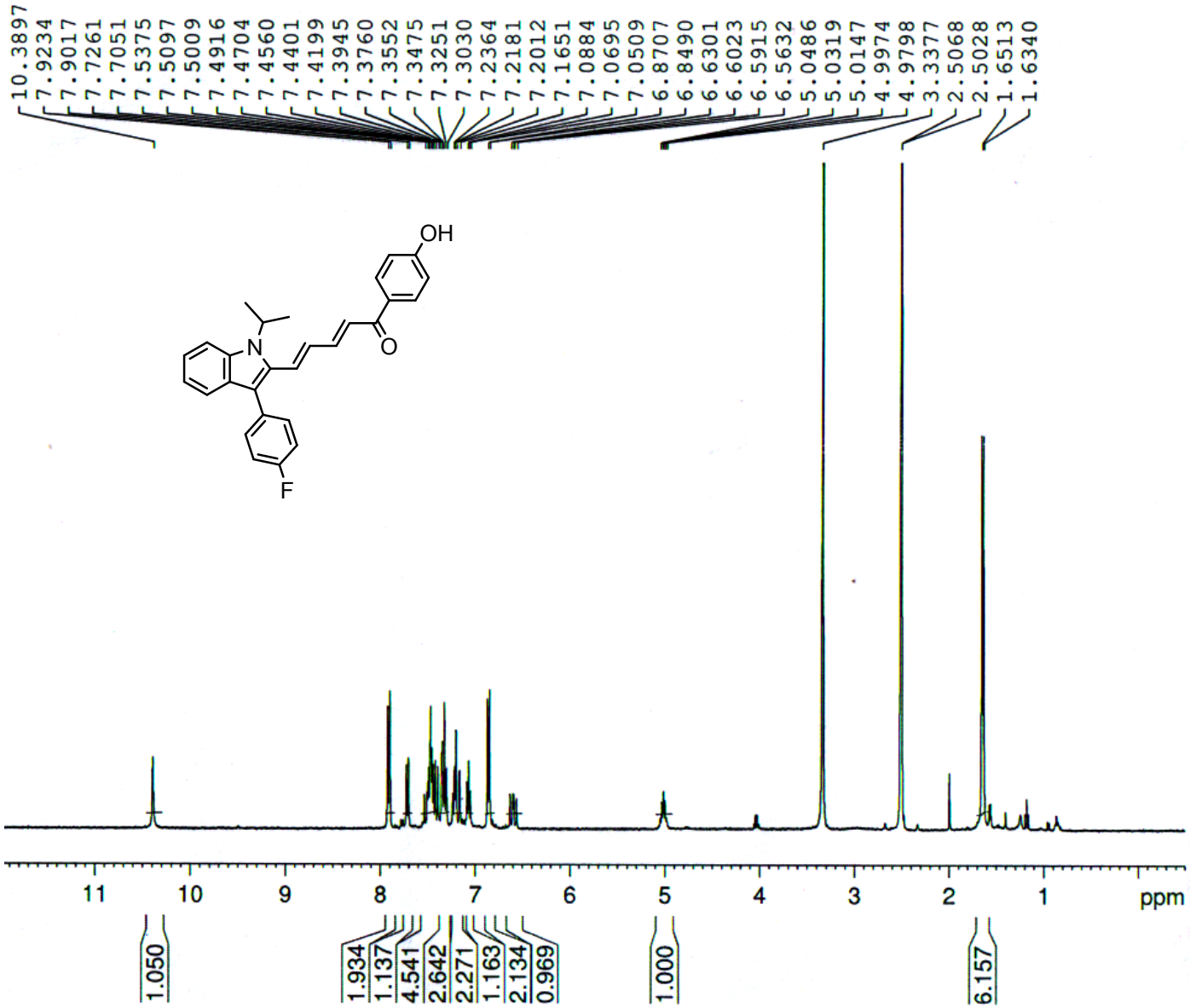
Peak No	RT min	Area	Area %
1	3.895	37.517	0.419
2	4.128	8460.143	98.540
3	4.561	430.721	0.813
4	5.215	20.389	0.228



FTIR spectrum of 5e

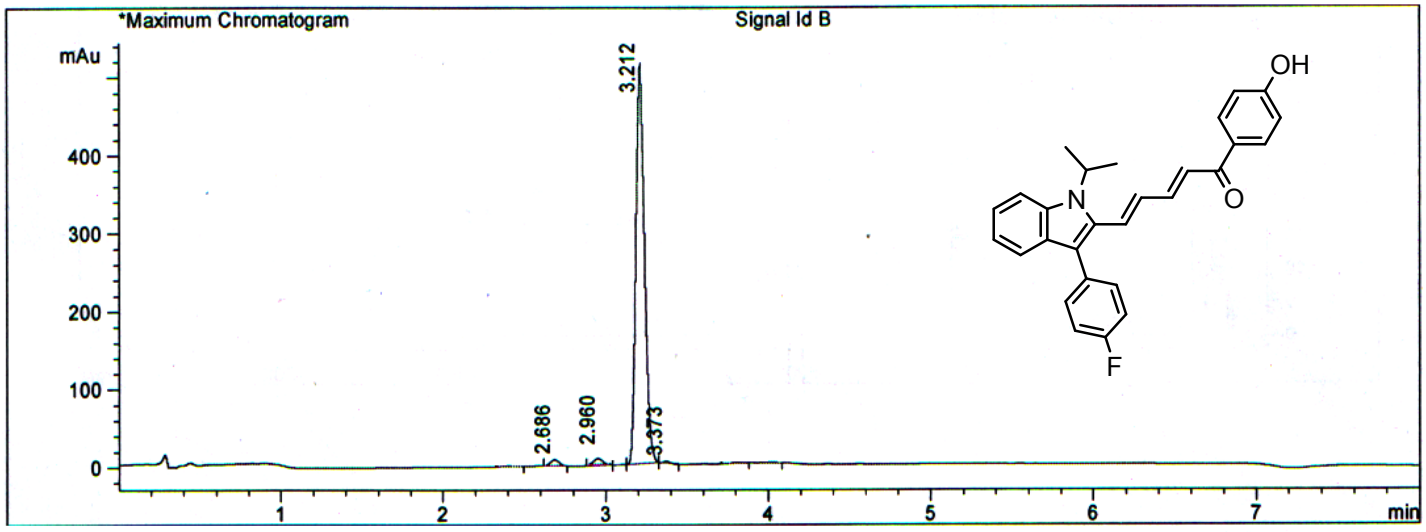


^{1}H NMR spectrum of 5e

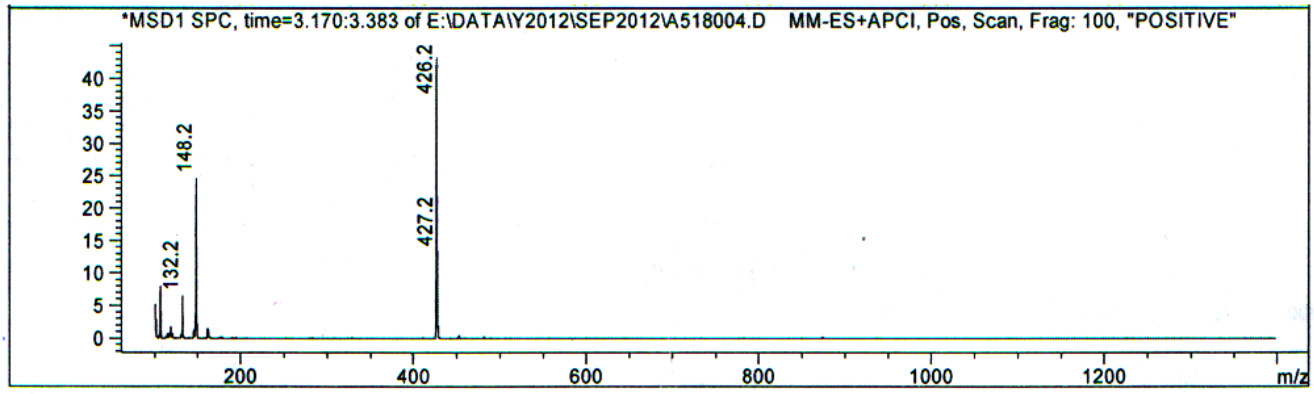


LCMS spectrum of 5e

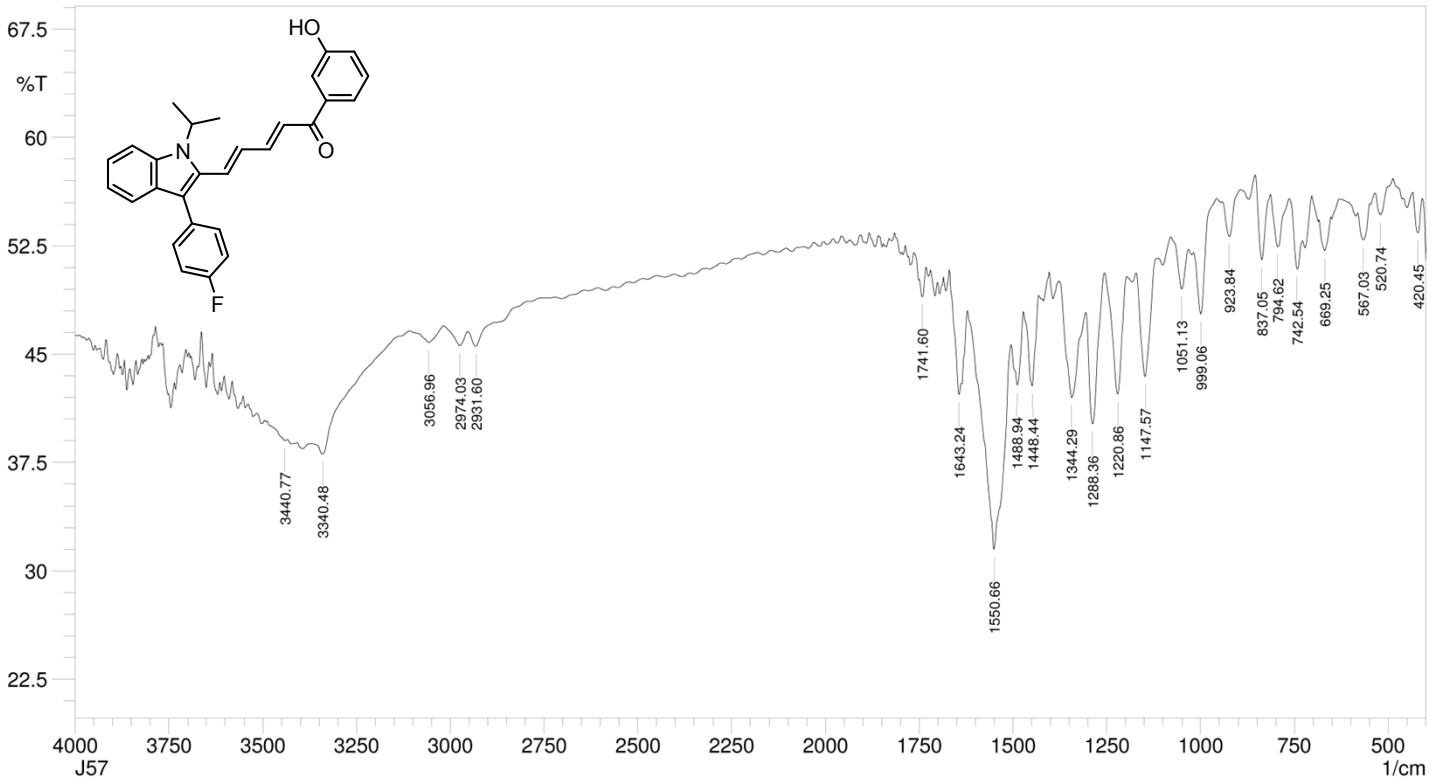
```
Method info  : A-0.1% HCOOH IN WATER ;B-ACN  Flow = 1.5ml/min,
               Column-Zorbax Extend  C18 (50X4.6mm-5µm, ) ,
              Time (min.):  0--3      3--6        6--7      7--8.0
               % B :        40-95     95       95-40       40
```



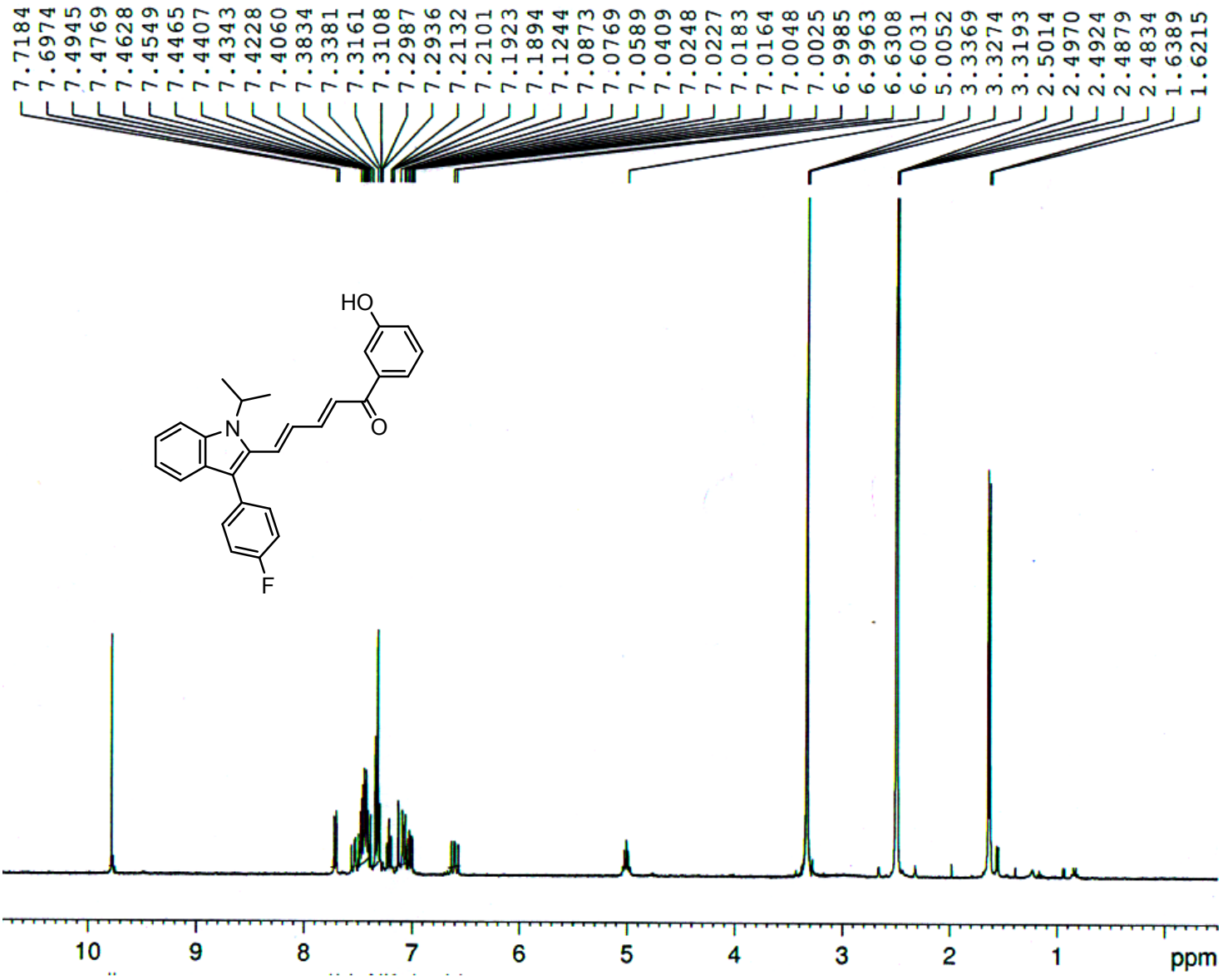
Peak No	RT min	Area	Area %
1	2.686	28.970	0.542
2	2.960	71.808	0.489
3	3.212	1928.325	98.688
4	3.373	5.794	0.281



FTIR spectrum of 5f



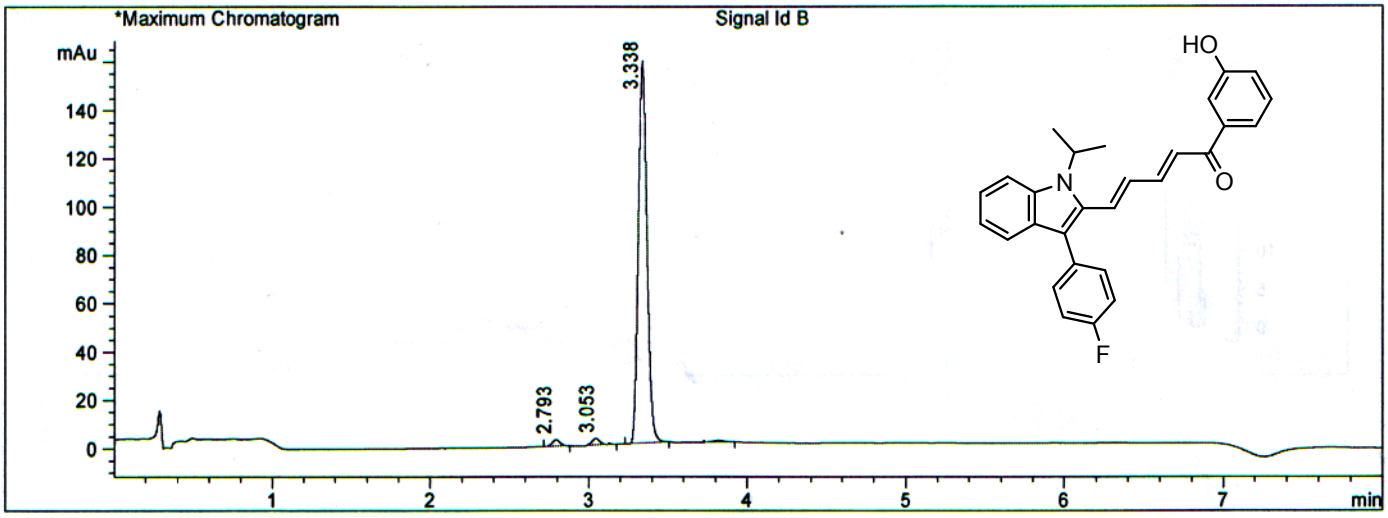
^{1}H NMR spectrum of 5f



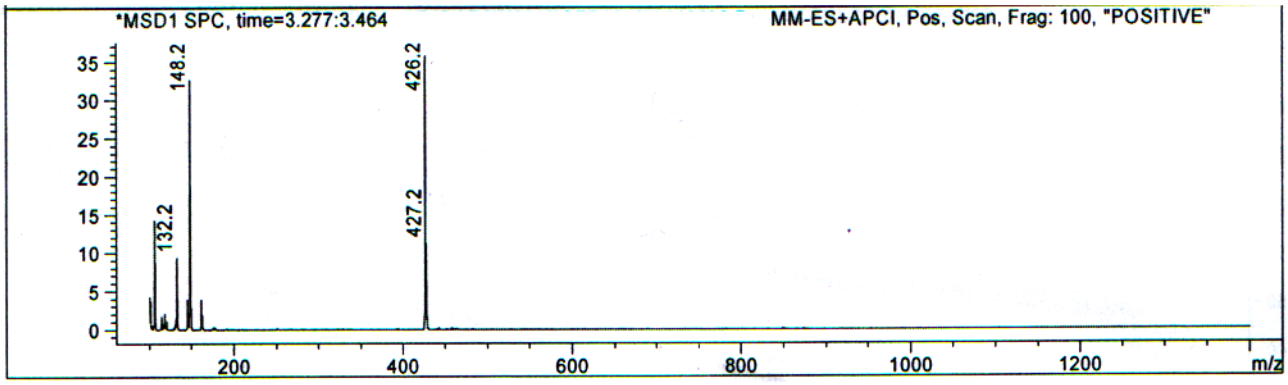
LCMS spectra of 5f

Method info : A-0.1% HCOOH IN WATER ;B-ACN Flow = 1.5ml/min,
Column-Zorbax Extend C18 (50X4.6mm-5µm,) ,

Time (min.):	0--3	3--6	6--7	7--8.0
% B :	40-95	95	95-40	40



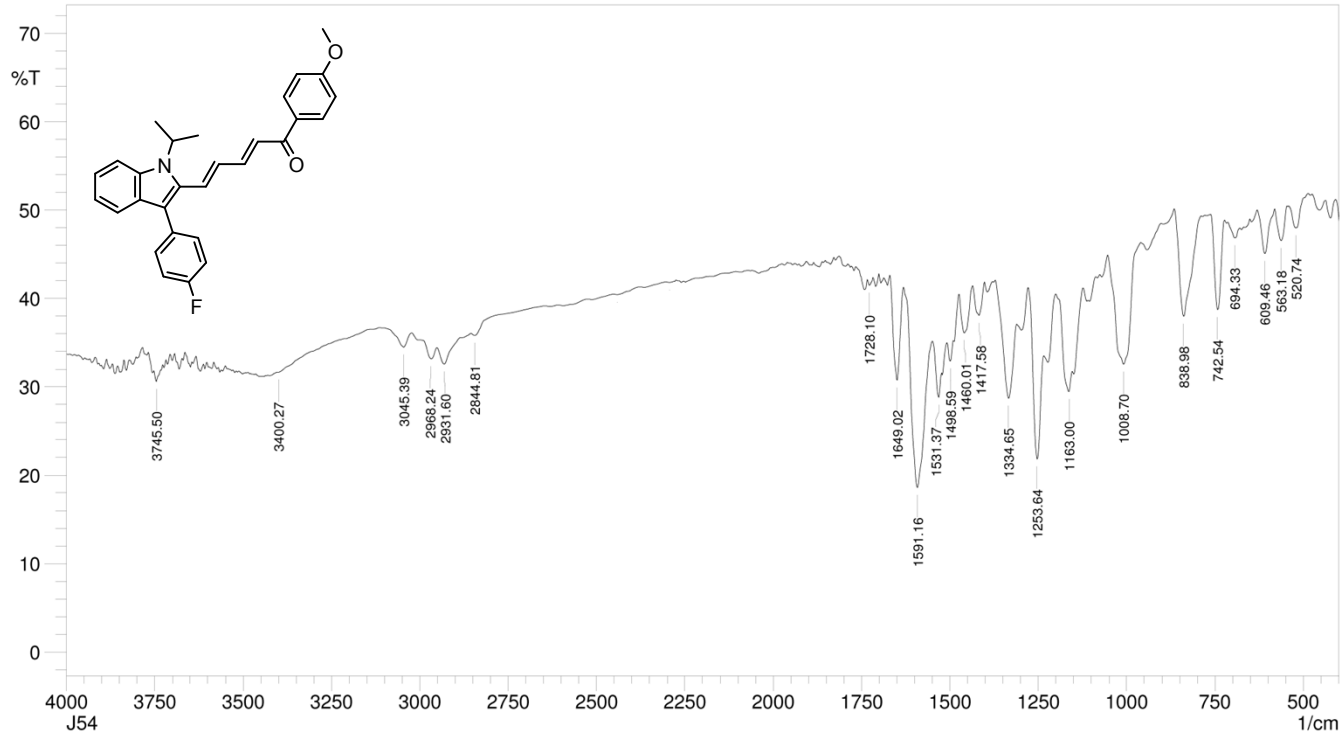
Peak No	RT min	Area	Area %
1	2.793	9.678	0.975
2	3.053	53.848	1.039
3	3.338	601.386	97.986



FTIR spectrum of 5g

C:\Program Files\Shimadzu\IRsolution\PrintTemplates\No Grids-No Table.ptm

1



Comment;aminphos

J54

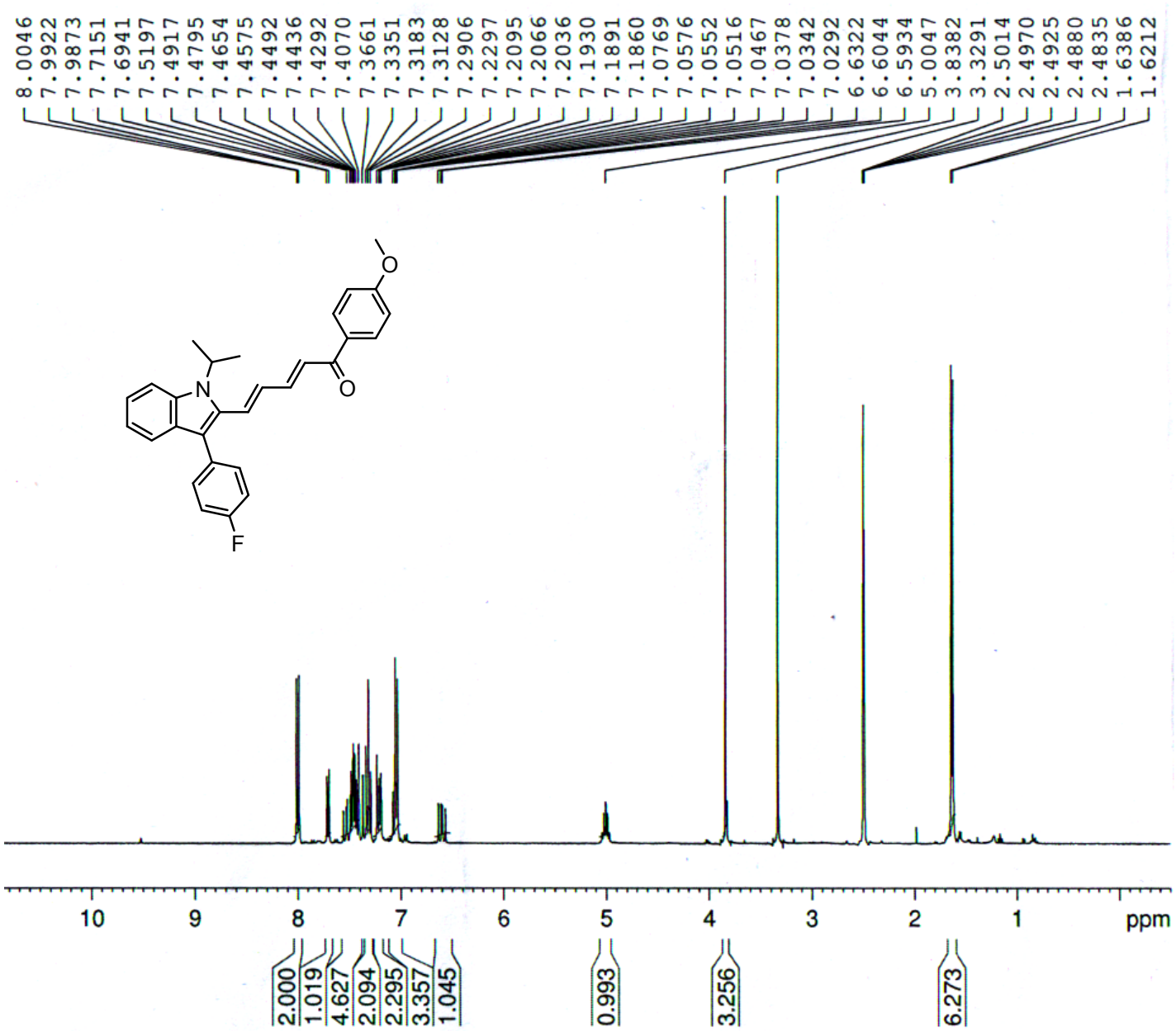
No. of Scans;

Resolution;

Date/Time; 10/18/2012 01:56:43 PM

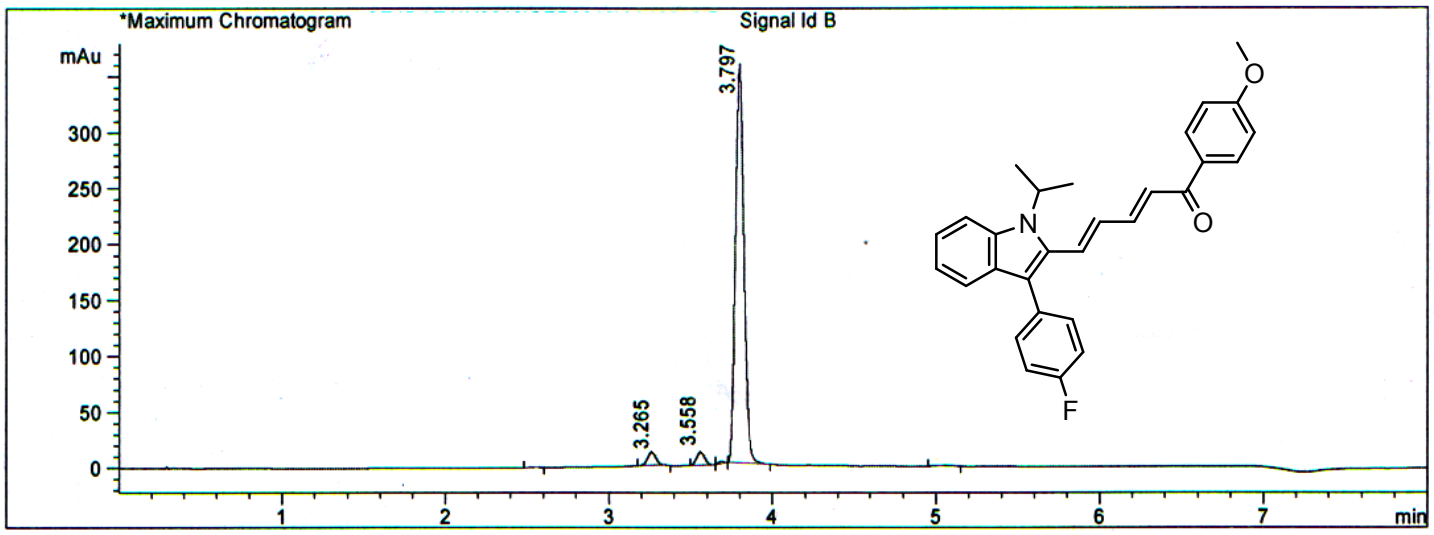
User; Administrator

^{1}H NMR spectrum of 5g

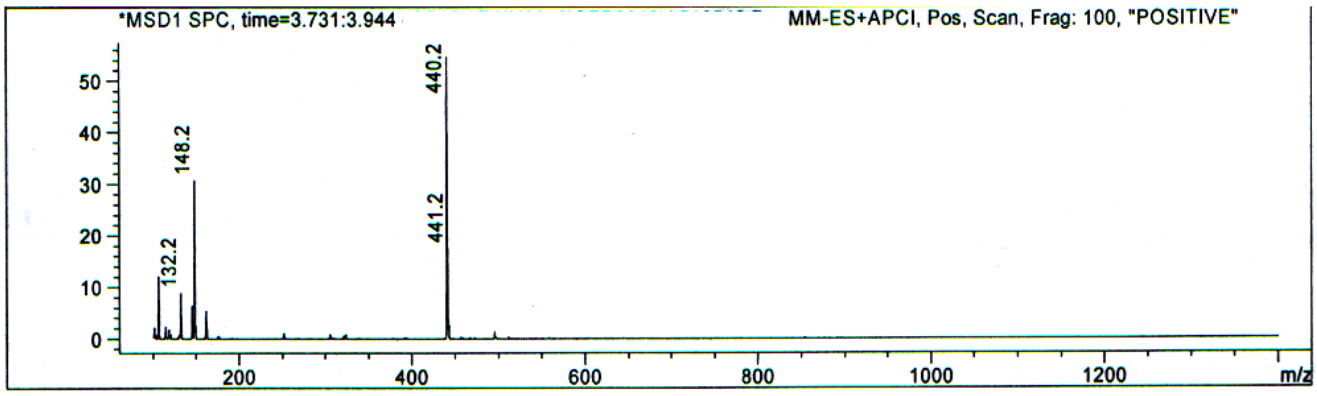


LCMS spectrum of 5g

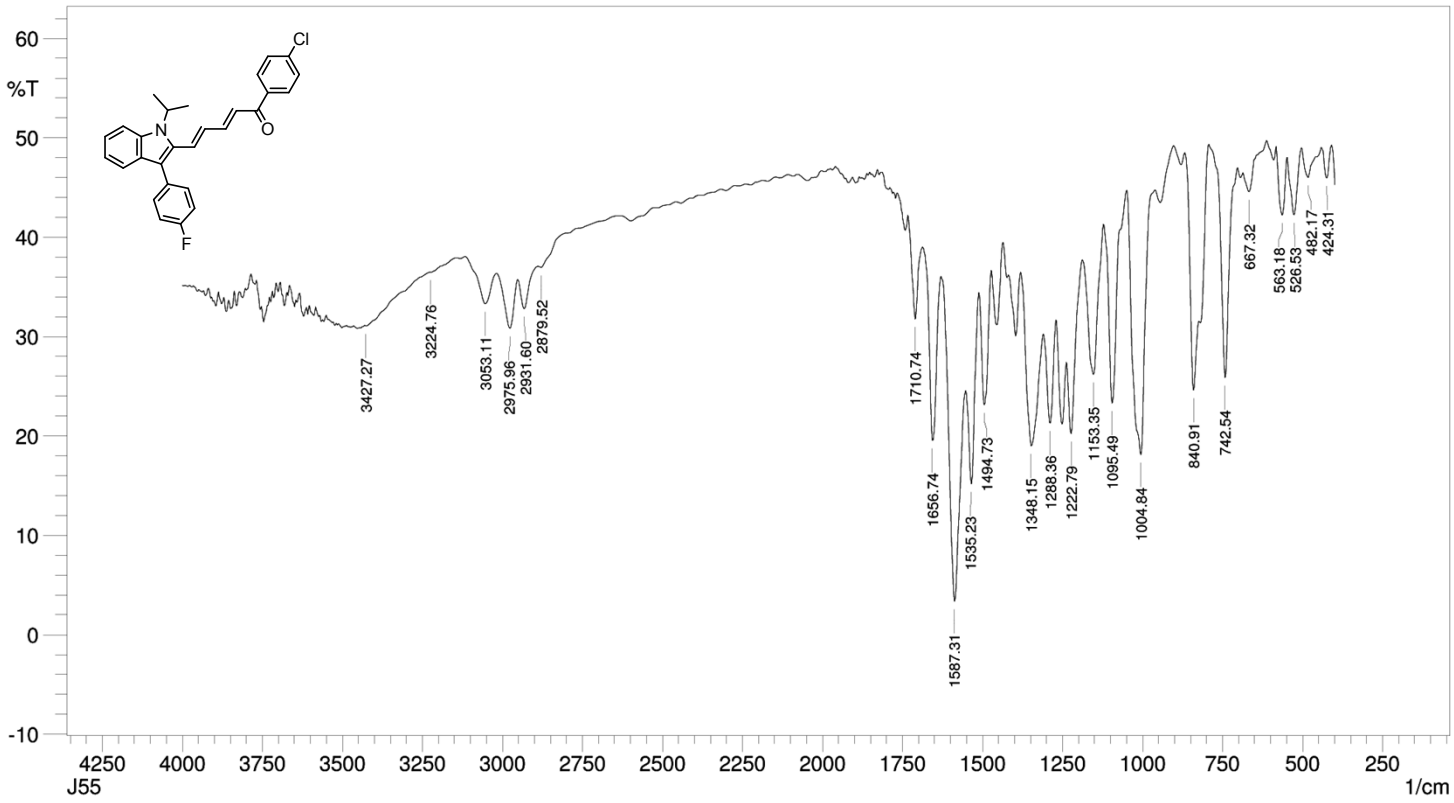
```
Method info  : A-0.1% HCOOH IN WATER ;B-ACN  Flow = 1.5ml/min,
               Column-Zorbax Extend  C18 (50X4.6mm-5µm, ) ,
              Time (min.):  0--3      3--6        6--7      7--8.0
               % B :        40-95     95       95-40       40
```



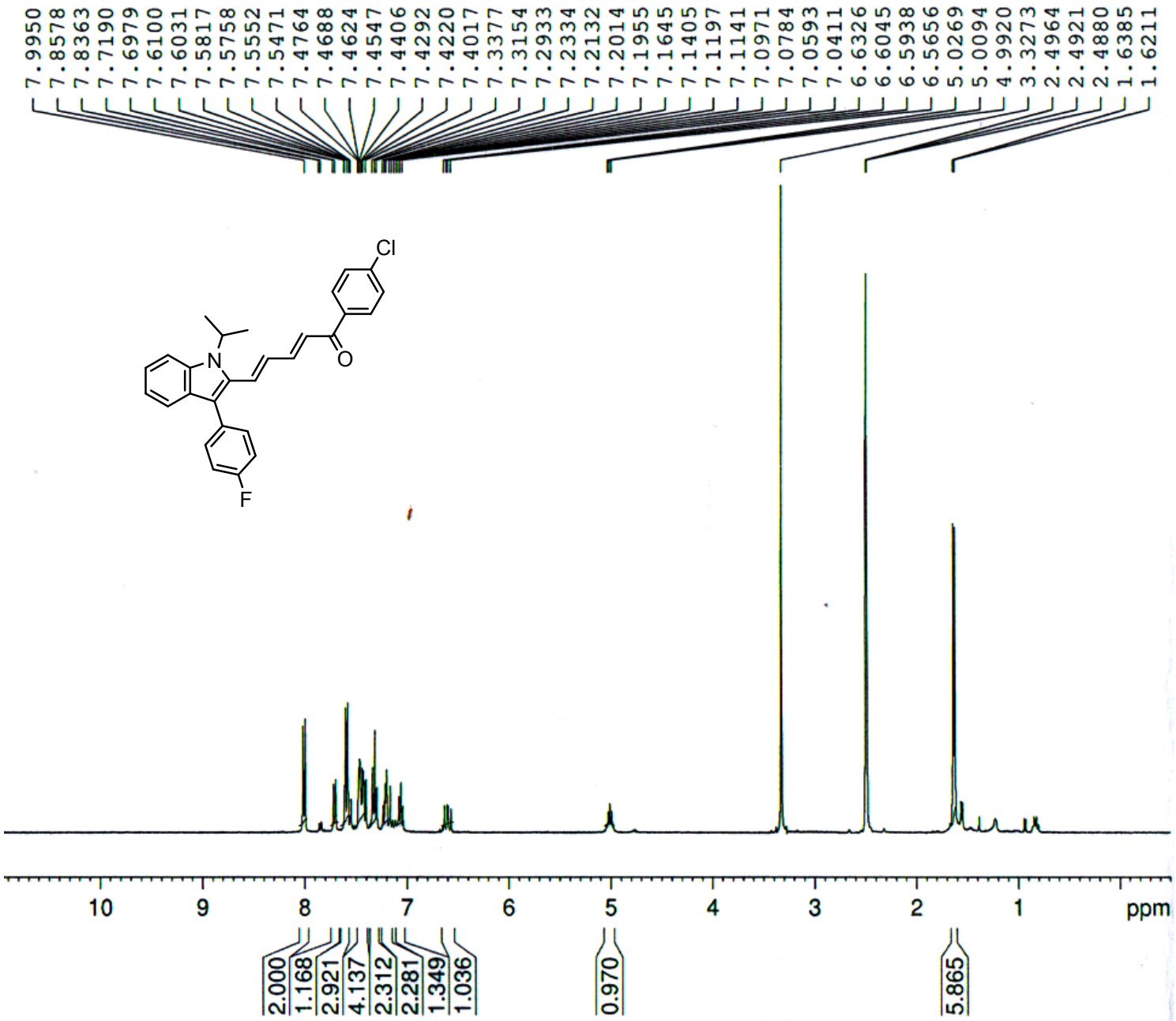
Peak No	RT min	Area	Area %
1	3.265	120.888	1.177
2	3.558	42.603	0.915
3	3.797	1284.571	97.908



FTIR spectrum of 5h



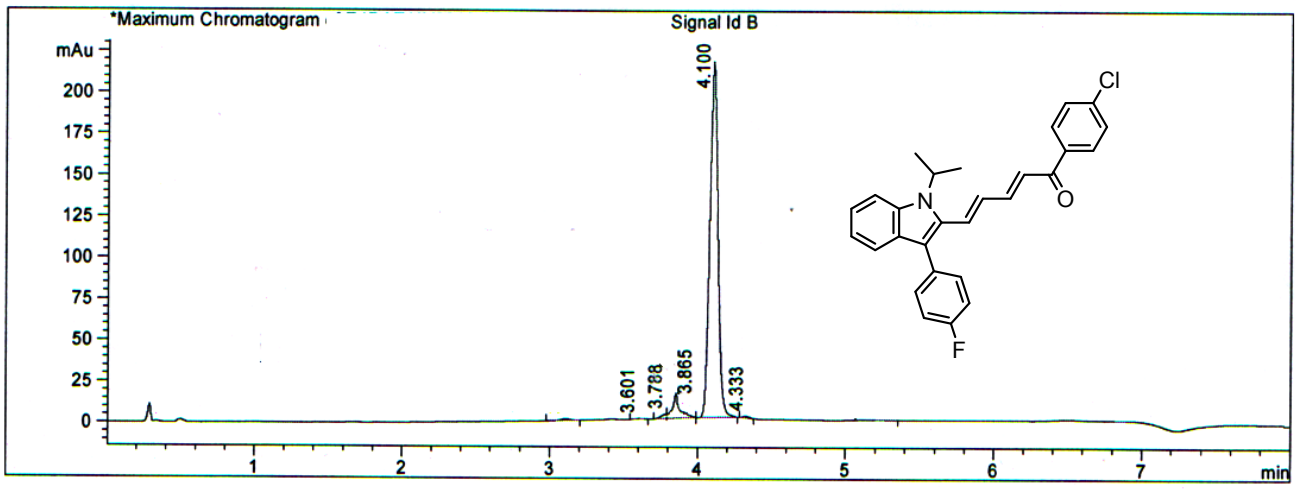
^{1}H NMR spectrum of 5h



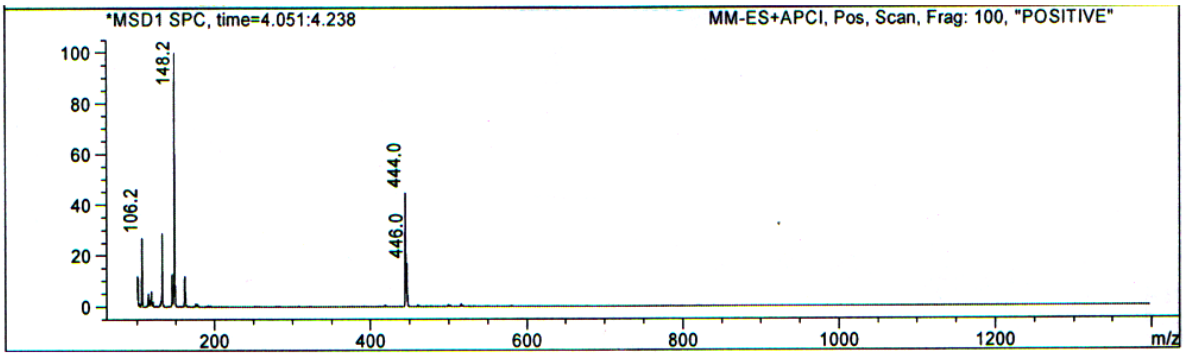
LCMS spectrum of 5h

Method info : A-0.1% HCOOH IN WATER ;B-ACN Flow = 1.5ml/min,
Column-Zorbax Extend C18 (50X4.6mm-5µm,) ,

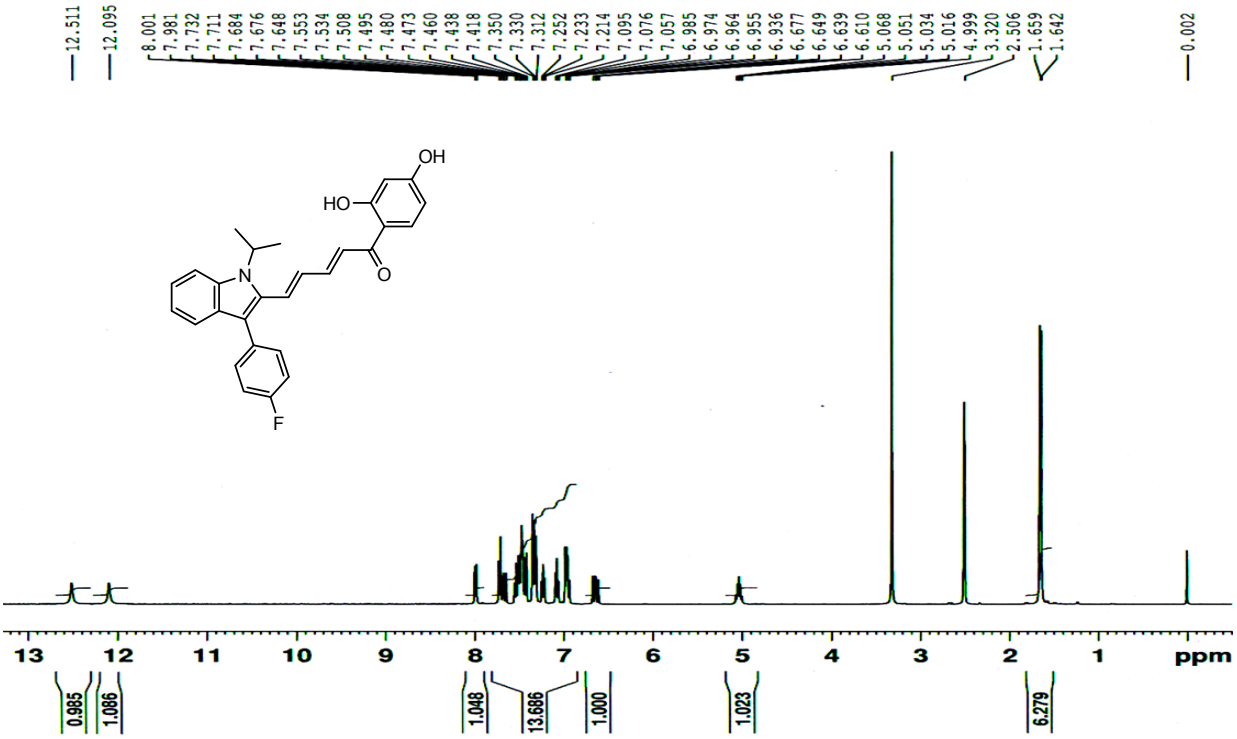
Time (min.):	0--3	3--6	6--7	7--8.0
% B :	40-95	95	95-40	40



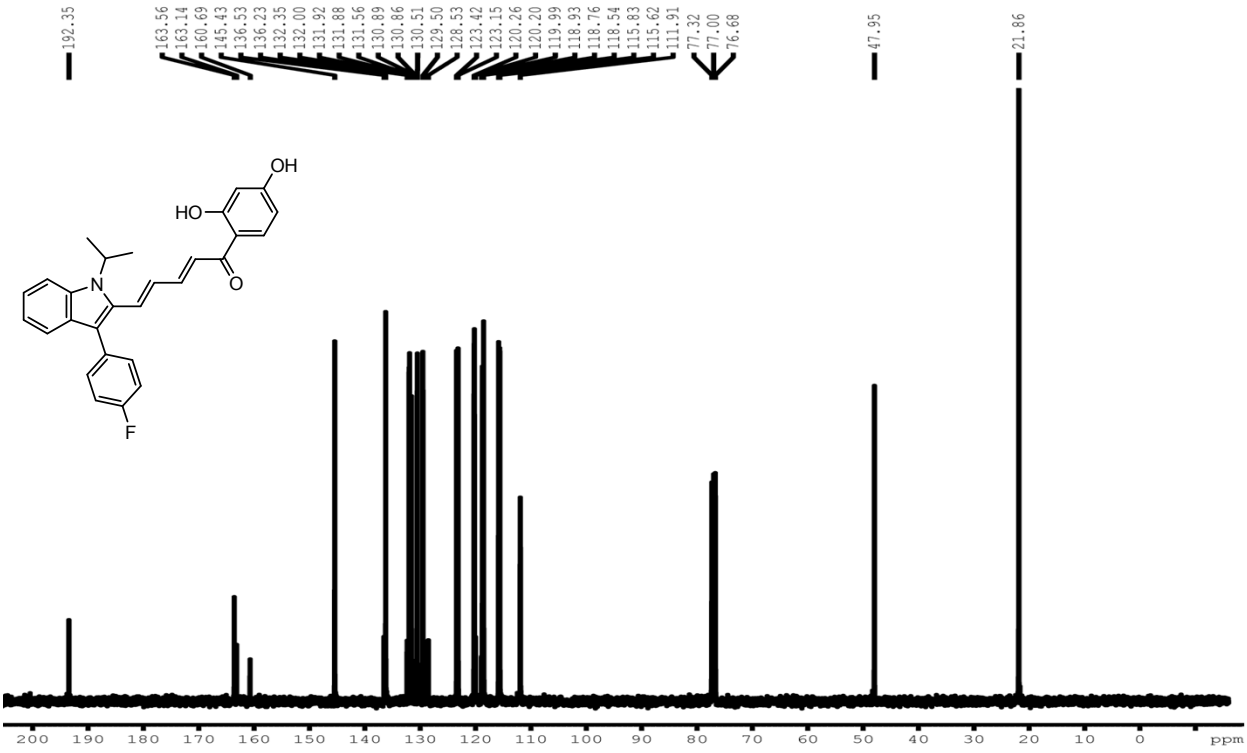
Peak No	RT min	Area	Area %
1	3.601	2.115	0.222
2	3.788	6.639	0.698
3	3.865	106.716	1.218
4	4.100	822.002	97.452
5	4.333	3.897	0.410



^{1}H NMR spectrum of 5i

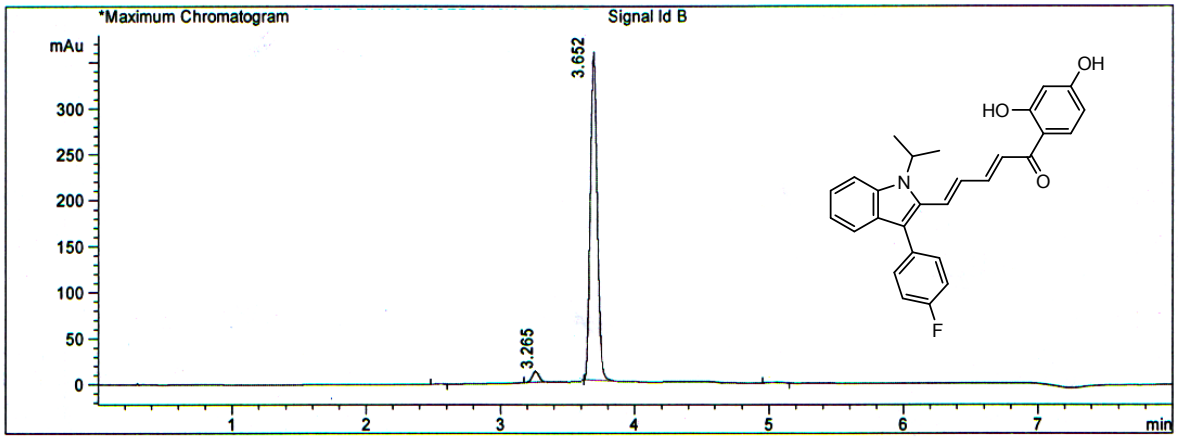


^{13}C NMR spectrum of 5i

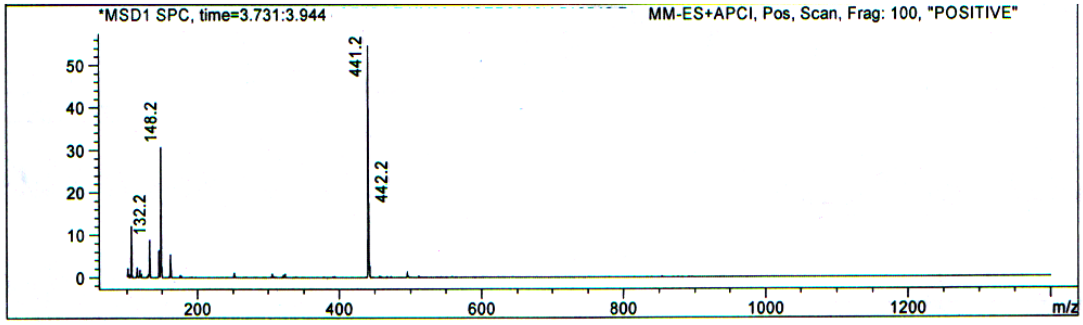


LCMS spectrum of 5i

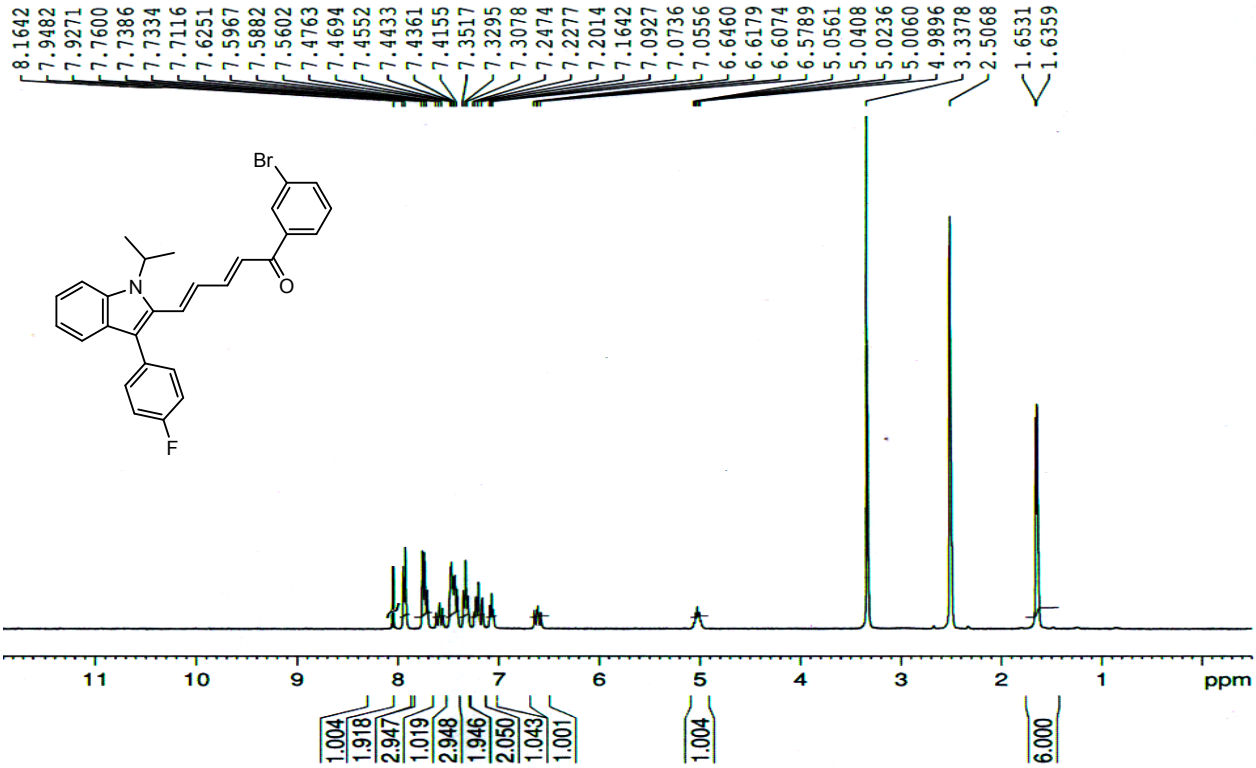
```
Method info  : A-0.1% HCOOH IN WATER ;B-ACN  Flow = 1.5ml/min,
               Column-Zorbax Extend  C18 (50X4.6mm-5µm, ) ,
              Time (min.):  0--3      3--6       6--7      7--8.0
               % B :        40-95     95       95-40       40
```



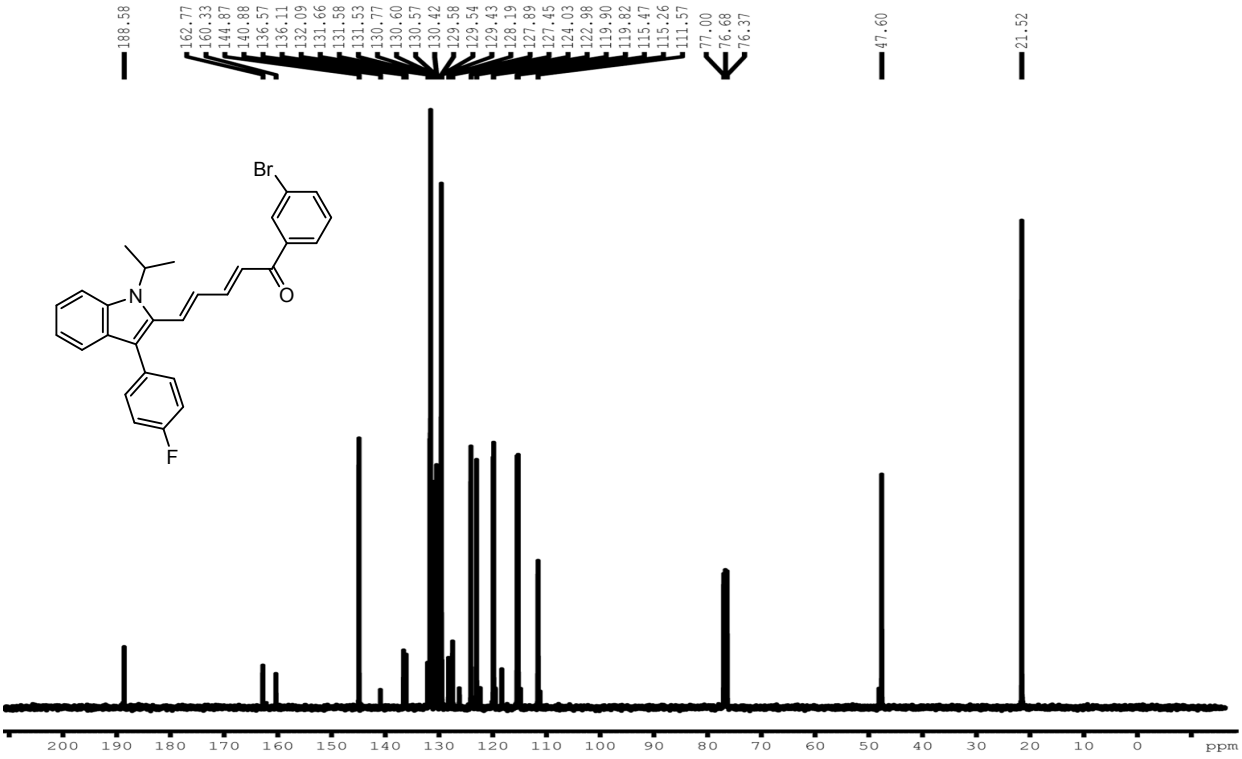
Peak No	RT min	Area	Area %
1	3.265	120.888	1.177
2	3.652	1284.571	98.823



^{1}H NMR spectrum of 5j

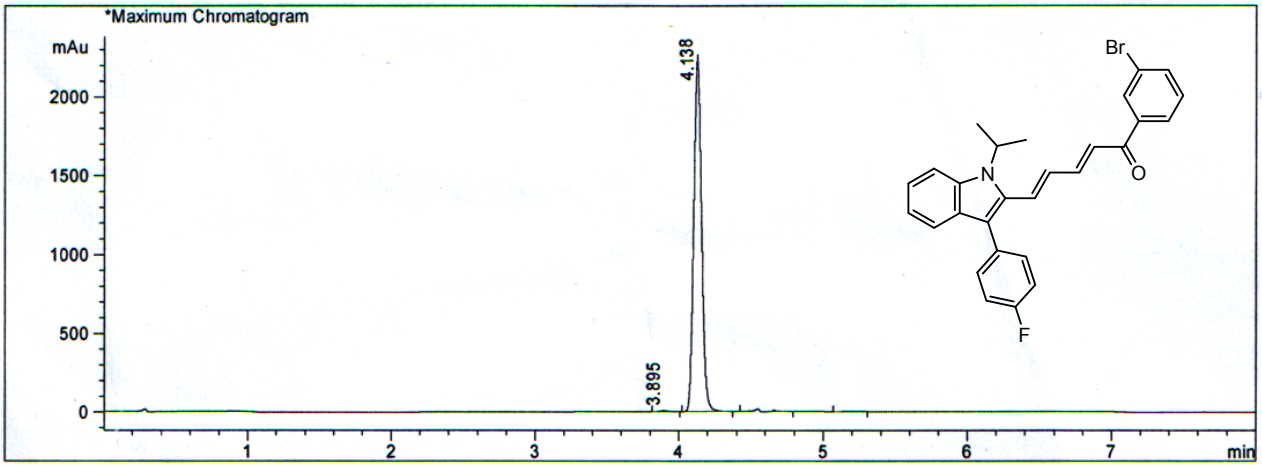


^{13}C NMR spectrum of 5j

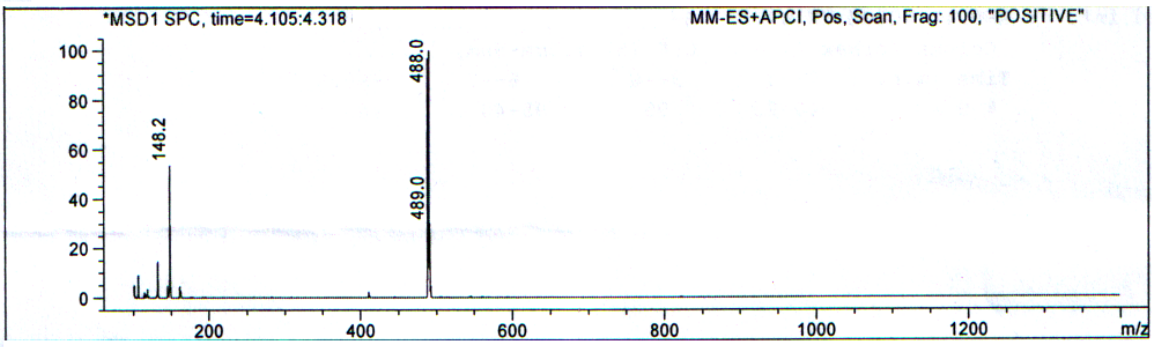


LCMS spectrum of 5j

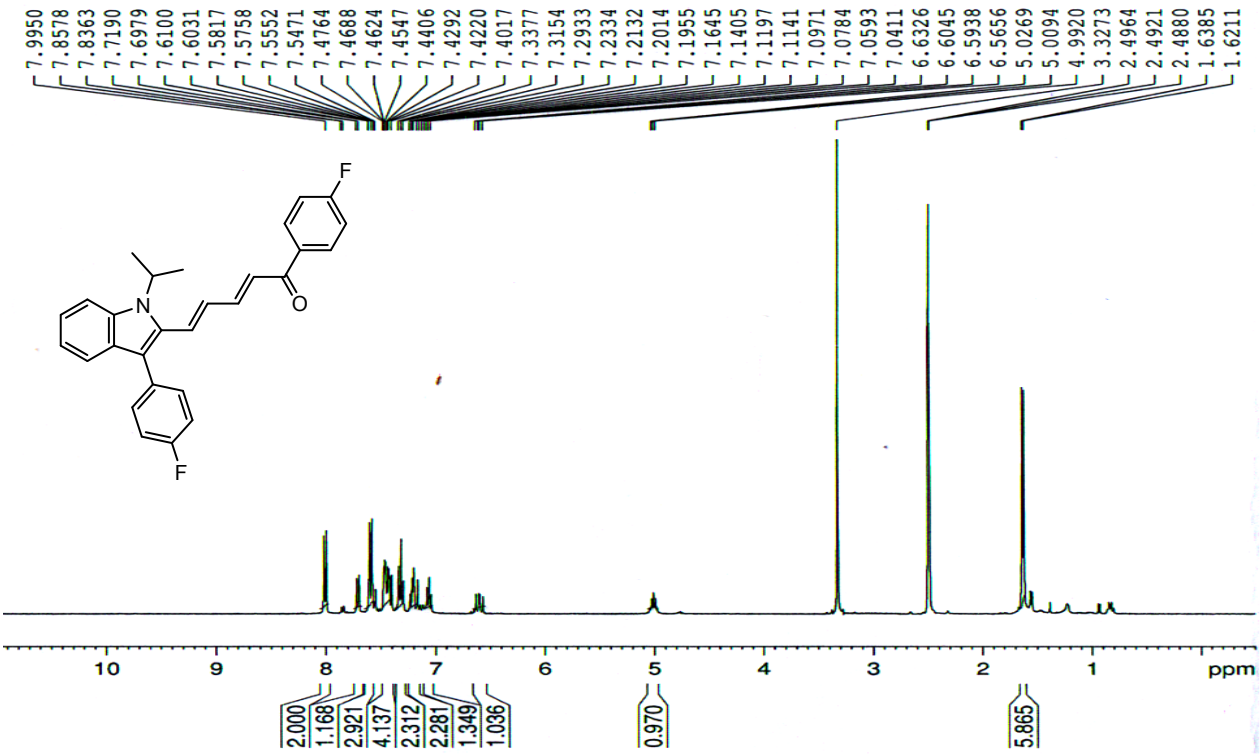
```
Method info  : A-0.1% HCOOH IN WATER ;B-ACN  Flow = 1.5ml/min,
               Column-Zorbax Extend  C18 (50X4.6mm-5µm, ) ,
              Time (min.):  0--3      3--6       6--7     7--8.0
               % B :        40-95     95       95-40      40
```



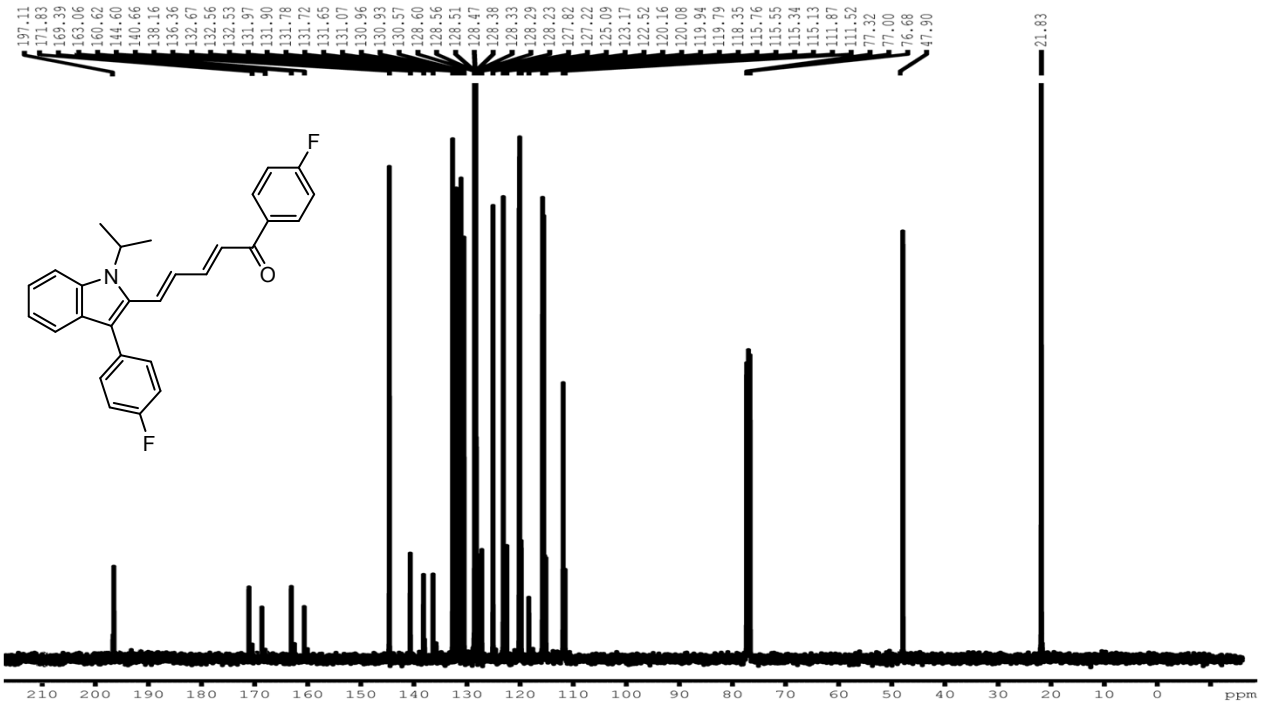
Peak No	RT min	Area	Area %
1	3.895	37.517	0.419
2	4.128	8460.143	99.581



^{1}H NMR spectrum of 5k



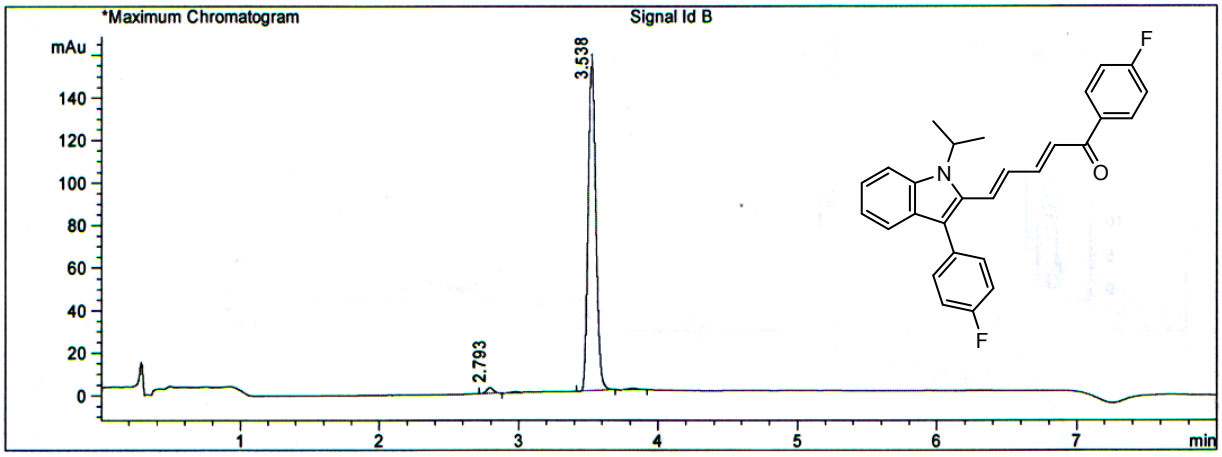
^{13}C NMR spectrum of 5k



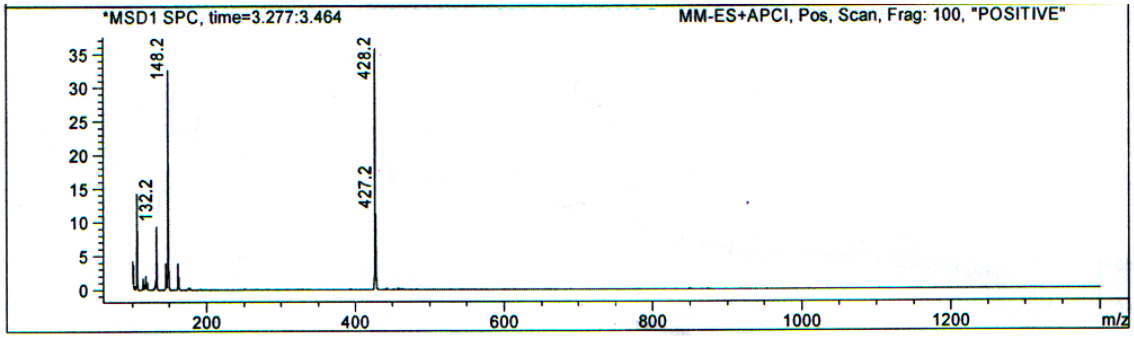
LCMS spectrum of 5k

Method info : A-0.1% HCOOH IN WATER ;B-ACN Flow = 1.5ml/min,
Column-Zorbax Extend C18 (50X4.6mm-5µm,) ,

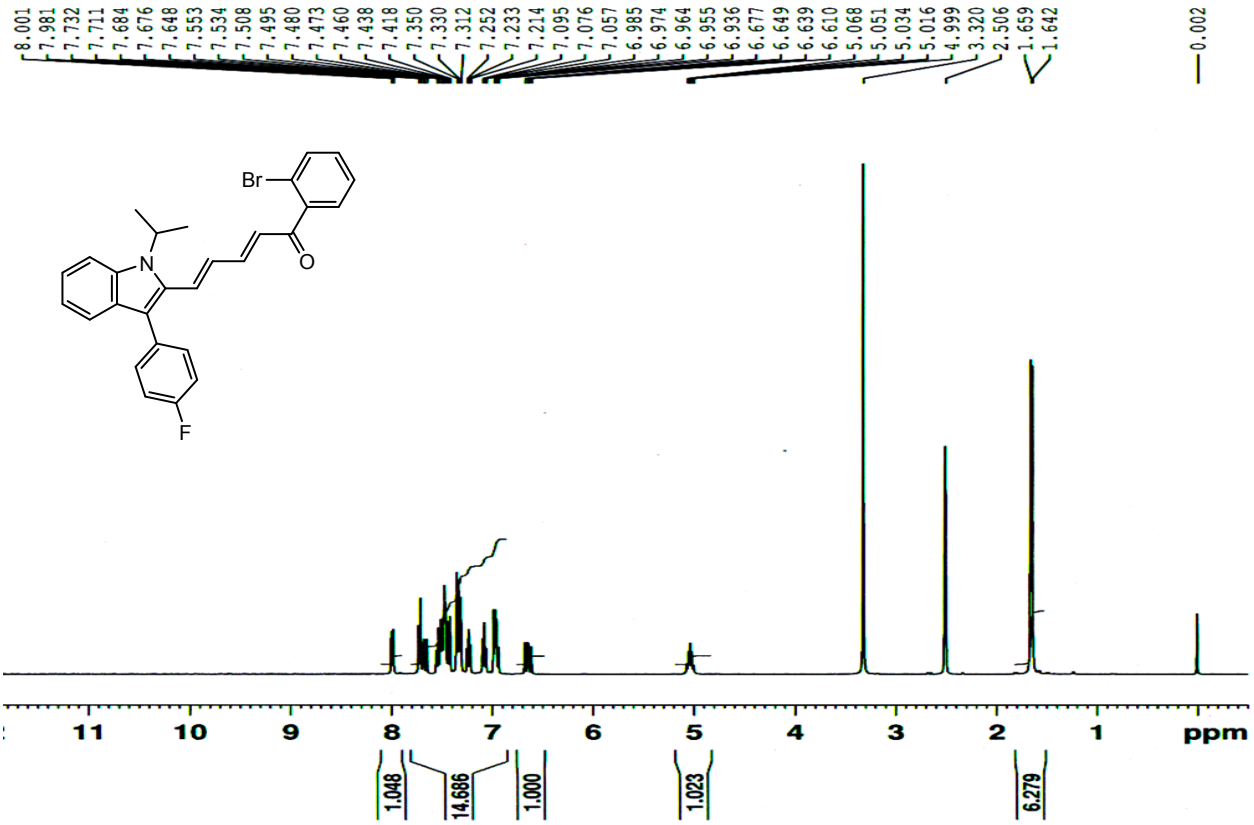
Time (min.):	0--3	3--6	6--7	7--8.0
% B :	40-95	95	95-40	40



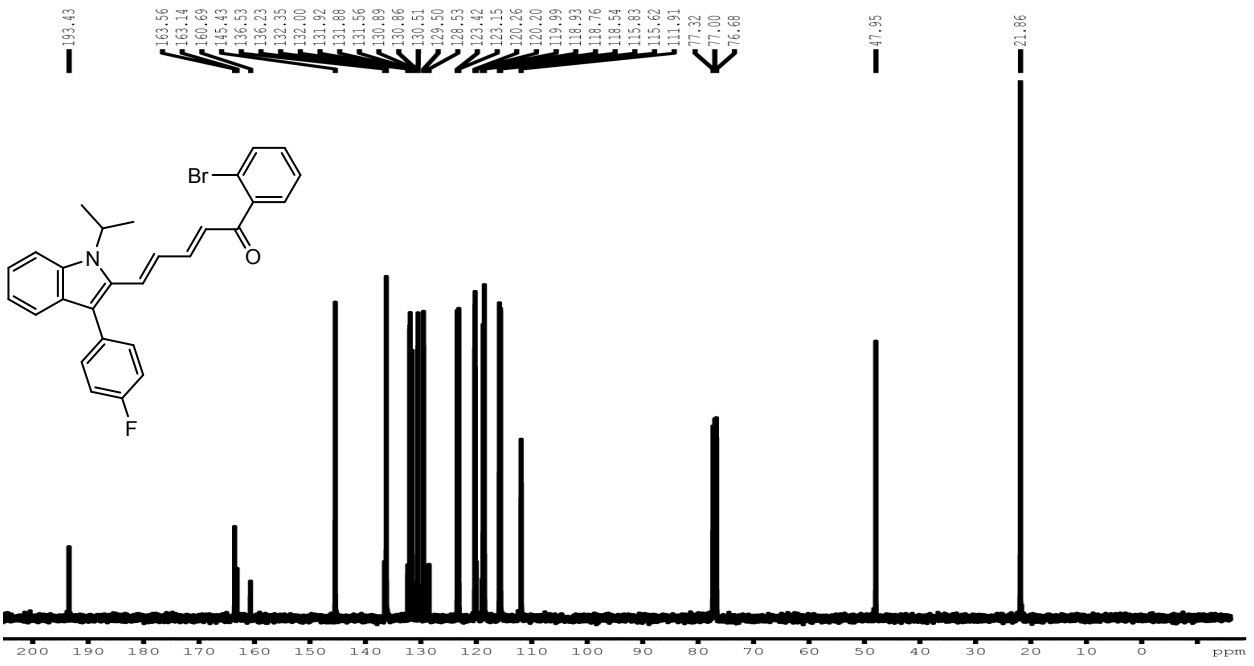
Peak No	RT min	Area	Area %
1	2.793	9.678	0.975
2	3.538	601.386	99.025



^{1}H NMR spectrum of 5l

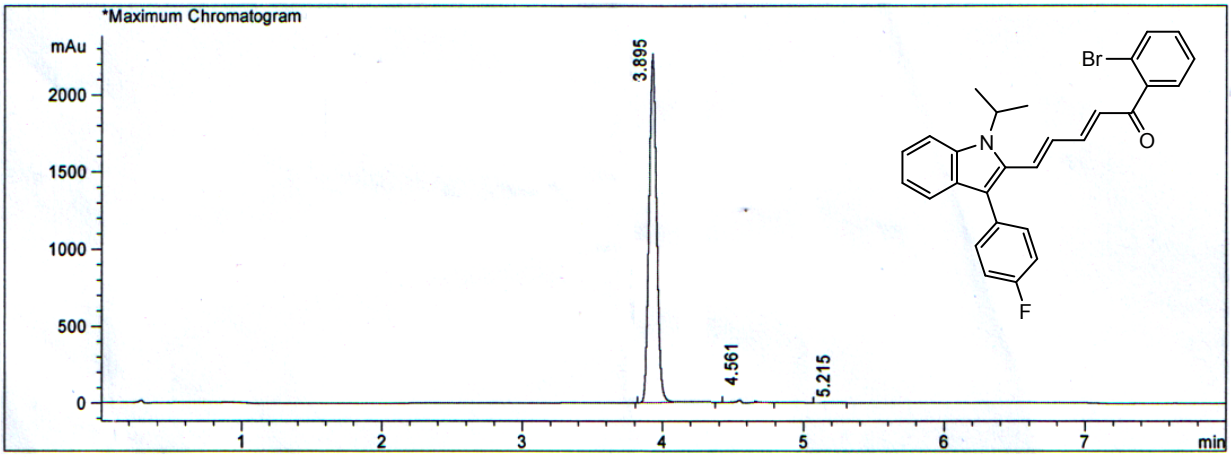


^{13}C NMR spectrum of 5l



LCMS spectrum of 5l

```
Method info  : A-0.1% HCOOH IN WATER ;B-ACN  Flow = 1.5ml/min,
               Column-Zorbax Extend  C18 (50X4.6mm-5µm, ) ,
              Time (min.):  0--3      3--6       6--7     7--8.0
               % B :        40-95     95       95-40      40
```



Peak No	RT min	Area	Area %
1	3.895	8460.143	98.959
2	4.561	430.721	0.813
3	5.215	20.389	0.228

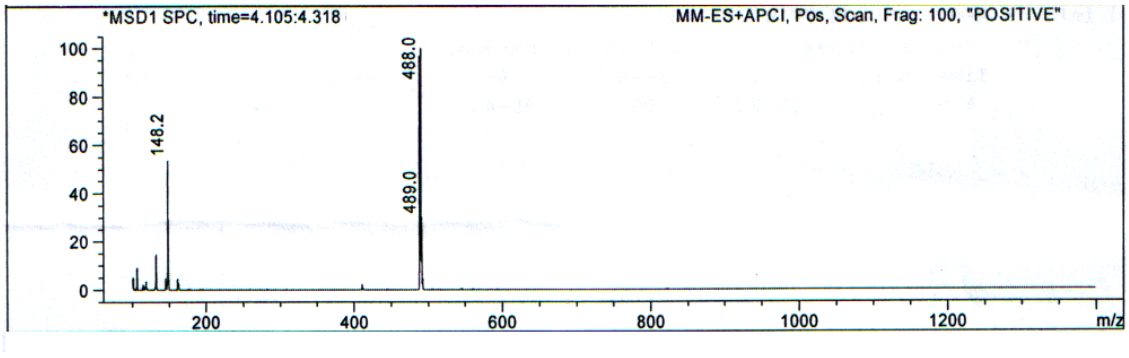


Fig. S1. Dihedral angle formed between 4-fluorophenyl ring and mean indole plane in compounds **5b**, **5c**, **5g** and **5h**.