

# Phenothiazine- and carbazole-cyanochalcones as dual inhibitors of tubulin polymerization and human farnesyltransferase

Andreea Zubaş<sup>1</sup>, Alina Ghinet<sup>1,2,3,\*</sup>, Amaury Farce<sup>4</sup>, Joëlle Dubois<sup>5</sup> and Elena Bîcu<sup>1,\*</sup>

<sup>1</sup> 'Alexandru Ioan Cuza' University of Iasi, Faculty of Chemistry, Bd. Carol I, nr. 11, 700506 Iasi, Romania.

<sup>2</sup> Junia, Health and Environment, Laboratory of Sustainable Chemistry and Health, F-59000 Lille, France.

<sup>3</sup> Univ. Lille, Inserm, CHU Lille, Institut Pasteur Lille, U1167 - RID-AGE - Facteurs de risque et déterminants moléculaires des maladies liées au vieillissement, F-59000 Lille, France.

<sup>4</sup> Univ. Lille, Inserm, CHU Lille, U1286 – Infinite-Institute for Translational Research in Inflammation, F-59000 Lille, France.

<sup>5</sup> Institut de Chimie des Substances Naturelles, UPR2301, CNRS, Centre de Recherche de Gif, 91190 Gif-sur-Yvette Cedex, France

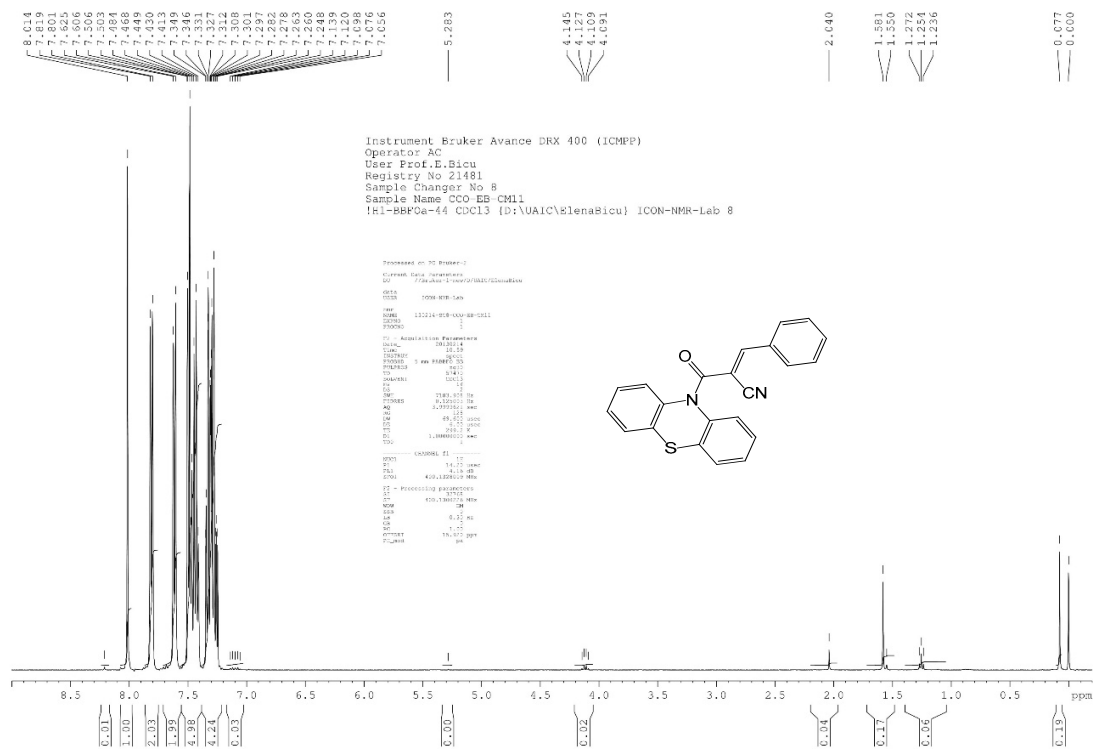
\* Correspondence: Corresponding authors. [alina.ghinet@junia.com](mailto:alina.ghinet@junia.com); [elena@uaic.ro](mailto:elena@uaic.ro)

## Supplementary information

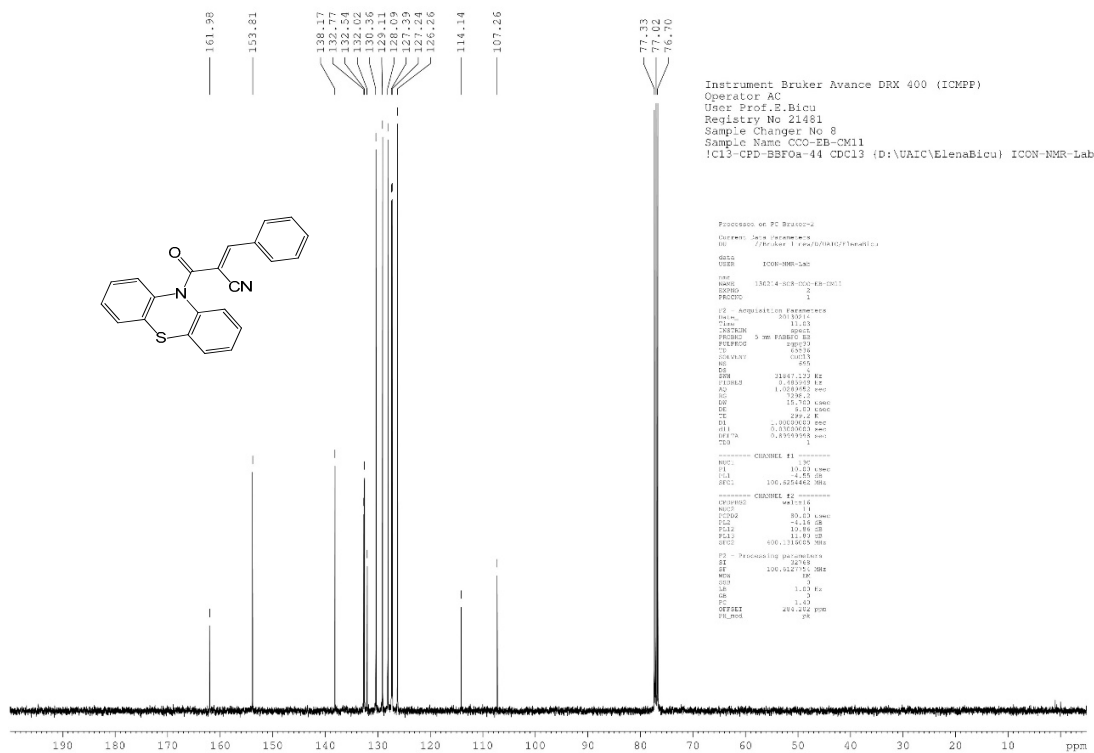
<sup>1</sup> H, <sup>13</sup> C NMR, 2D NMR and IR spectra of compounds	2
One-dose full graphs obtained on NCI-60 cancer cell lines panel	81
<b>Figure S1.</b> Results of the <i>in vitro</i> human cancer cell growth inhibition for selected compounds <b>2k</b> , <b>2l</b> and <b>2o</b> .	84
<b>Figure S2.</b> Docking of all dual FTIs/MTIs identified in this study on farnesyltransferase and colchicine binding sites	85

## Spectra of compounds

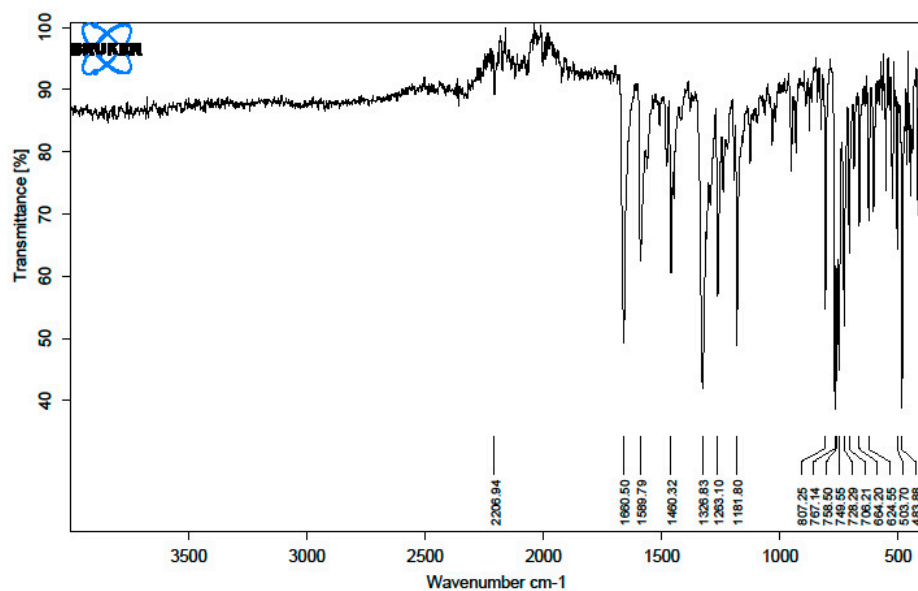
### $^1\text{H}$ NMR (400 MHz, $\text{CDCl}_3$ )-1a



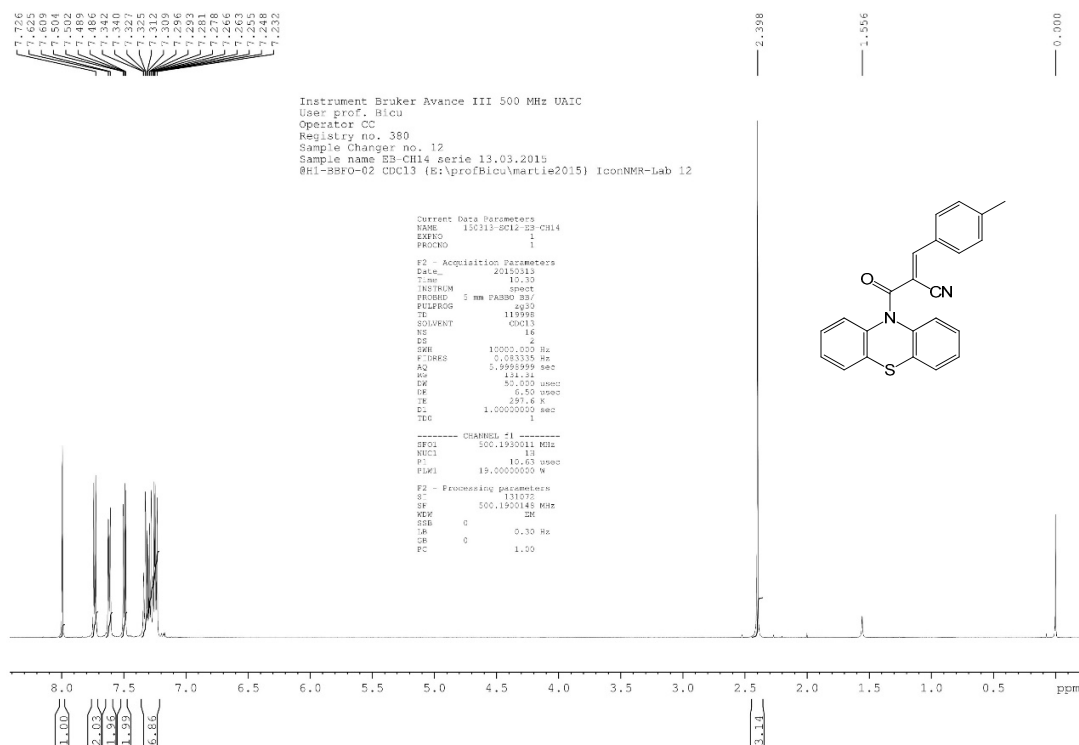
### $^{13}\text{C}$ NMR (100 MHz, $\text{CDCl}_3$ )-1a



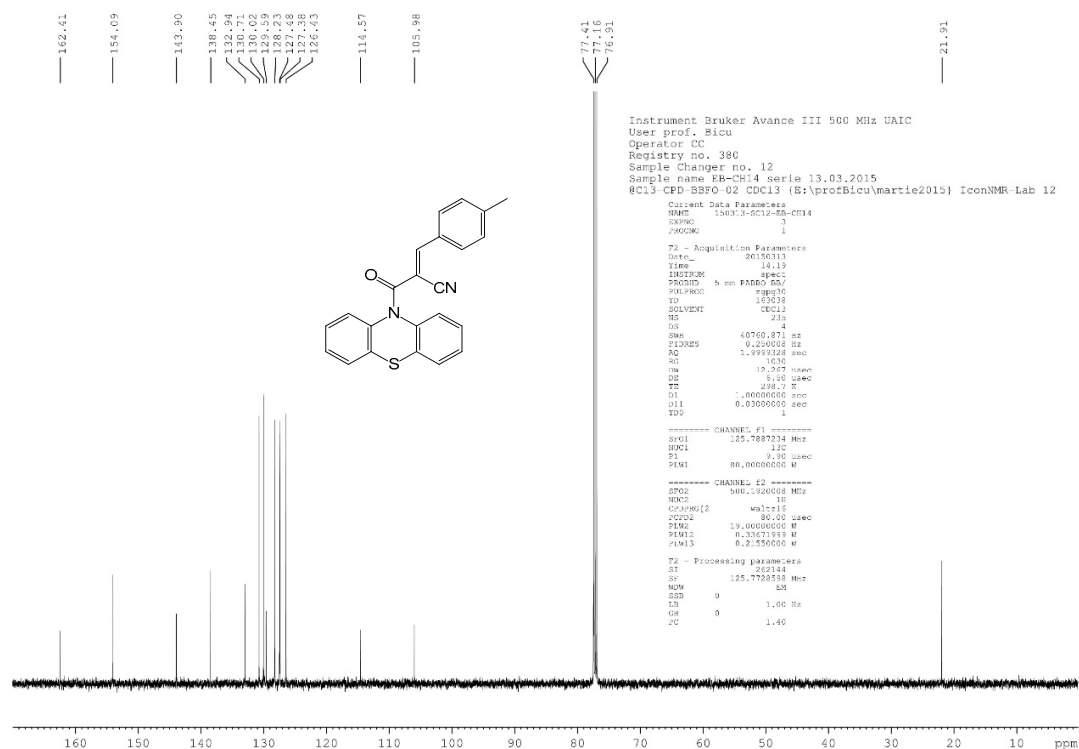
## IR-1a



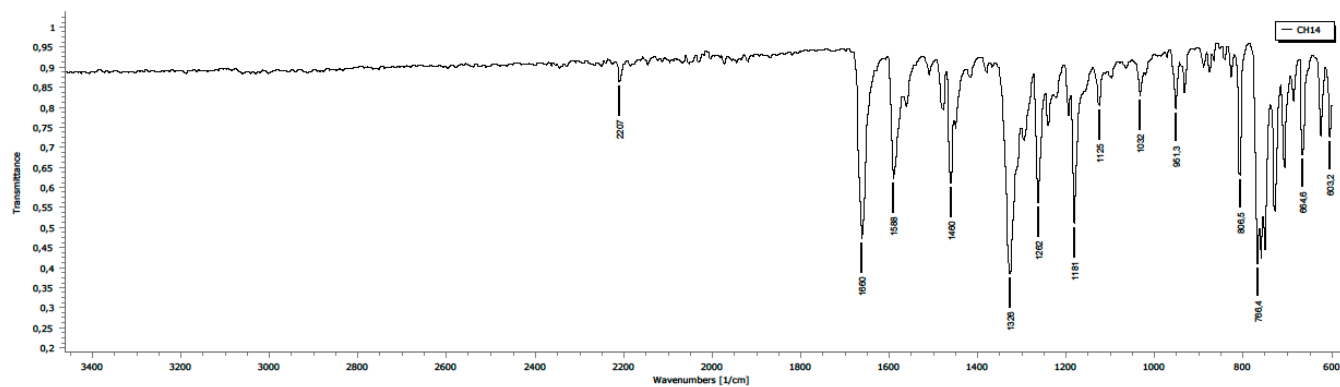
## <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-1b



# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-**1b**



## IR-**1b**





7.972  
7.920  
7.896  
7.858  
7.856  
7.843  
7.841  
7.835  
7.825  
7.470  
7.467  
7.403  
7.396  
7.293  
7.293  
7.282  
7.260  
7.256  
7.253  
7.253  
6.956  
6.955

Instrument Bruker Avance III 500 MHz UAIC  
User prof. Bicu  
Operator CC  
Registry no. 29  
Sample Changer no. 8  
Sample name BR-AZD1775 serie20.01.2022  
9H1-BBFO-02 CDCl<sub>3</sub> (E:\profBicu\2022\ian) IconNMR-Lab 8

CN(C)C1=CC=C(C=C1)/C=C/C2=CC=C3C(=C2)N(C(=O)C4=CC=CC=C4S5C=CC=CC=C53)C6=CC=CC=C6

3.074  
1.564

Current Data Parameters  
NAME 20170-SCB-BB-A001000  
EXPNO 1  
PROCNO 1

F2 - Acquisition Parameters  
DATE\_ 20220120  
TIME 11.02  
INSTRUM spect  
PULPROG 5 mm WALTZ16  
PCPPROG 2  
TD 131072  
SOLVENT CDCl<sub>3</sub>  
NS 16  
DS 4  
SWH 10000.400 Hz  
FIDRES 0.00313199 Hz  
AQ 0.99981999 sec  
RG 170.10  
EW 30.000 uHz  
SR 6.50 uHz  
TE 292.2 K  
H1 1.00000000 sec  
TD0 1

----- CHANNEL f1 -----  
NUC1 13C-130911 MHz  
PULP1 12.00 uHz  
RG1 19.00000000 N  
PC1 130912  
PC2 500.1300119 MHz  
F2 - Processing parameters  
SI 32768  
SF 500.1300119 MHz  
RG 655  
SSB 0  
DS 2  
SW 6.50 Hz  
PC 1.00

1.00  
2.00  
2.00  
2.05  
2.13  
0.78  
1.42  
2.00  
6.05

ppm

Chemical structure of compound 10: CN(C)Cc1ccc(cc1)/C=C/C2C(=O)N(c3ccccc3)S4C(=O)C#NCC42

**Peak List (ppm):**  
 163.74, 154.55, 153.30, 139.06, 133.54, 132.90, 128.12, 127.27, 126.46, 120.16, 116.18, 111.55, 98.57, 77.41, 77.16, 76.91, 40.15

**Instrument:** Bruker Avance III 500 MHz UAIC  
**User:** prof. Bicu  
**Operator:** CC  
**Registry no.:** 29  
**Sample Changer no.:** 6  
**Sample name:** EB-A2D170 serie20.01.2022  
**File:** 8c13-CPD-SBFO-02 CD13 (E:\profBicu\2022\lan) IconNM- Lab 8

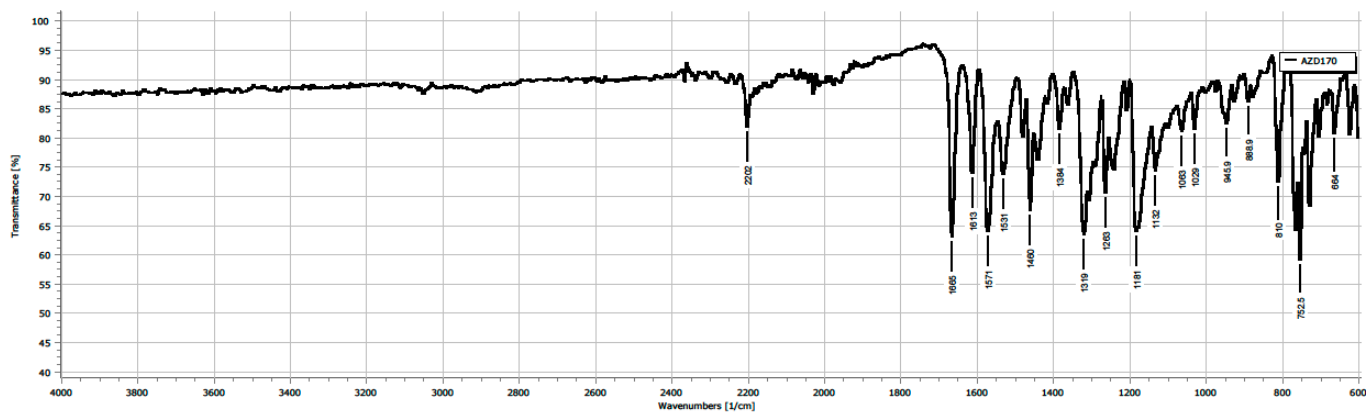
**Current Data Parameters:**  
 NAME: 220120-SCB-EB-A2D170C  
 EXPNO: 3  
 PROCNO: 1  
 F2 - Acquisition Parameters  
 Date\_: 20230120  
 Time: 13.42  
 INSTRUM: spect  
 PROCOR: 5 mm PABBO BB/  
 PULPROG: zgpg30  
 TD: 163878  
 SFO: 500.13  
 XD: 1024  
 YD: 4  
 ZD: 4  
 FWHM: 46760.871 Hz  
 FIDRES: 0.250008 Hz  
 AQ: 1.3399328 sec  
 RG: 1030  
 DW: 12.247 usec  
 DE: 6.30 usec  
 TE: 300.2 K  
 D1: 1.0000000 sec  
 D11: 0.0300000 sec  
 TEO

**Channel 1:**  
 RF01: 125.7681244 MHz  
 NUC1: 13C  
 P1: 9.30 usec  
 PL1: 0.0000000 W

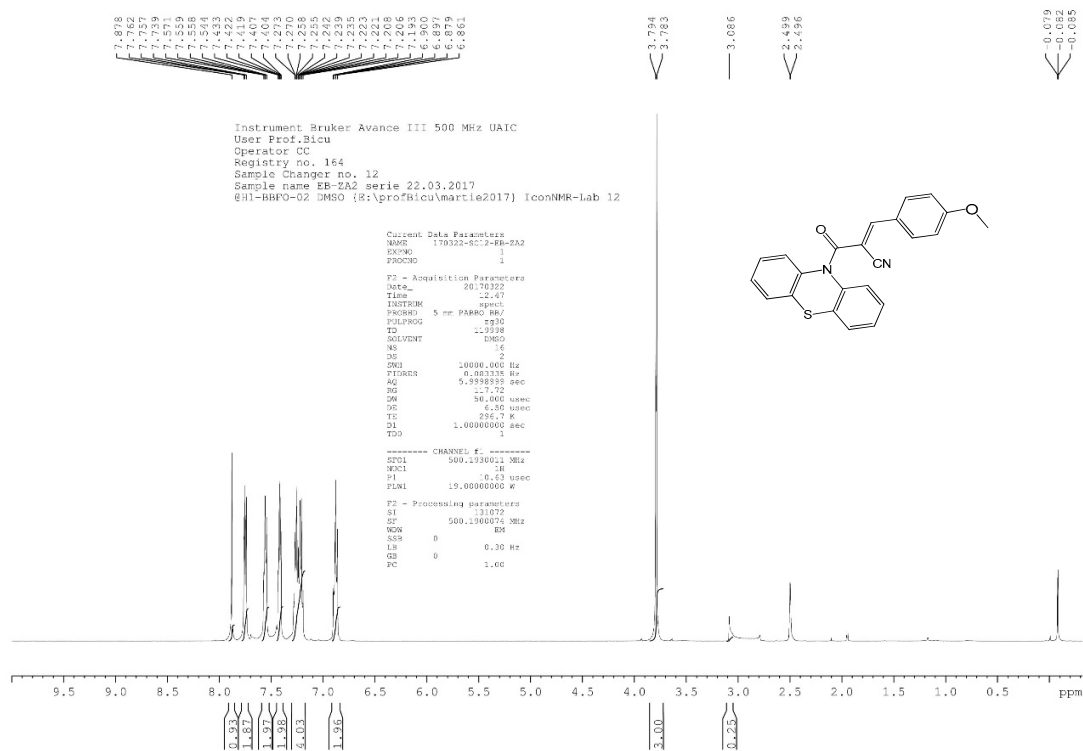
**Channel 2:**  
 RF02: 500.1300000 MHz  
 NUC2: 1H  
 CPDPRG2: waltz16  
 PCPD2: 86.00 usec  
 P1A0: 19.0000000 W  
 PL1A2: 0.1381559 W  
 PL1A3: 0.2155000 W

**F2 - Processing parameters:**  
 SI: 32768  
 SF: 125.7728598 MHz  
 DS: 4  
 SEB: 0  
 LB: 1.00 Hz  
 GB: 0  
 PC: 1.40

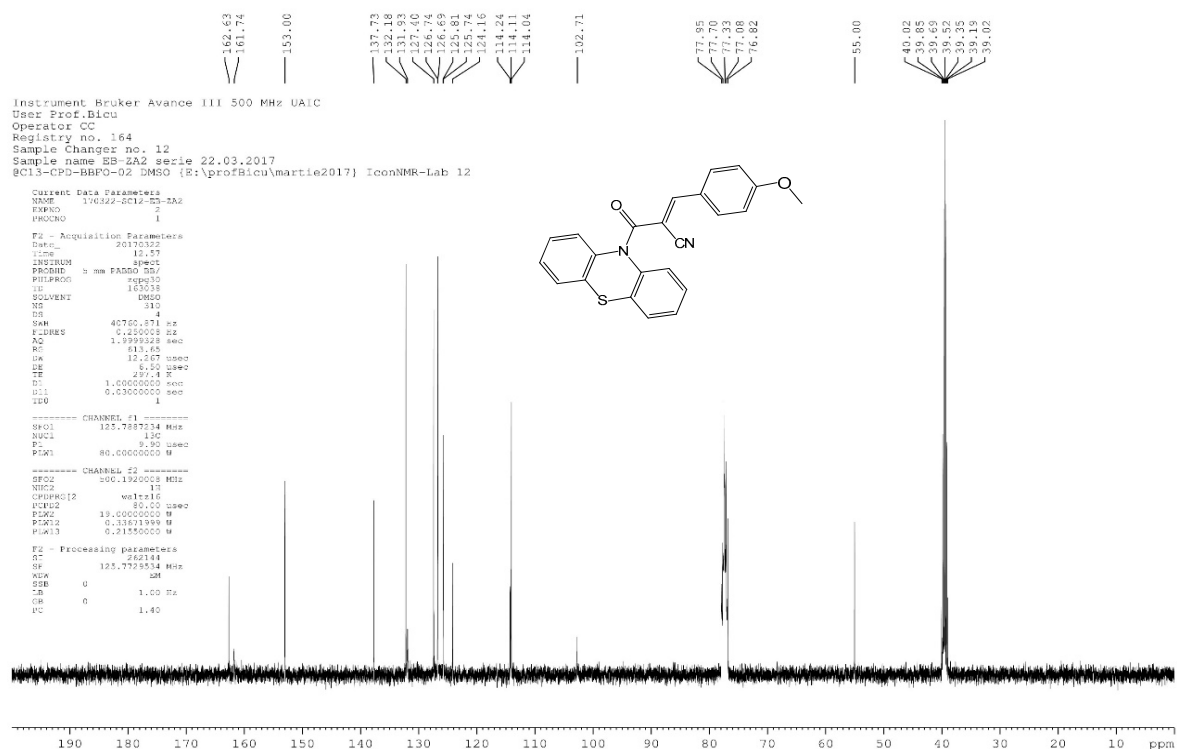
## IR-1c



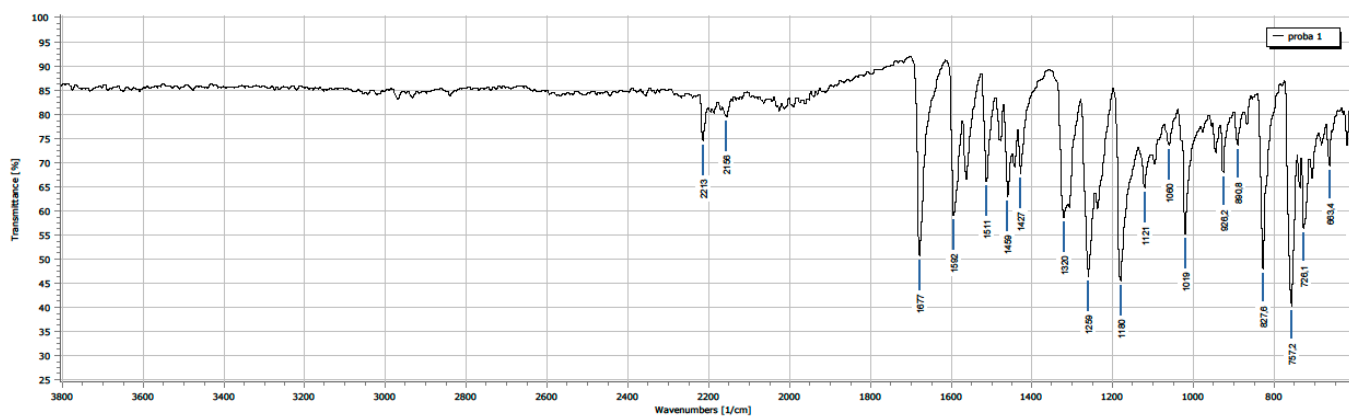
## <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-1d



# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-1d



## IR-1d



Instrument Bruker Avance III 500 MHz UAIC  
 User prof. Bicu  
 Operator CC  
 Registry no. 30  
 Sample Changer no. 9  
 Sample name EB-AZD171 serie20.01.2022  
 @H1-BBFO-02 CDCl3 (E:\profBicu\2022\lan) IconNMR-Lab 9

Current Data Parameters  
 NAME 20220120-EB-AZD171DC  
 EXPNO 1  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20220120  
 Time 11:07  
 INSTRUM spect  
 PROBM 5 mm F400 BBO  
 PULPROG zgpg30  
 TD 65536  
 TE 300.2  
 SOLVENT CDCl3  
 NS 16  
 DS 4  
 SWH 13000.000 Hz  
 FIDRES 0.300333 Hz  
 AQ 0.39999999 sec  
 RG 327.68  
 DP 50.0000000 sec  
 DC 0.40000000 sec  
 TT 200.0 Hz  
 D1 1.00000000 sec  
 TDC 1

----- CHANNEL f1 -----  
 SFO1 500.1360113 MHz  
 NUC1 1H  
 P1 19.00000000 sec  
 PL1 0.00000000 dB

F2 - Processing Parameters  
 SI 131072  
 SF 500.1360113 MHz  
 CP 4  
 NS 640  
 DS 4  
 GB 0.30 Hz  
 GR 0.00 Hz  
 PC 1.00

7.693  
7.692  
7.674  
7.673  
7.592  
7.587  
7.570  
7.565  
7.515  
7.503  
7.500  
7.343  
7.327  
7.324  
7.316  
7.303  
7.298  
7.260

1.558

8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

1.00  
2.04  
3.91  
2.03  
4.07

161.82  
132.56  
138.19  
132.94  
132.66  
132.56  
130.97  
130.71  
128.31  
127.67  
127.54  
127.48  
126.38  
114.07  
108.00  
77.41  
77.16  
76.91

Chemical structure: 1-methyl-2-methylthiophene

Instrument: Bruker Avance III 500 MHz UAIC  
User: prof. Bicu  
Operator: CC  
Registry no.: 30  
Sample name: KB-AZD171 serie20.01.2022  
Sample changer no.: 9  
gC13-CPD-BBFO-02 CDC13 {B:\profBicu\2022\ian} IconNMR-Lab 9

Current Data Parameters  
NAME: ZD131-SCYR-BAZD171SC  
EXPNO: 3  
PROCNO: 1

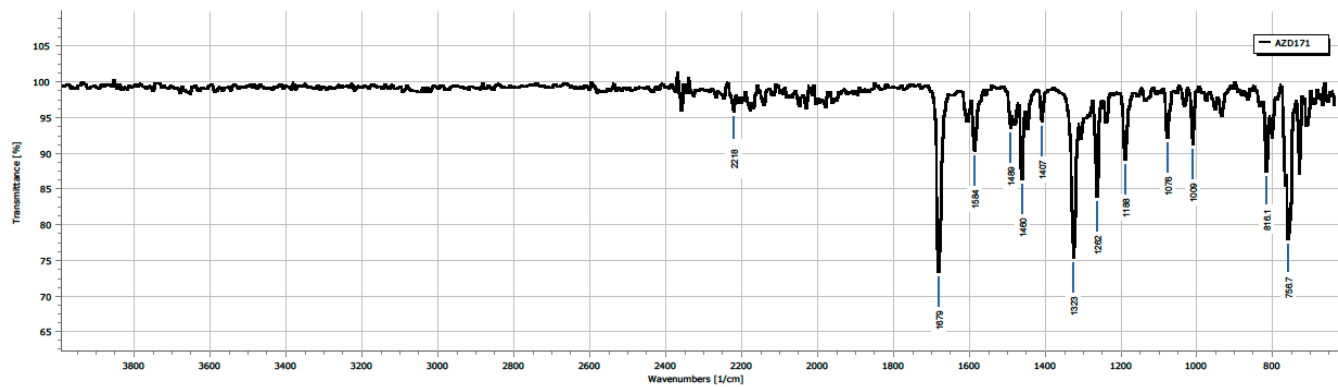
F2 Acquisition Parameters  
Date\_: 20220120  
Time: 15:14  
INSTRUM: spect  
PROCNO: 3  
F2NAME: 3 mm F4002 MR/  
PULPROG: zgpg30  
TD: 131072  
SFO: 500.136097  
C13: 125.13  
DS: 4  
QF: 40760.871 Hz  
ZF2DR2: 0.230508 Hz  
A2: 1.494835  
ANG: 539.65  
NS: 12  
DS: 12  
DE: 12.25, usec  
TE: 298.0 K  
DE: 6.30, usec  
D1: 1.0000000 sec  
D11: 0.0000000 sec  
TDO: 1

Channel 1: 125.130478 MHz  
132  
4.30, 80.0000000 W

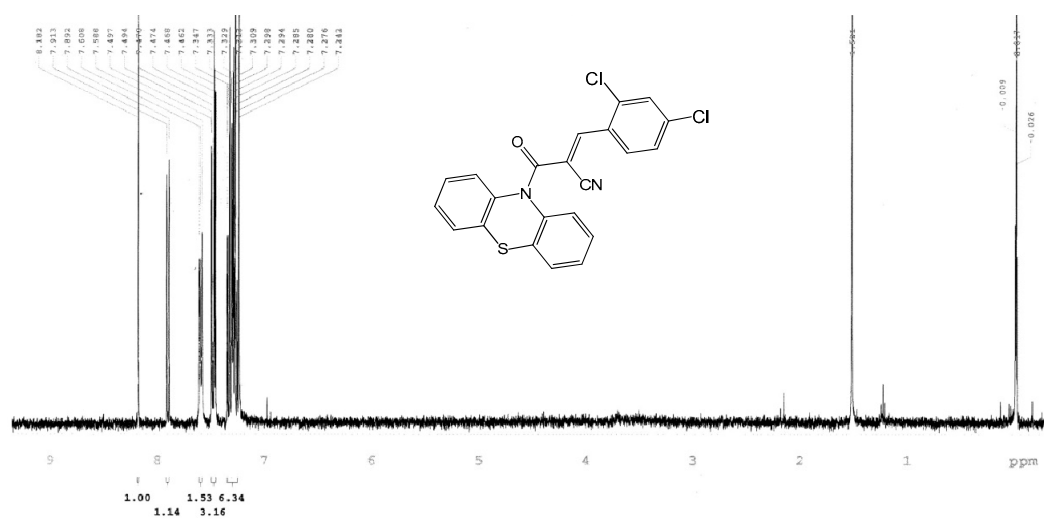
Channel 2: 100.624008 MHz  
16  
40.00, 19.0000000 W  
0.2367189 W  
0.2333000 W

F2 Processing parameters  
SI: 32768  
F2: 125.130478 MHz  
SF: 500.136097  
NS: 0  
DS: 0  
DE: 1.00  
TE: 298.0  
PC: 1.60

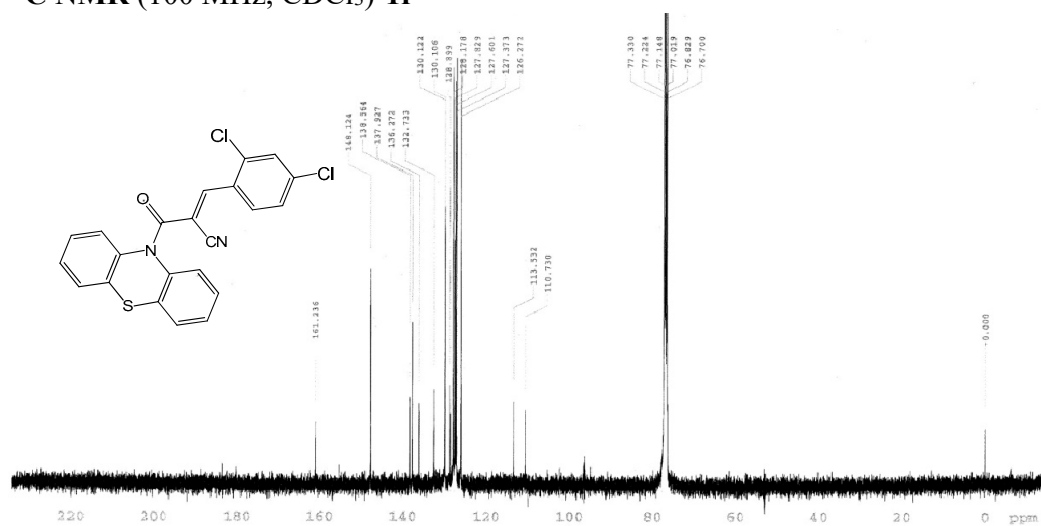
IR-1e



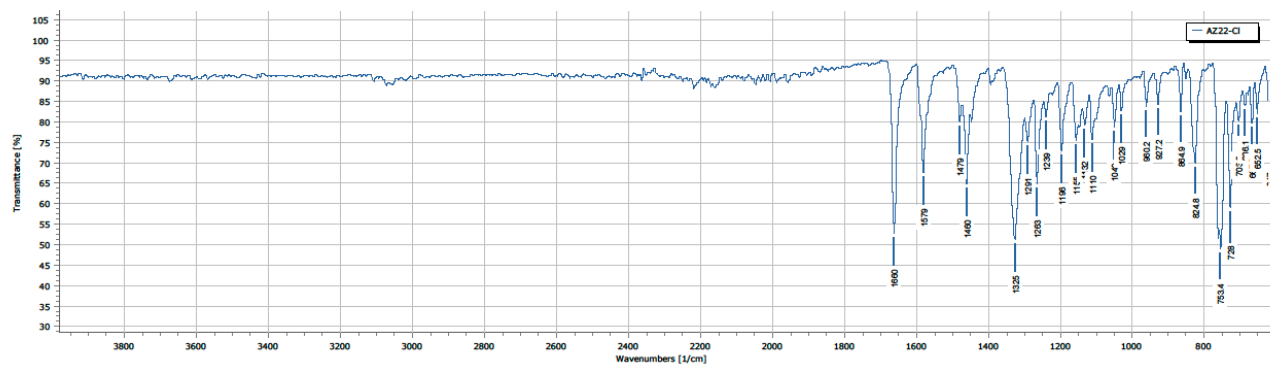
**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )-1f**



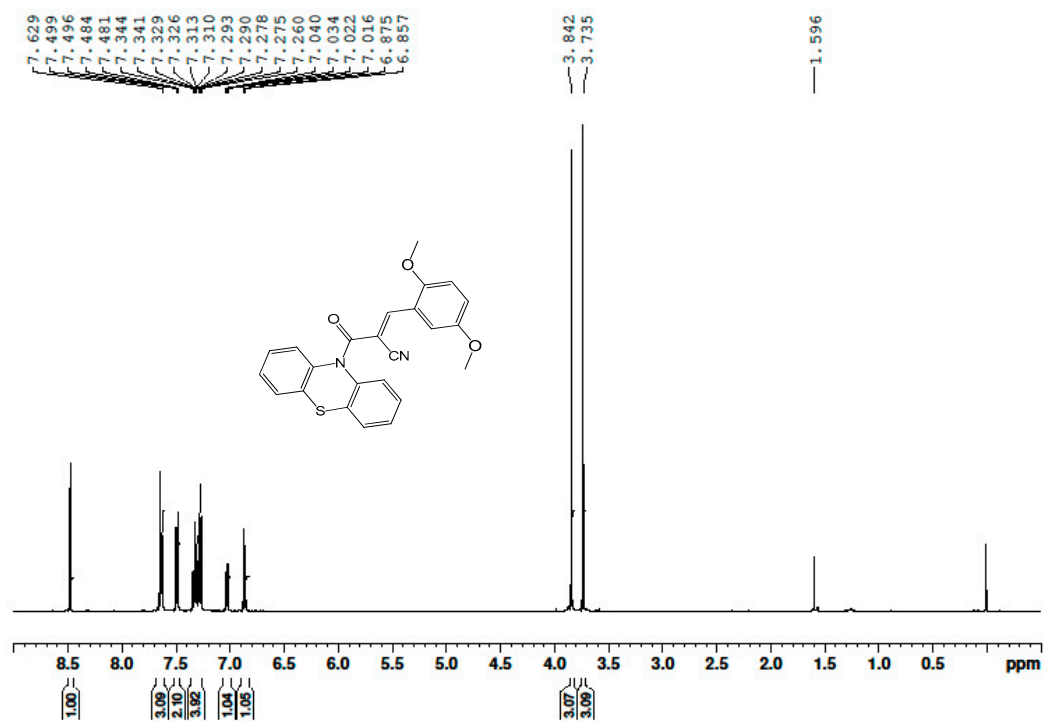
**$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )-1f**



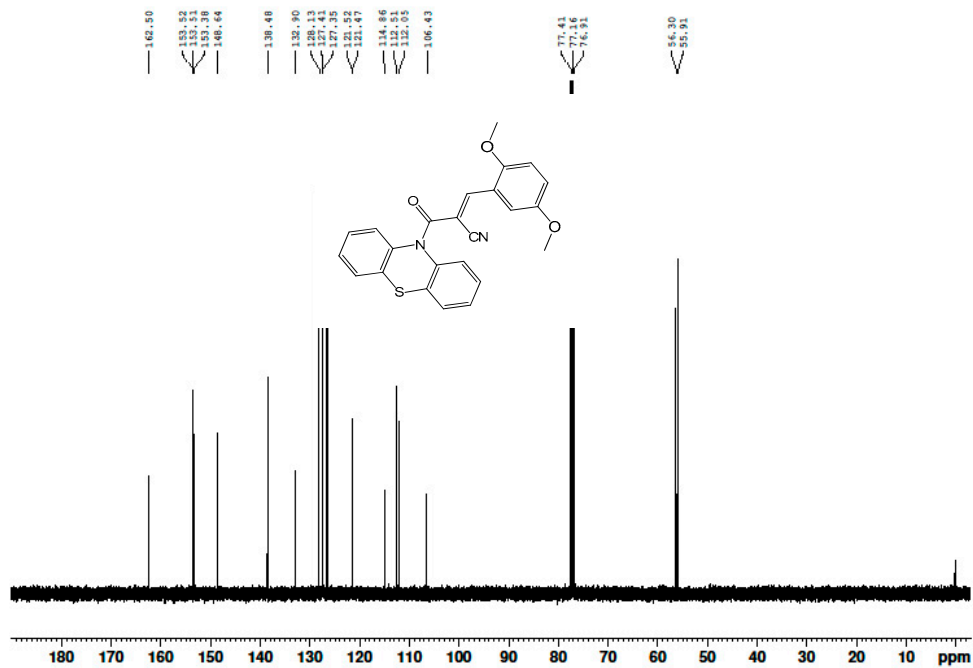
**IR-1f**



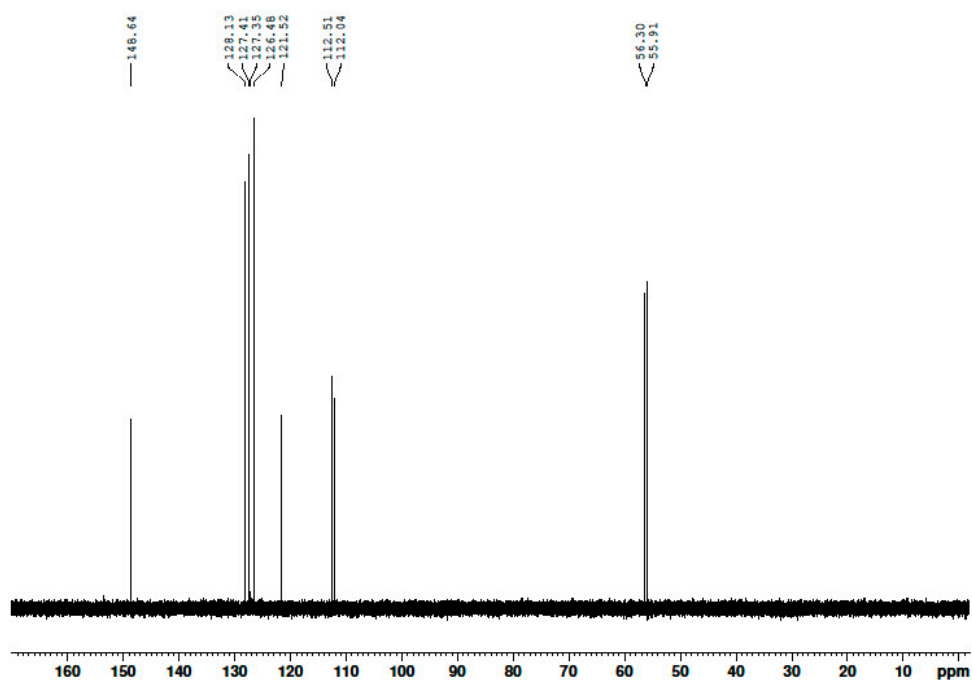
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-**1g**



<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-**1g**

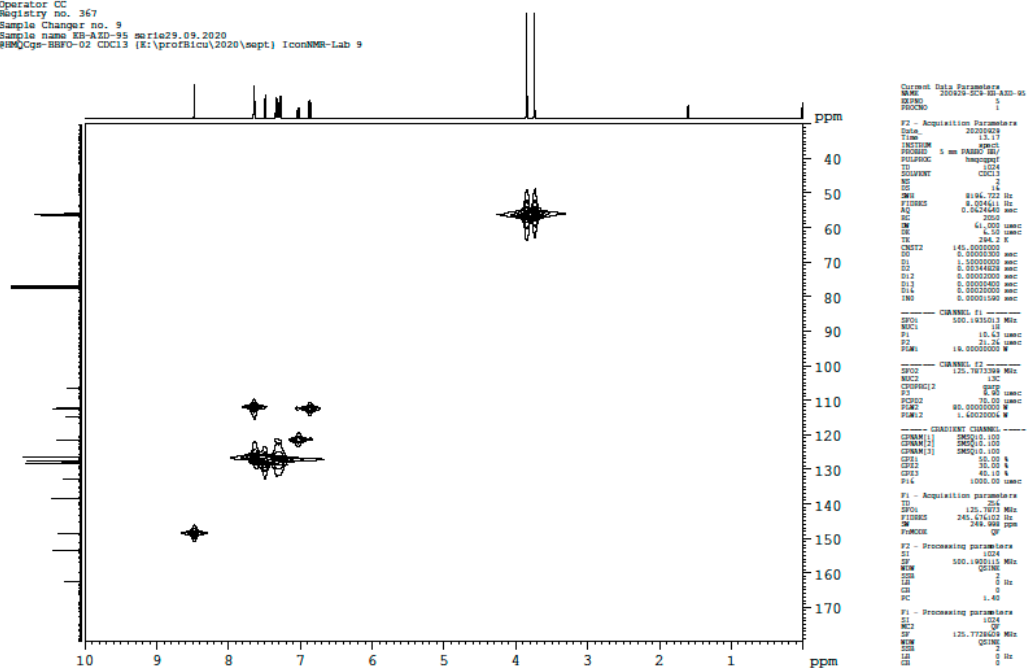


# <sup>13</sup>C-DEPT NMR (125 MHz, CDCl<sub>3</sub>)-1g



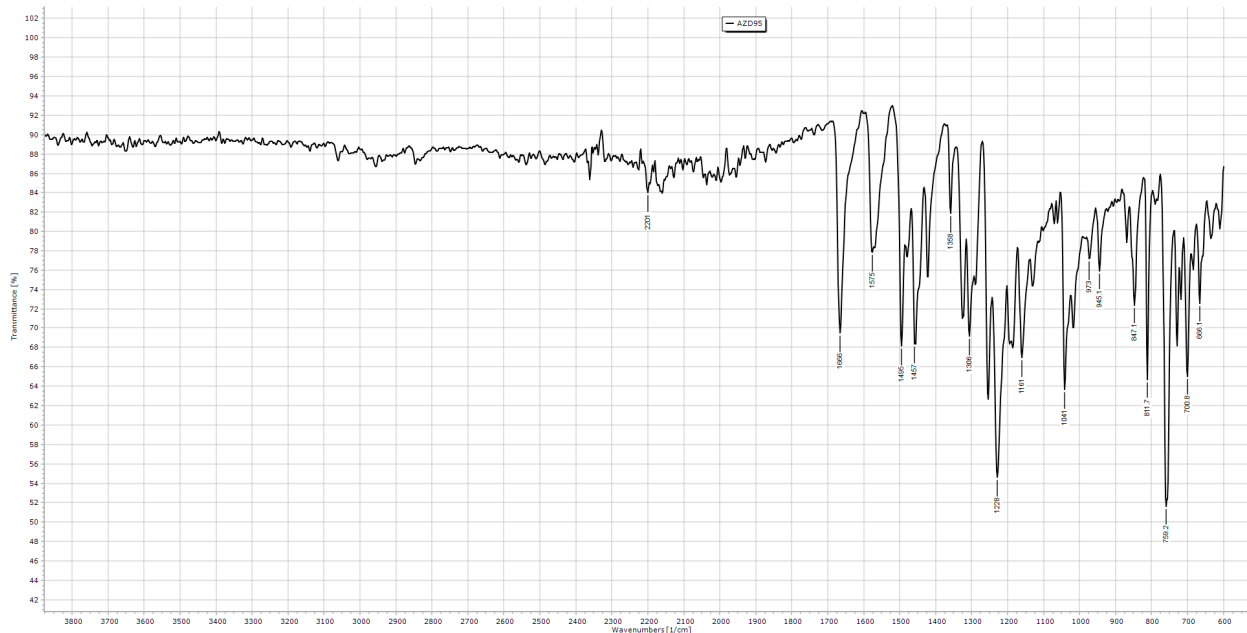
# HMQC NMR (500 MHz, CDCl<sub>3</sub>)-1g

Instrument Bruker Avance III 500 MHz UAIC  
 User prof. Bicu  
 Operator CC  
 Registry no. 367  
 Sample Changer no. 9  
 Sample name KB-AED-95 Series29.09.2020  
 @BBO-Cp- BBFO-02 CDCl3 [E:\profBicu\2020\sept] IconNMR-Lab 9

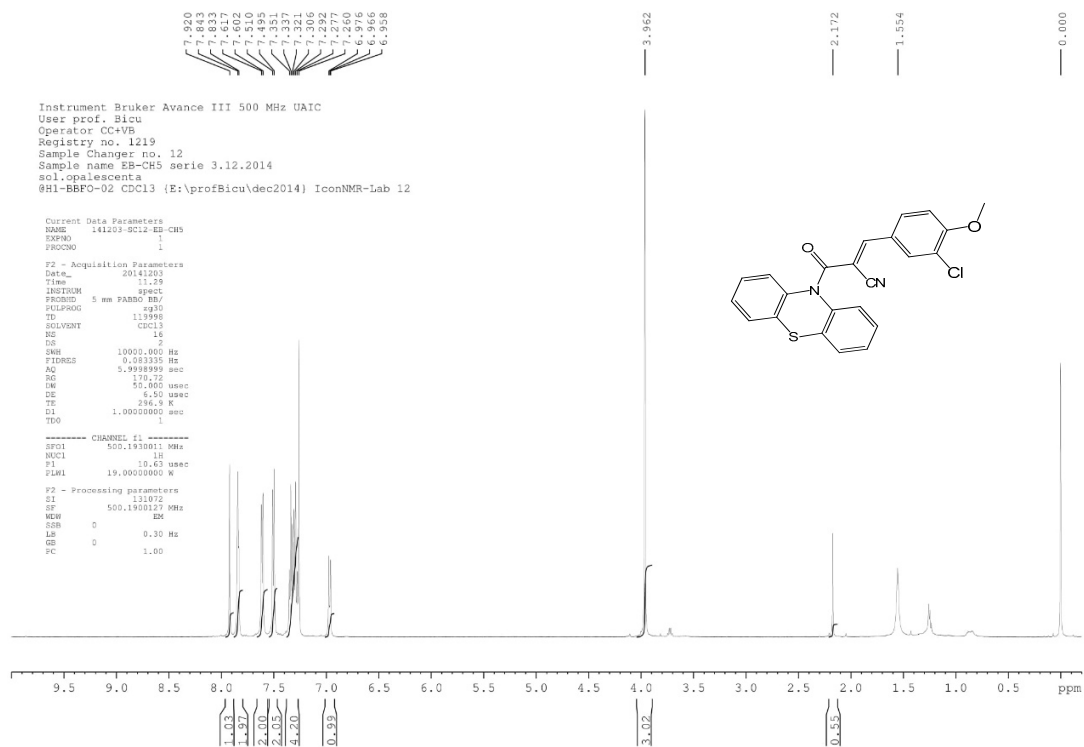




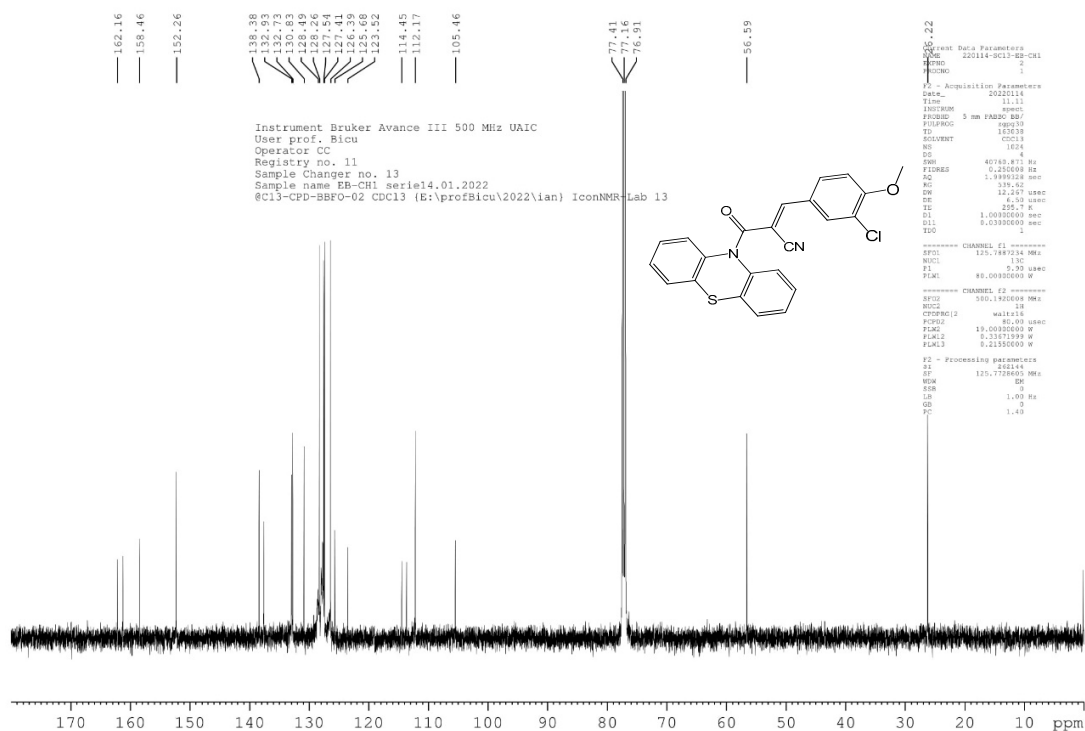
## IR-1g



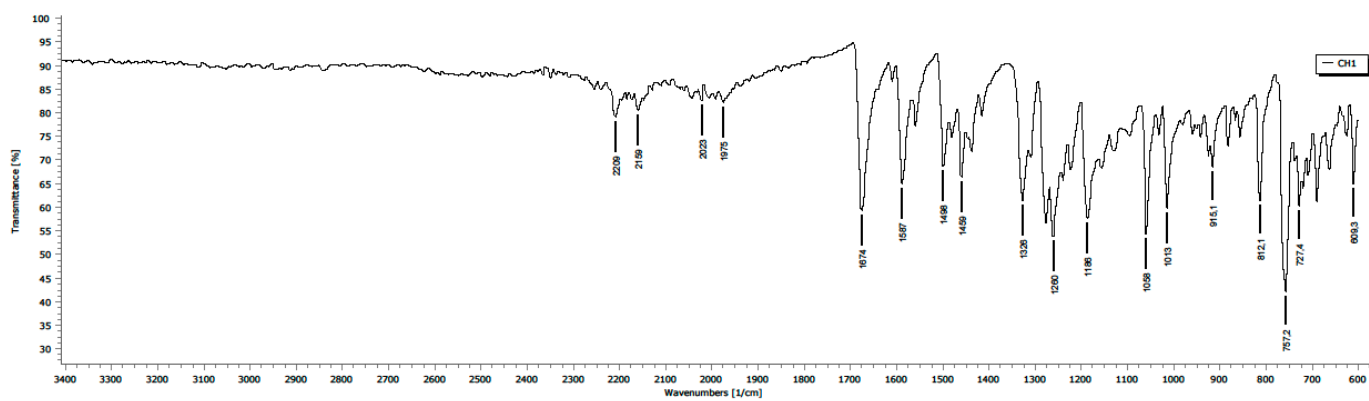
## <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)- 1h



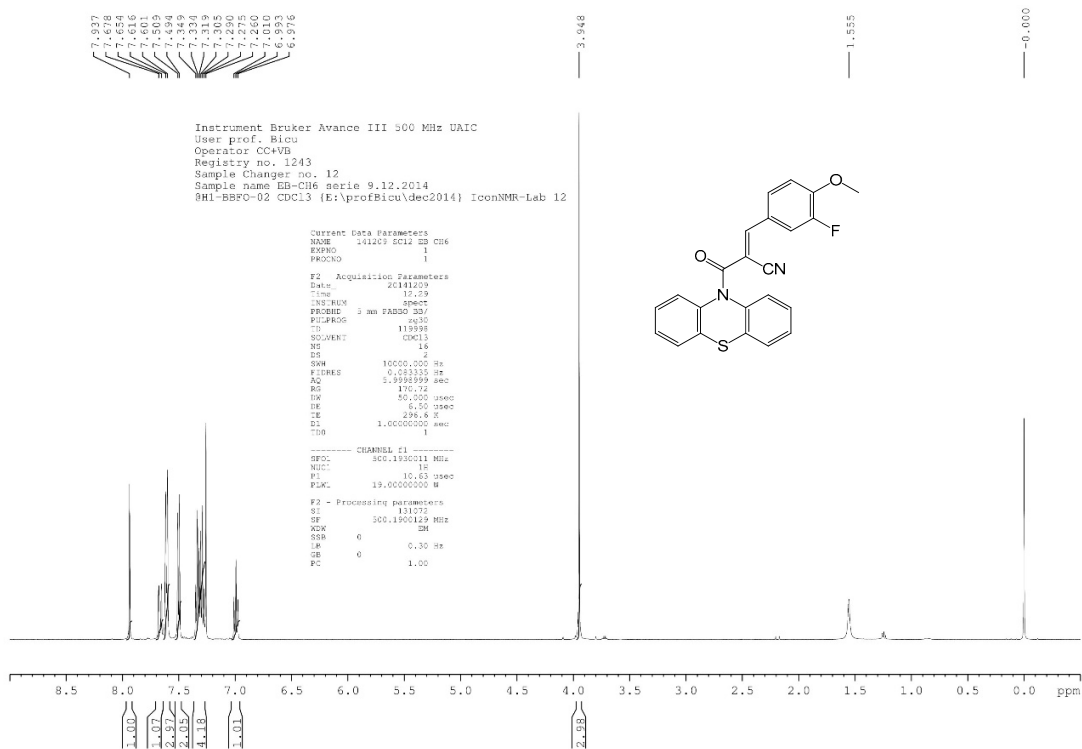
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-1h



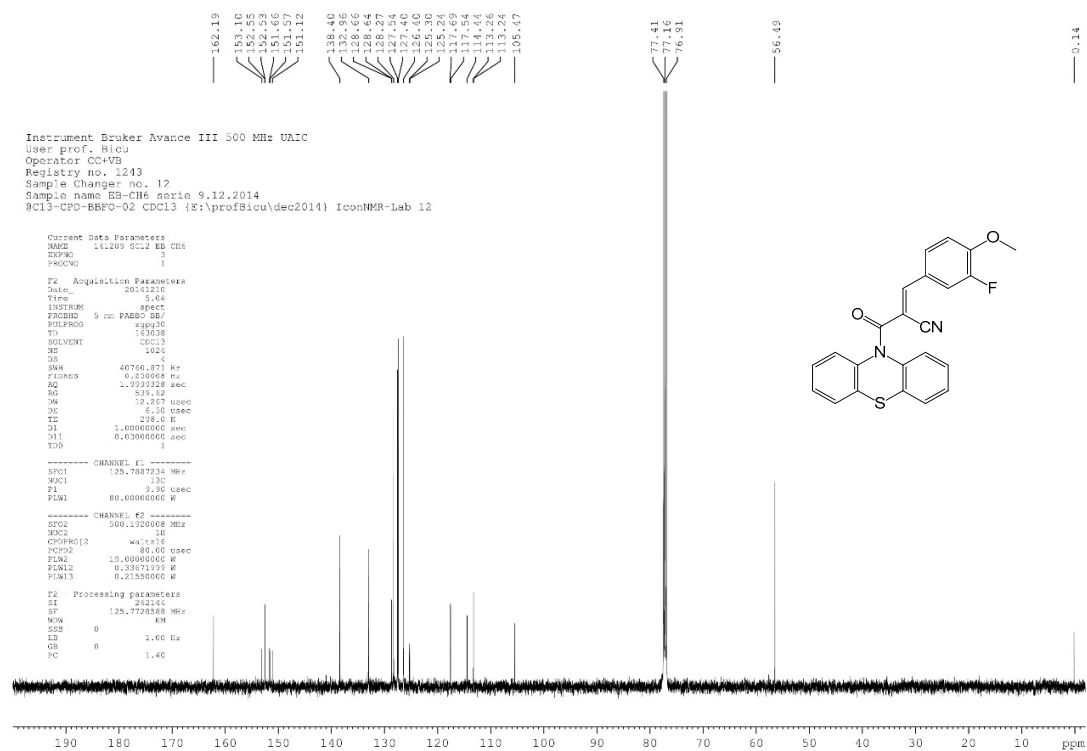
# IR-1h



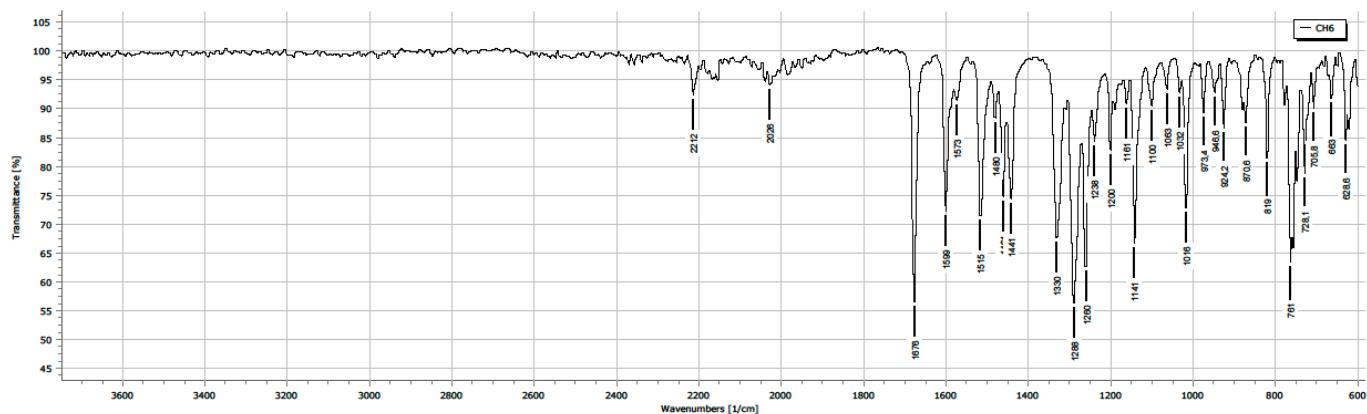
# <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)- **1i**



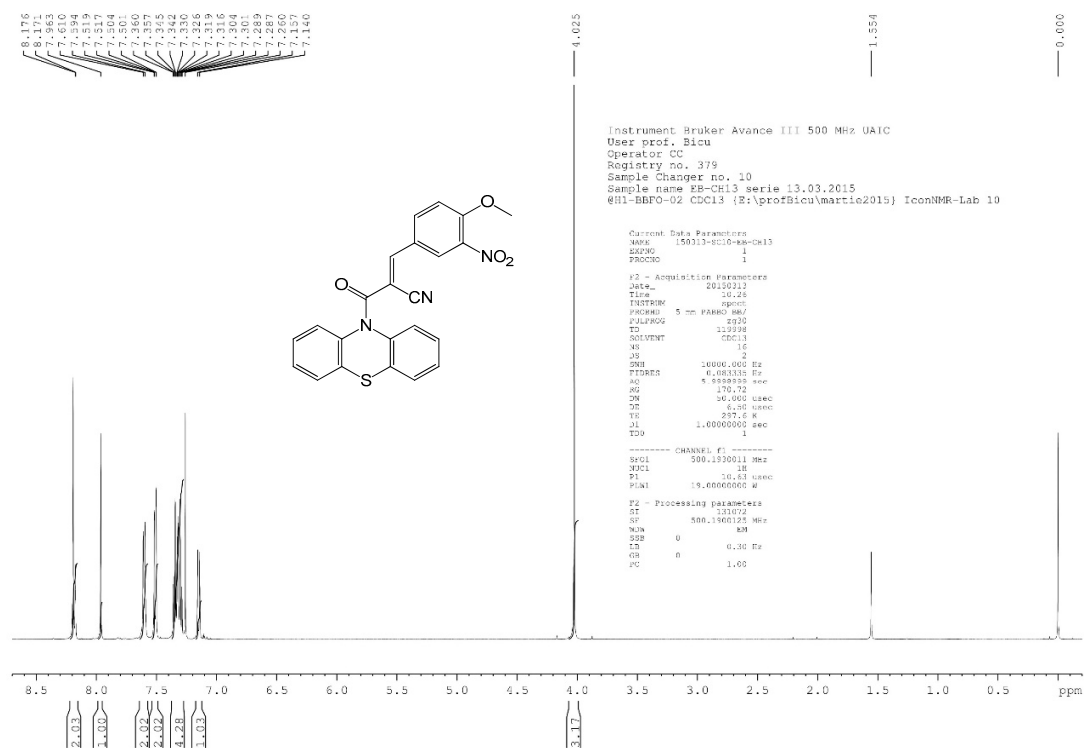
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)- **1i**



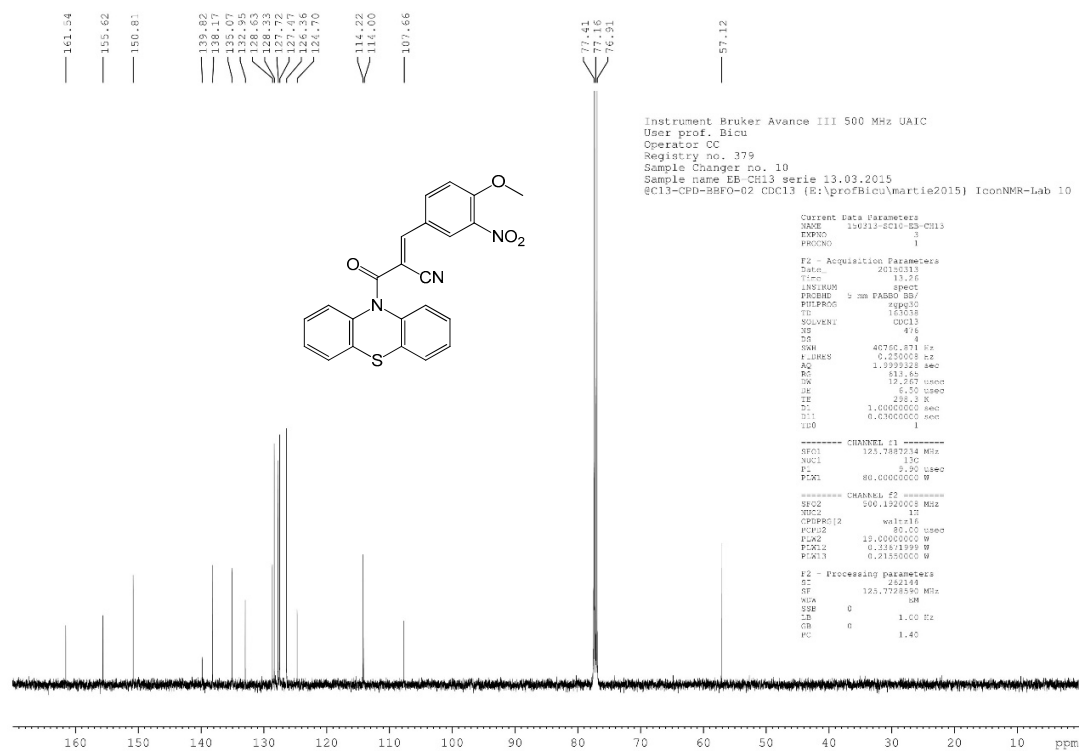
## IR-1i



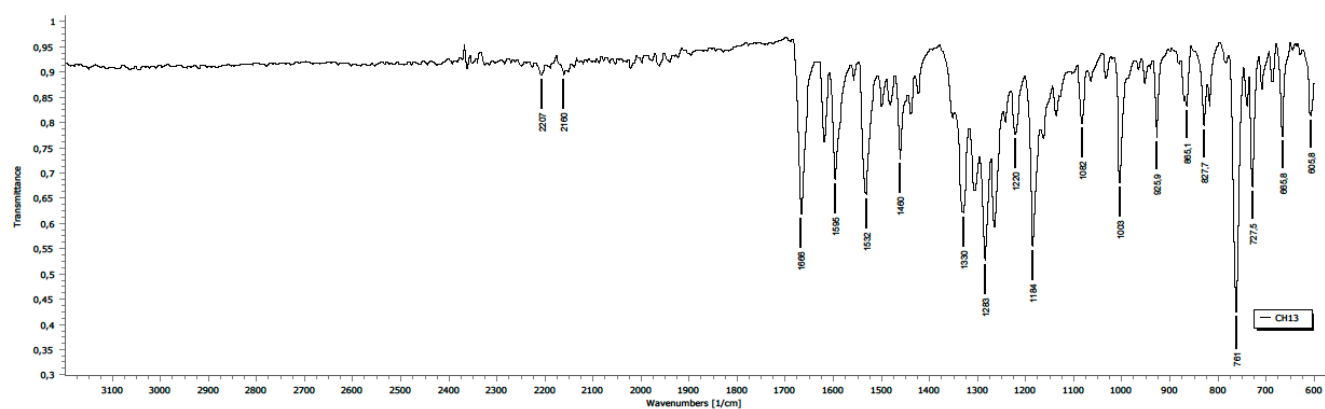
## <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)- 1j



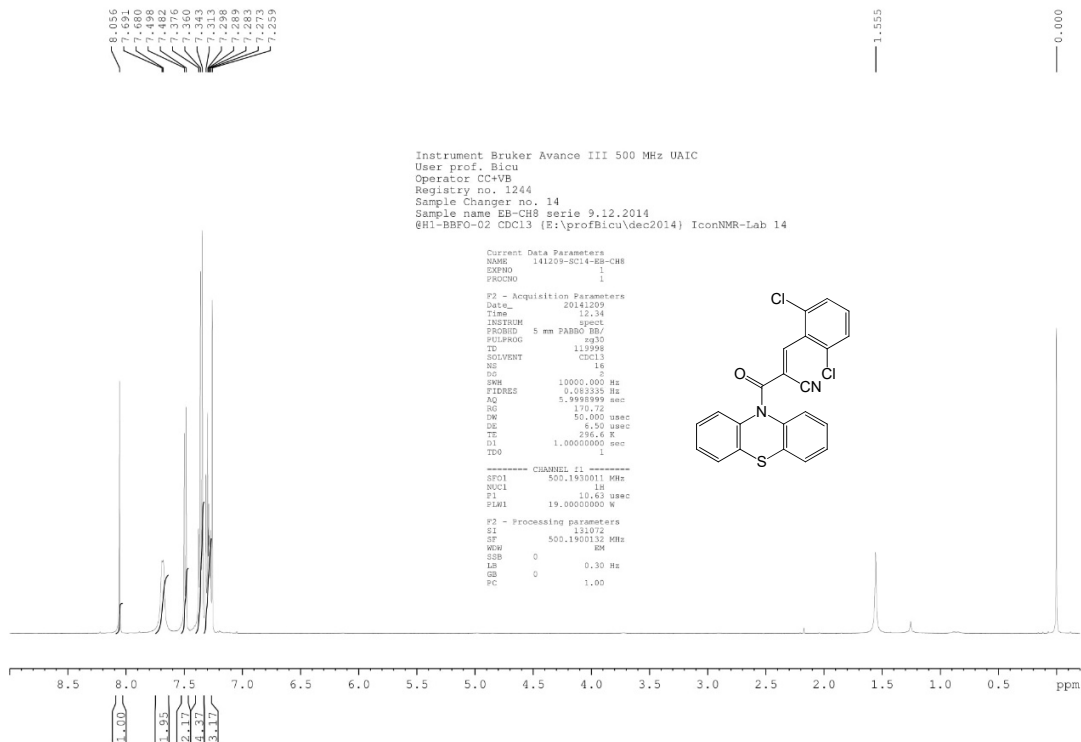
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-**1j**



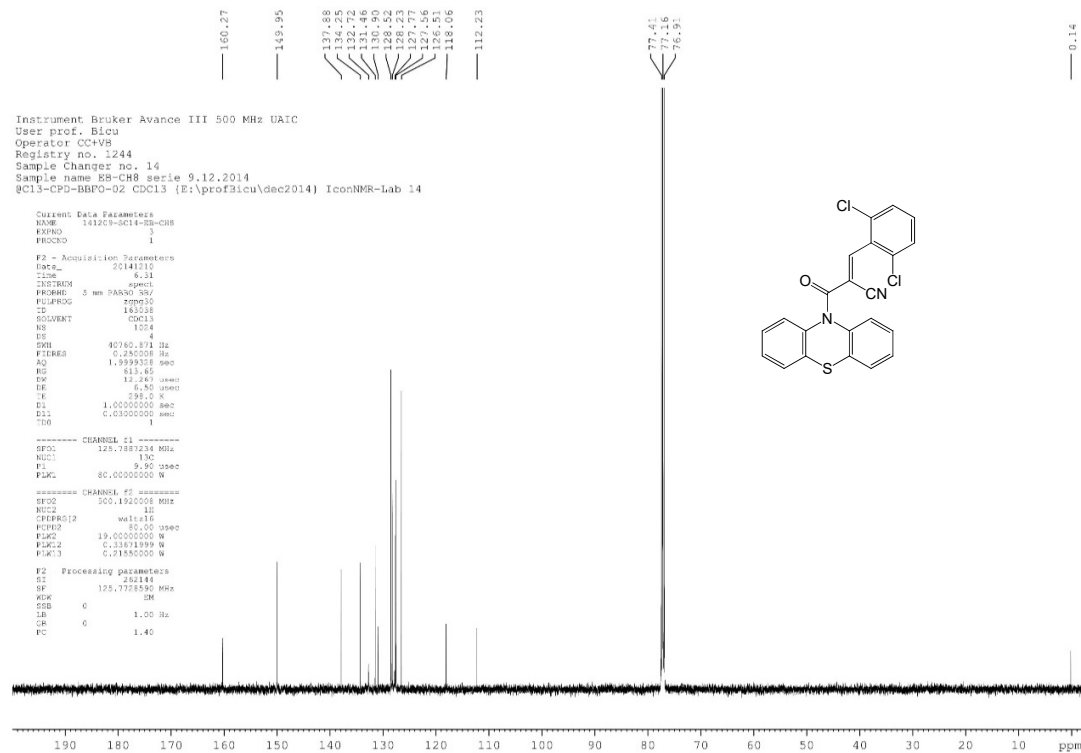
# IR-**1j**



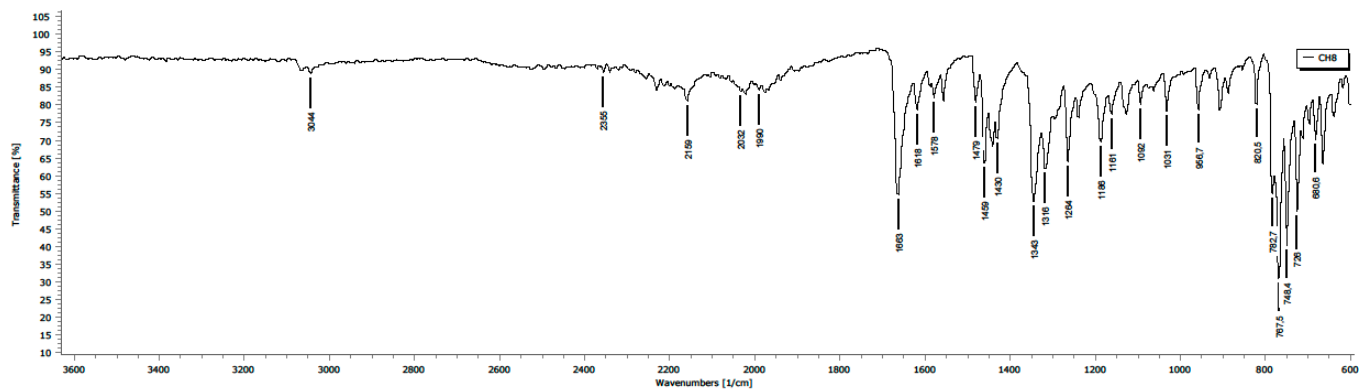
# <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)- 1k



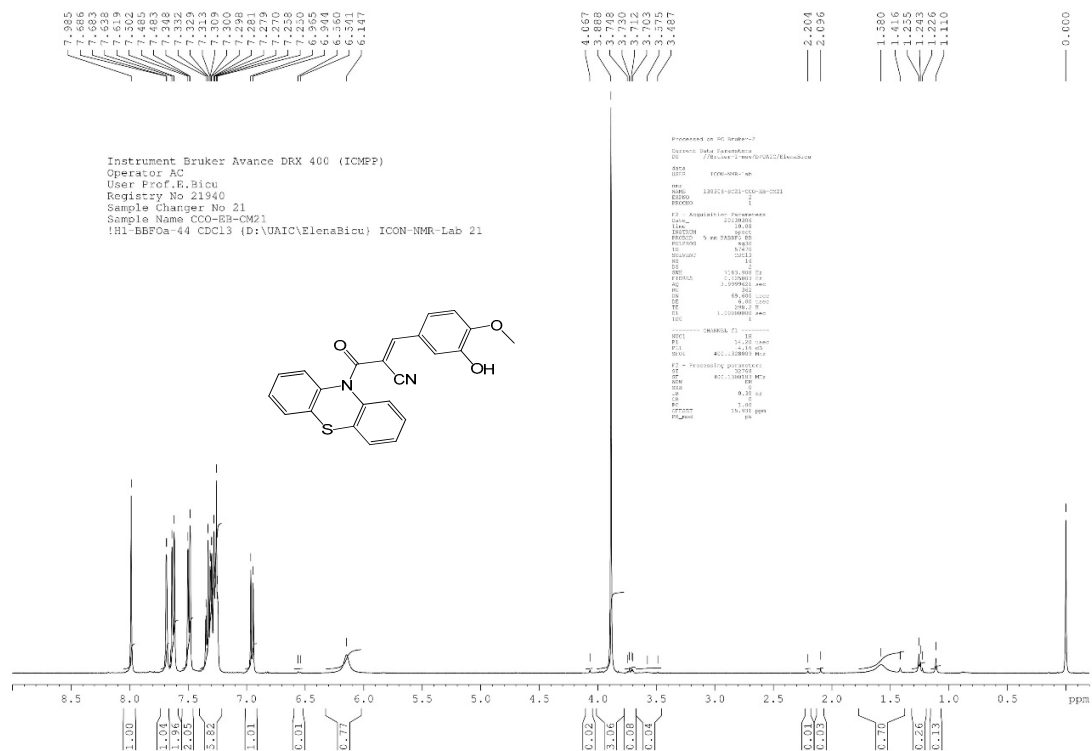
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-1k



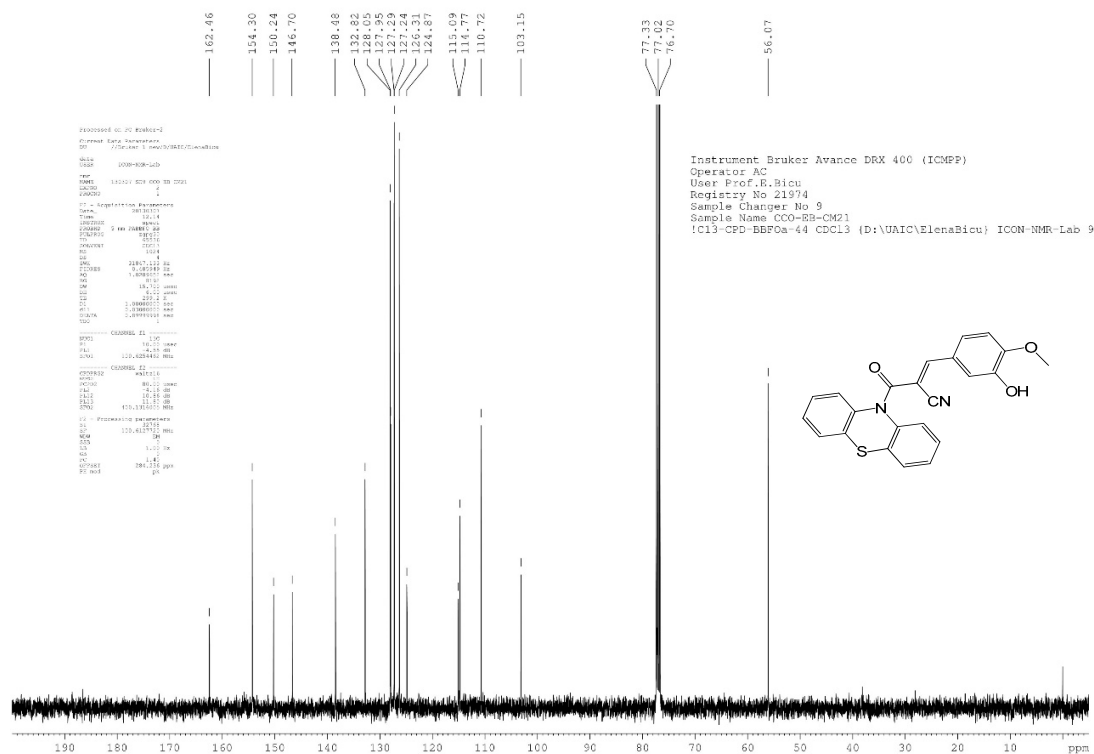
## IR-1k



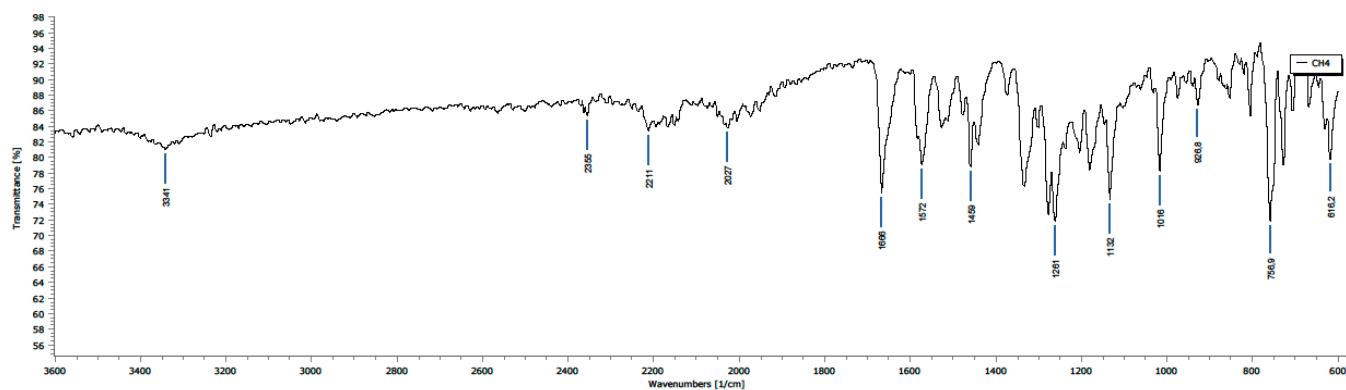
## <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)- 11



# <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)-II

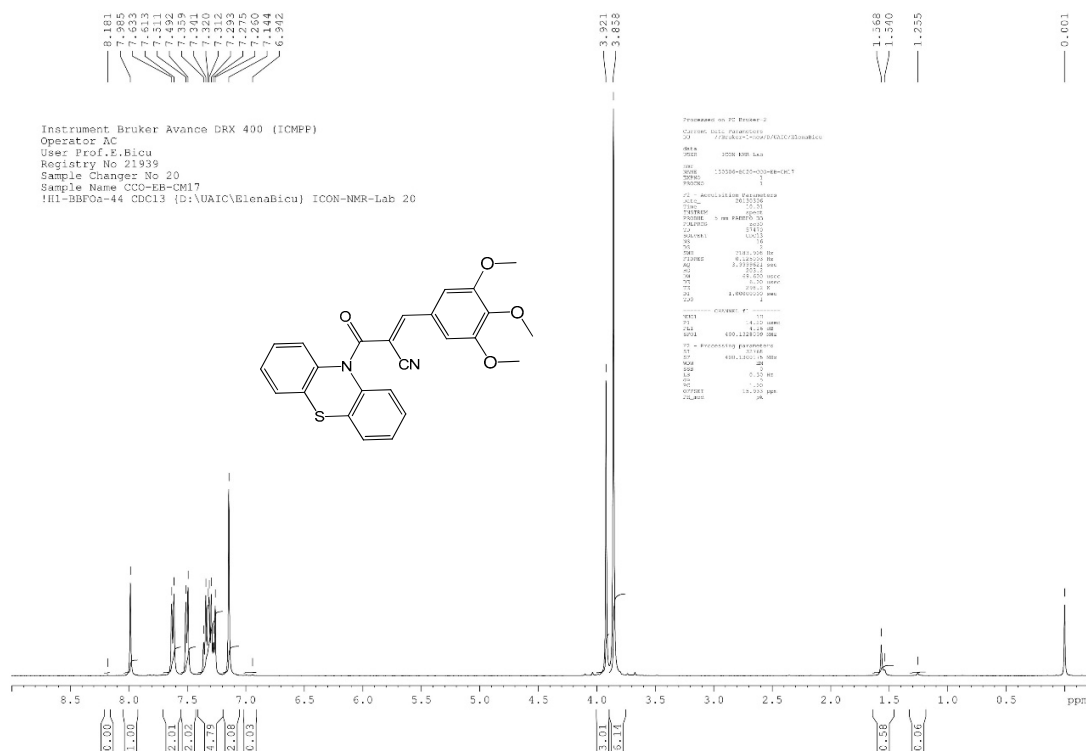


# IR-II

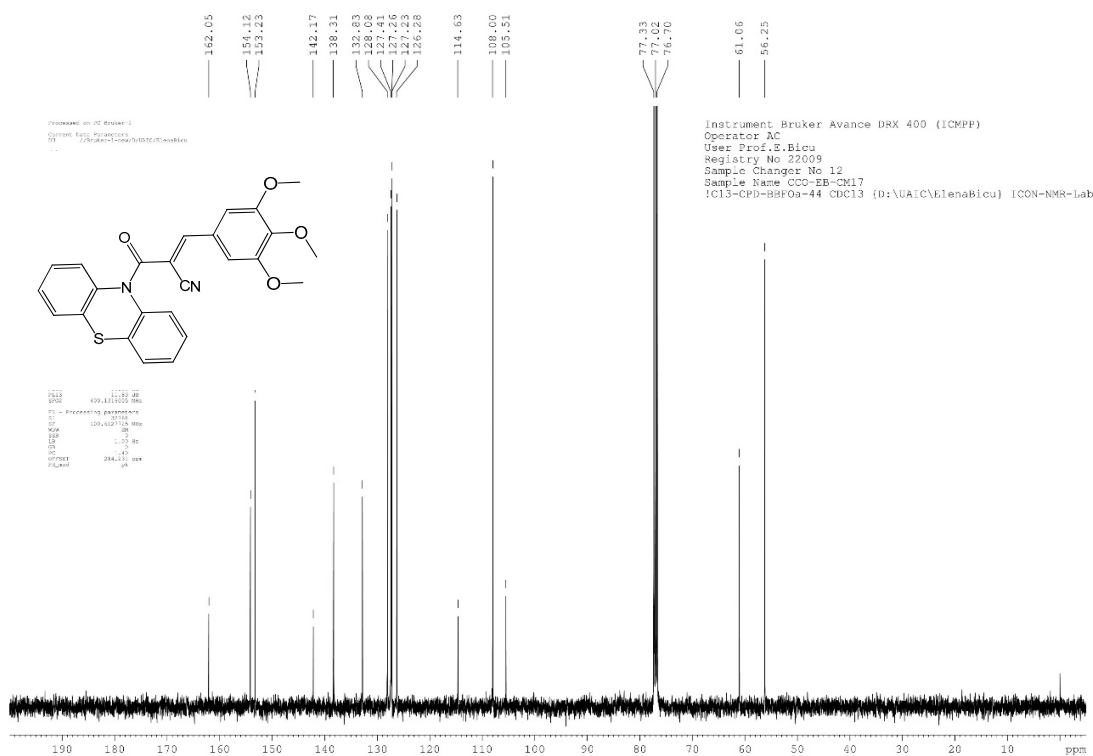




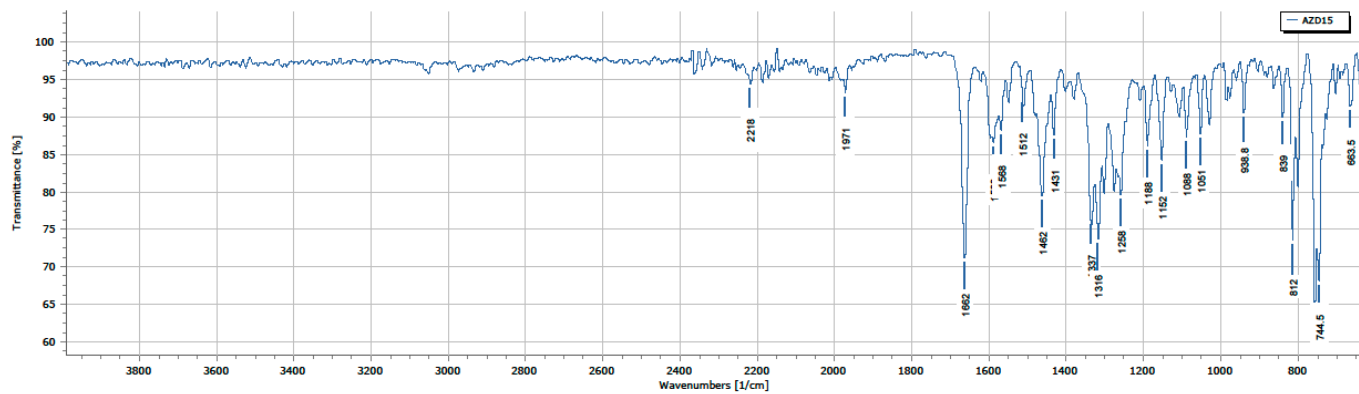
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)-1m



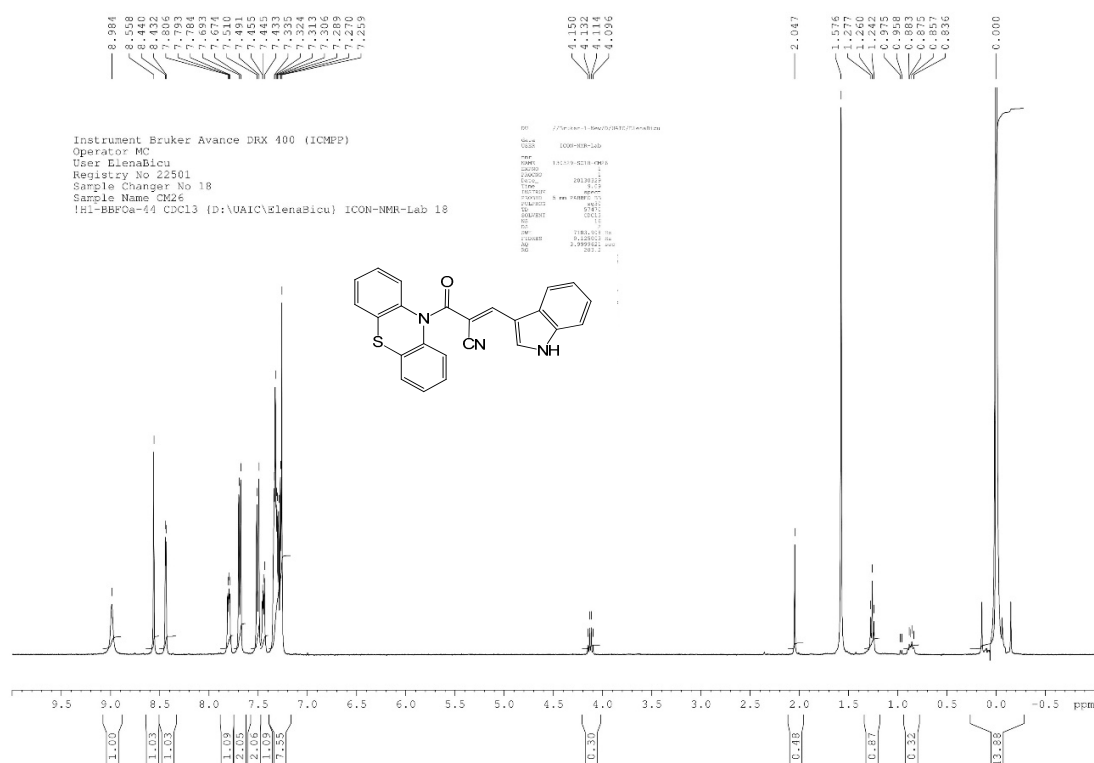
# <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)-1m



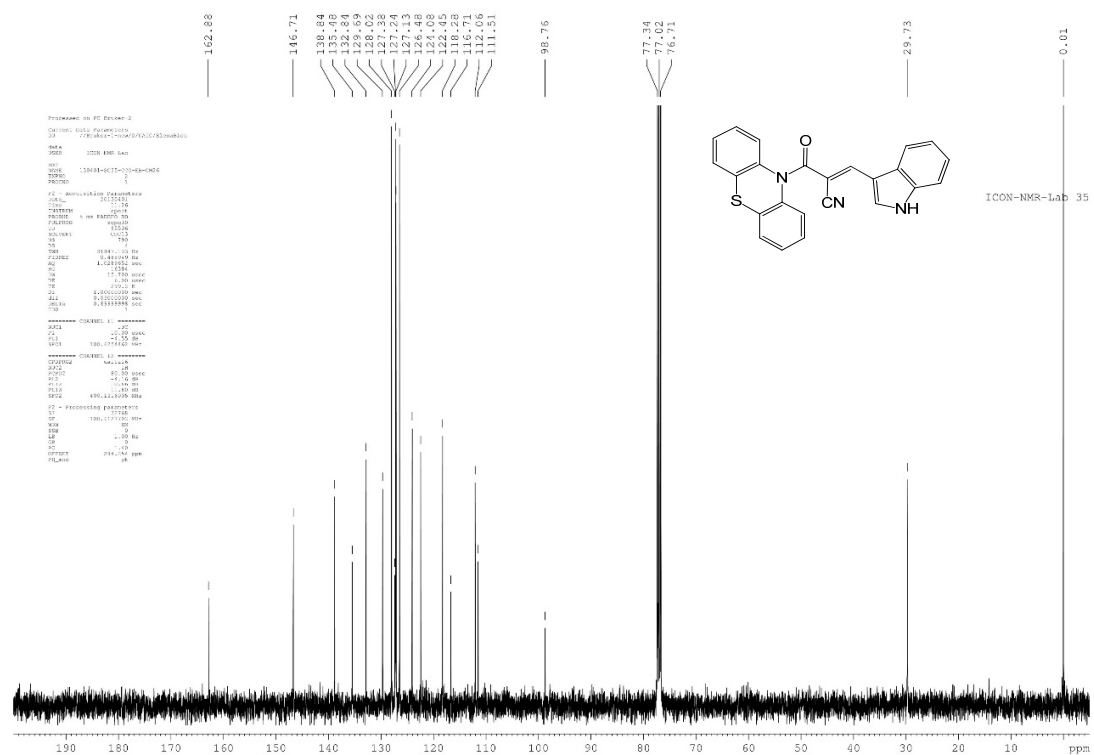
## IR-1m



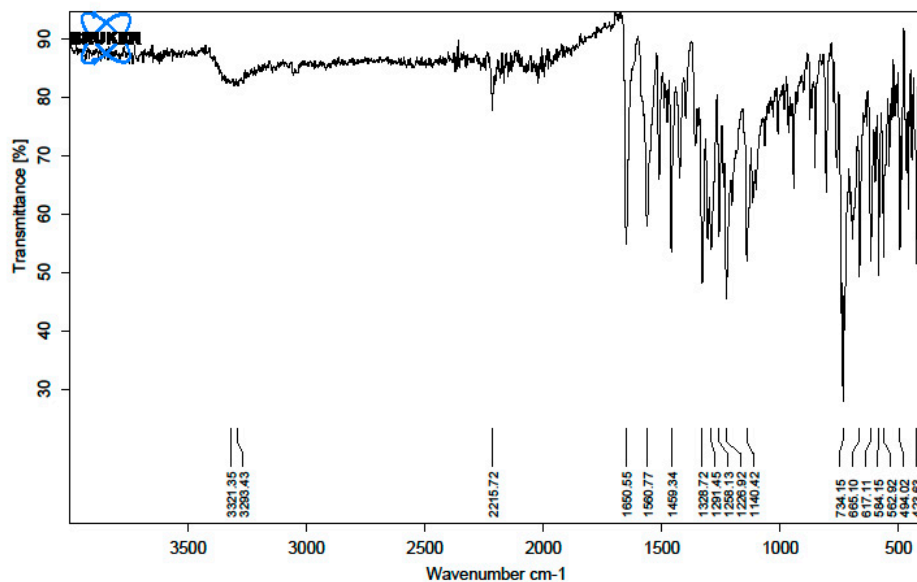
# <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)- 1n



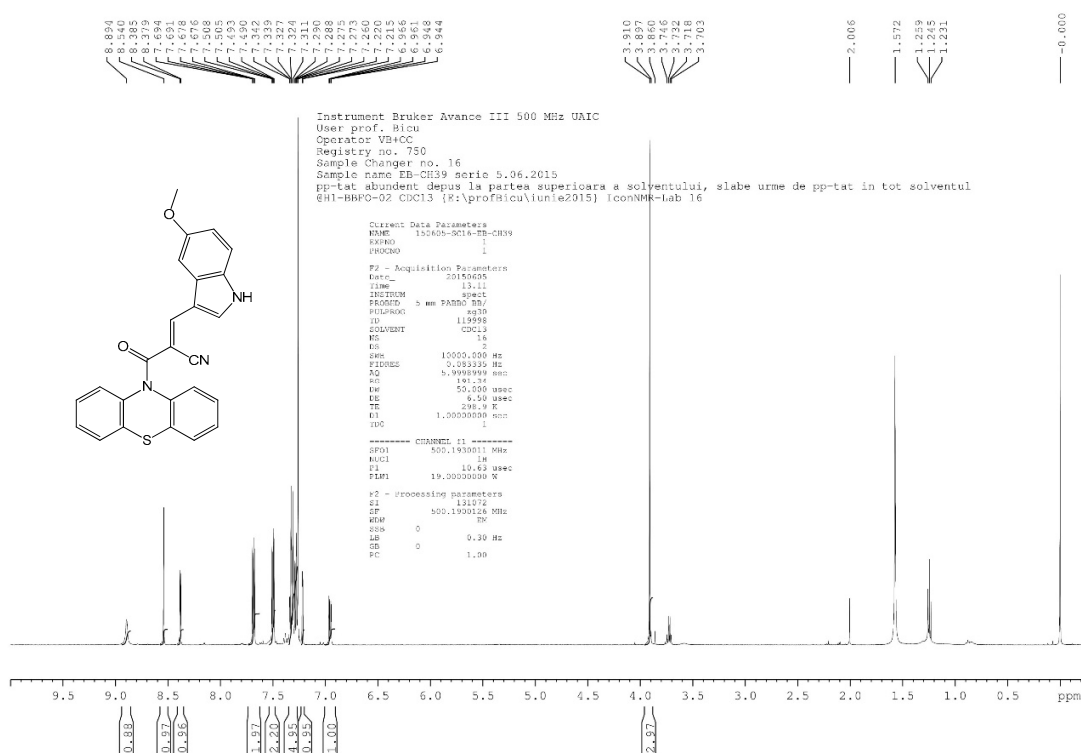
# <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)-1n



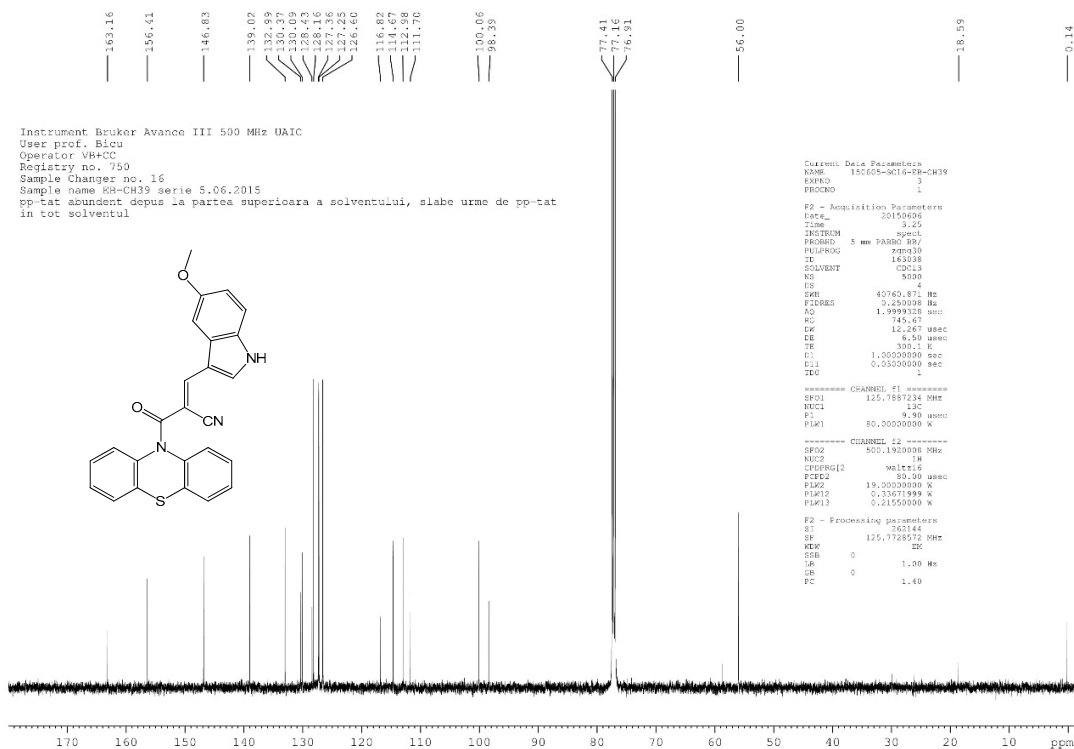
## IR-1n



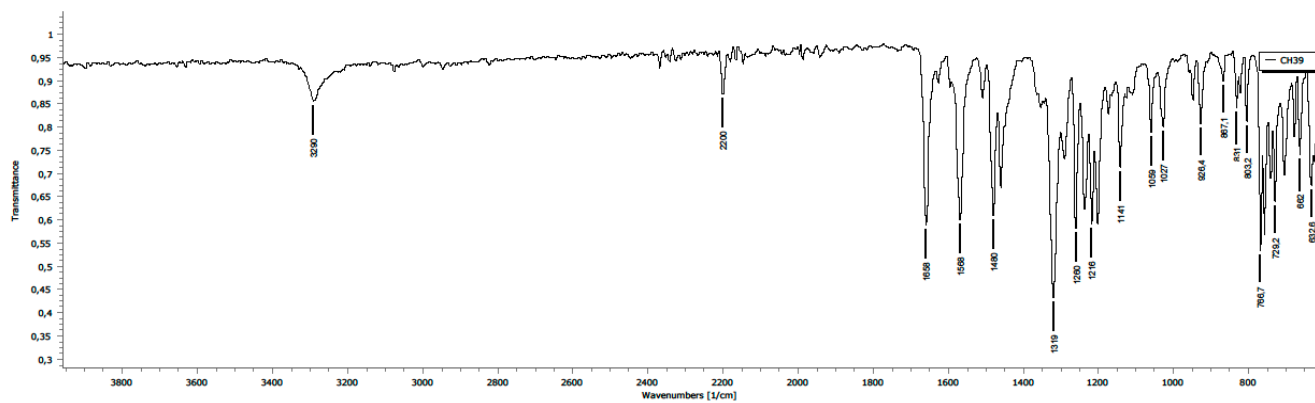
## <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)- 1o



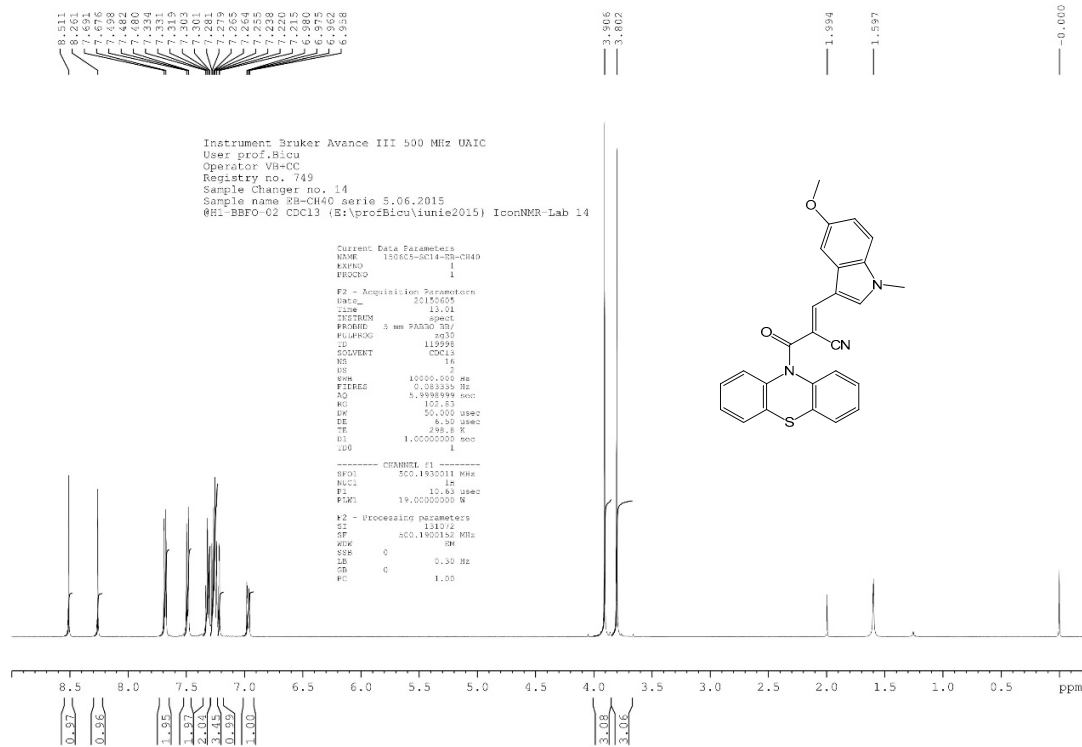
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-10



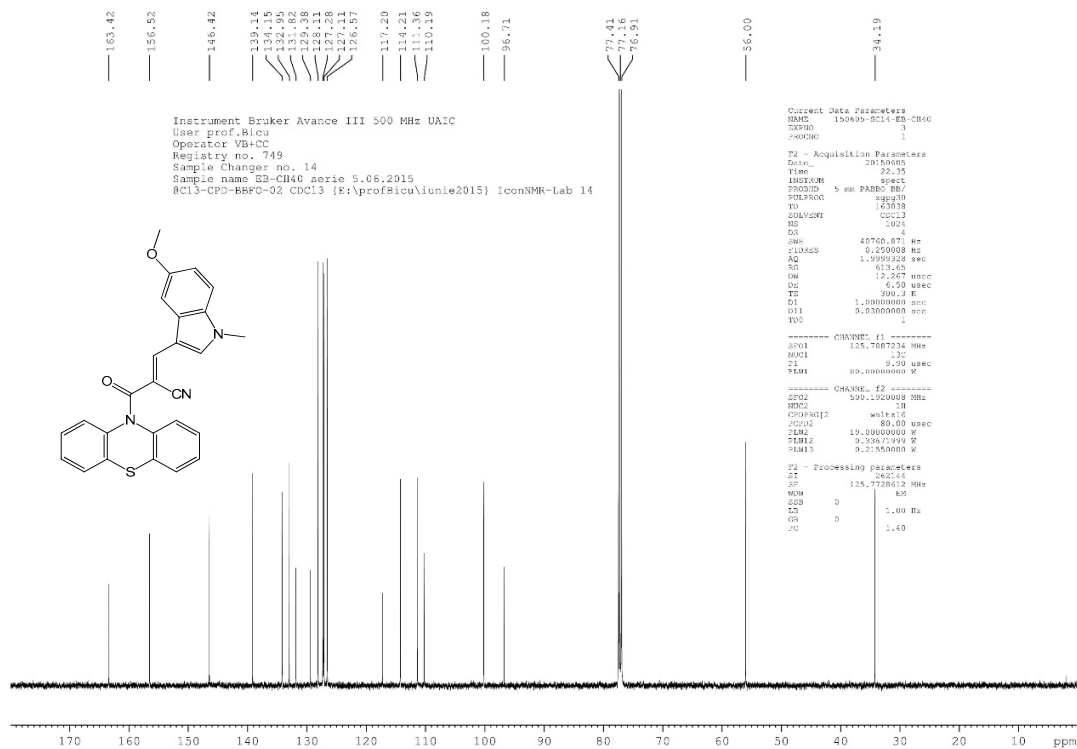
## IR-10



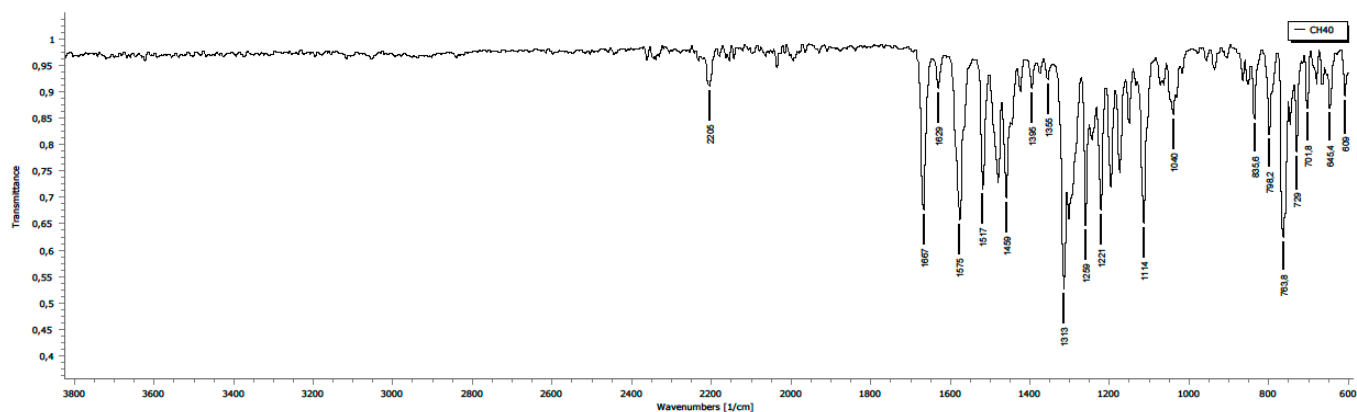
# <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)- 1p



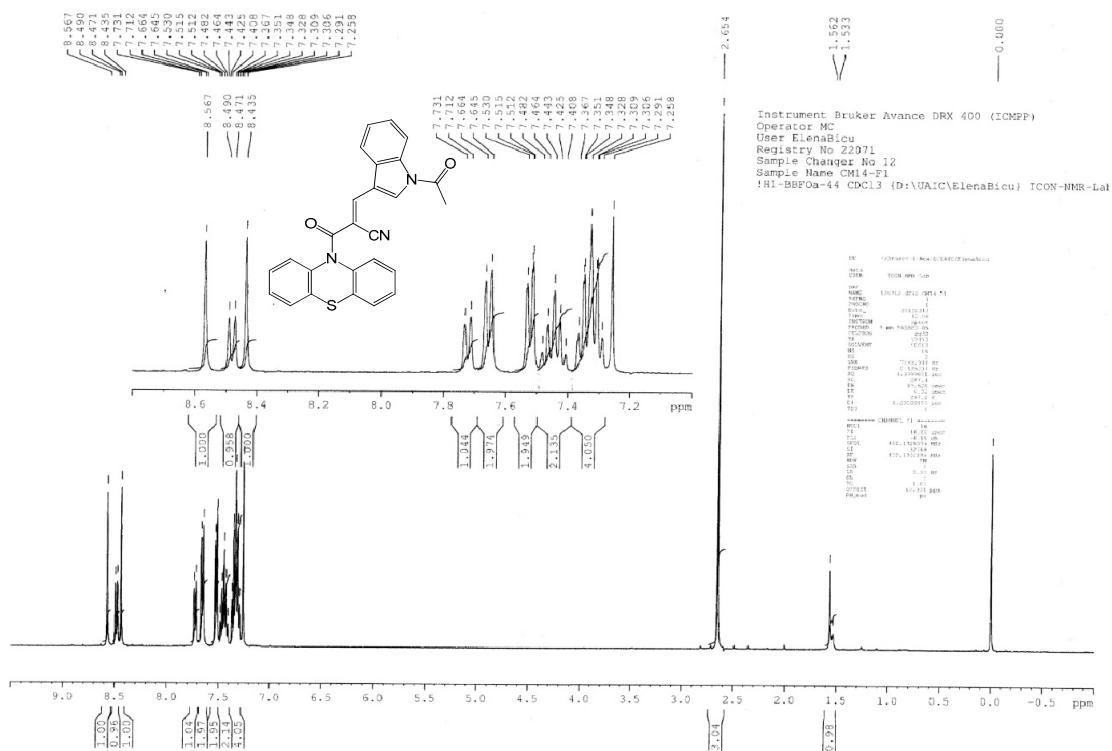
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-1p



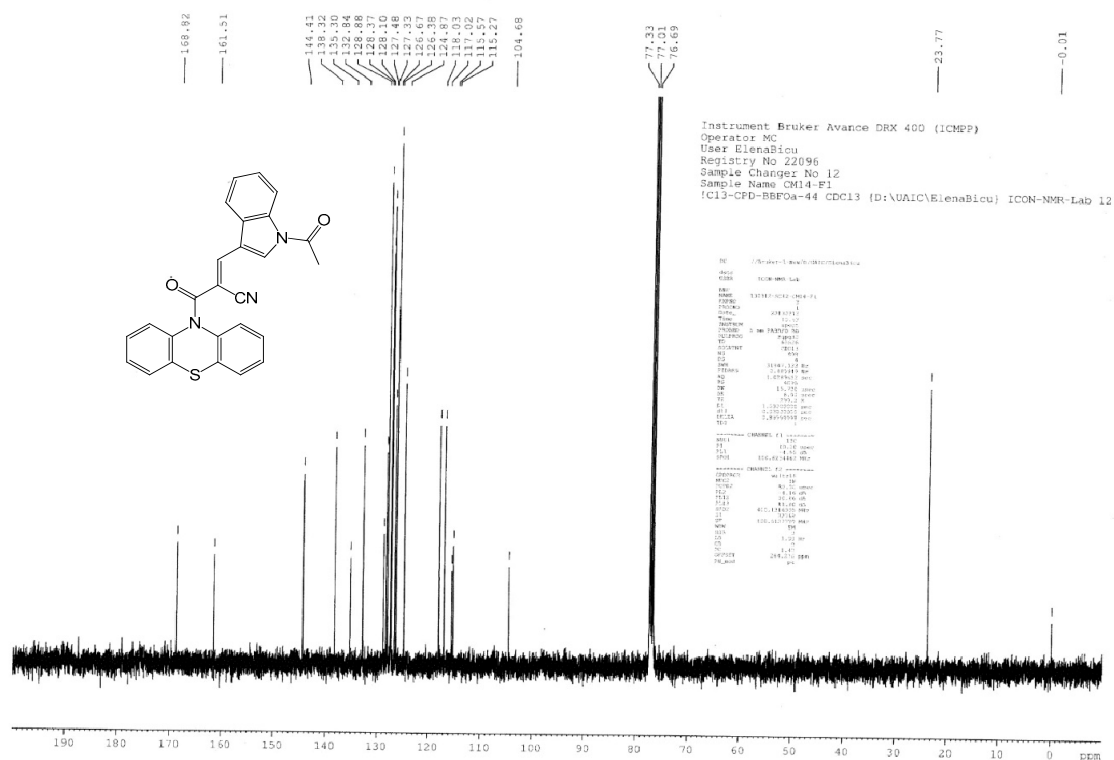
# IR-1p



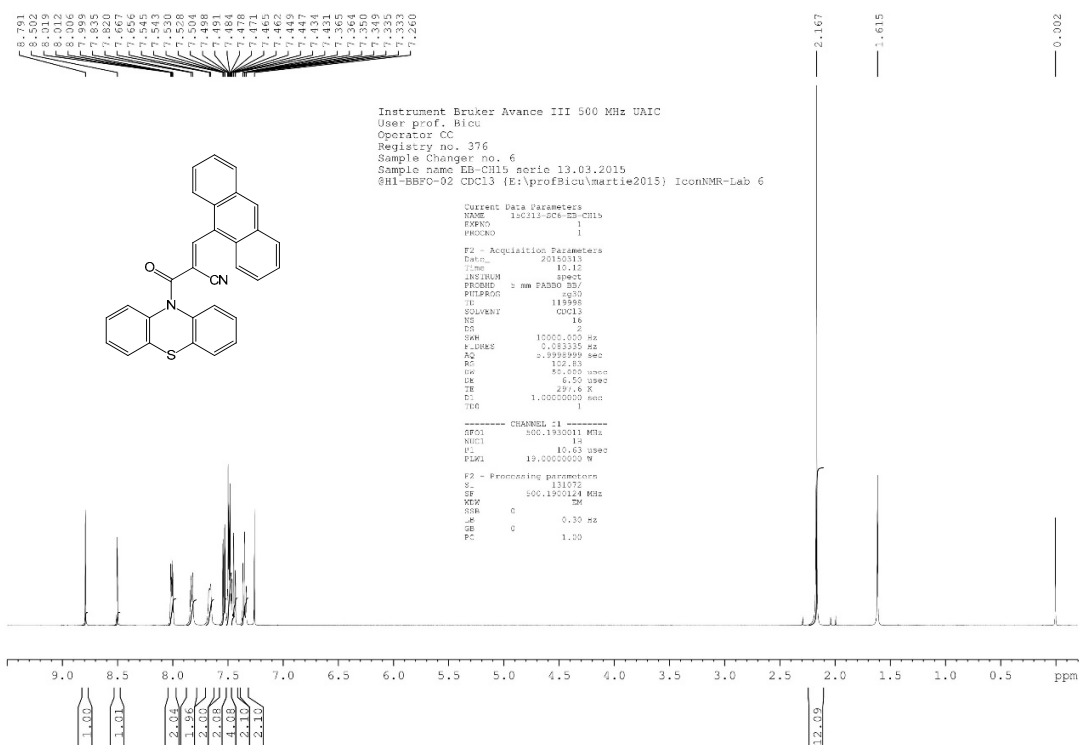
## <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)- 1q



**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)-1q**

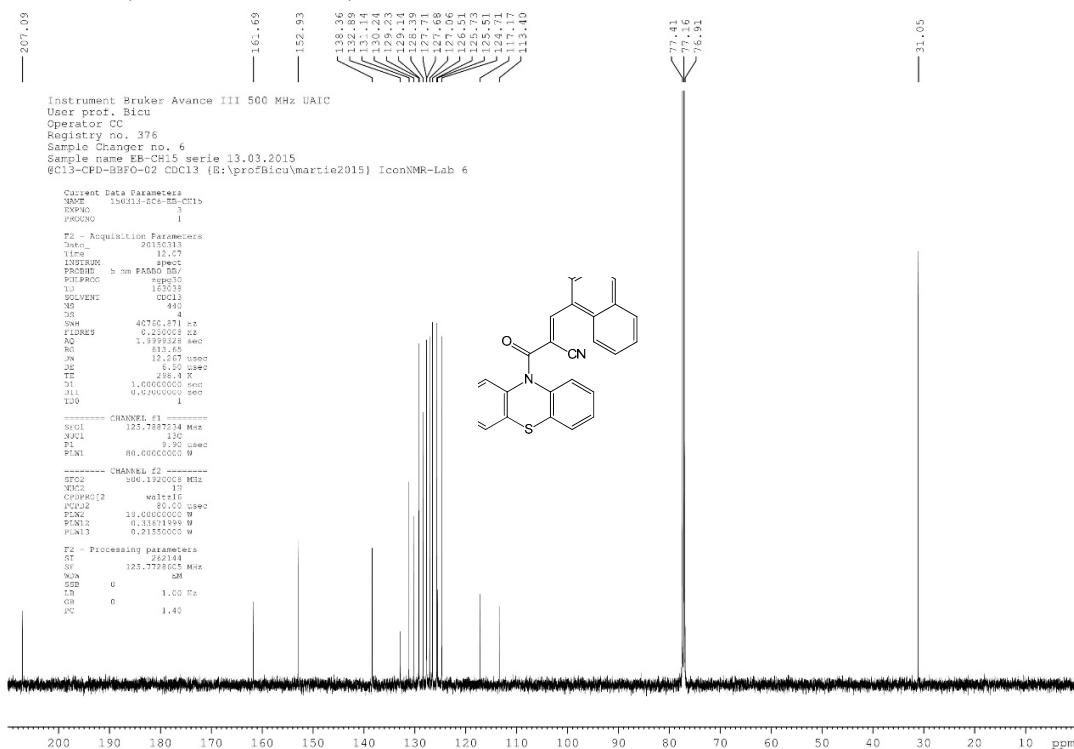


**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-1r**

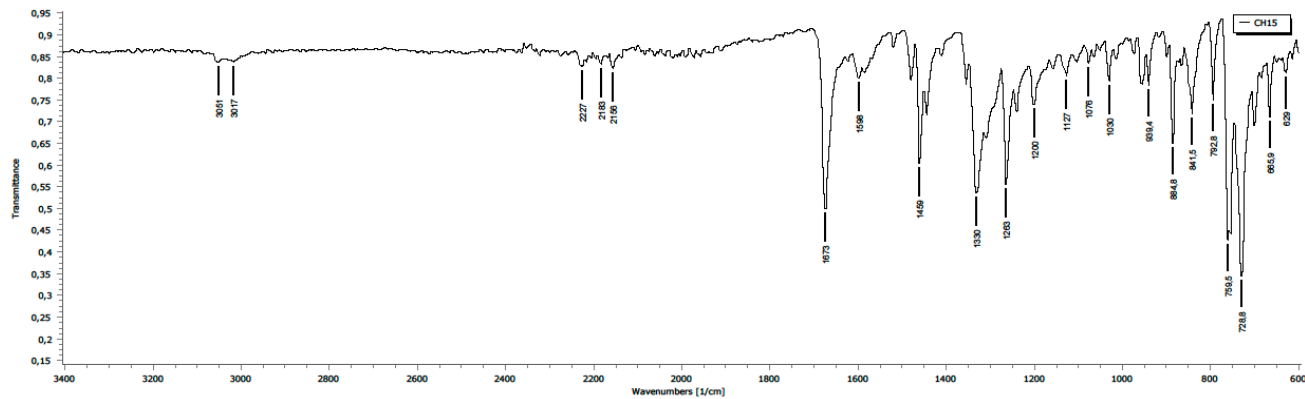




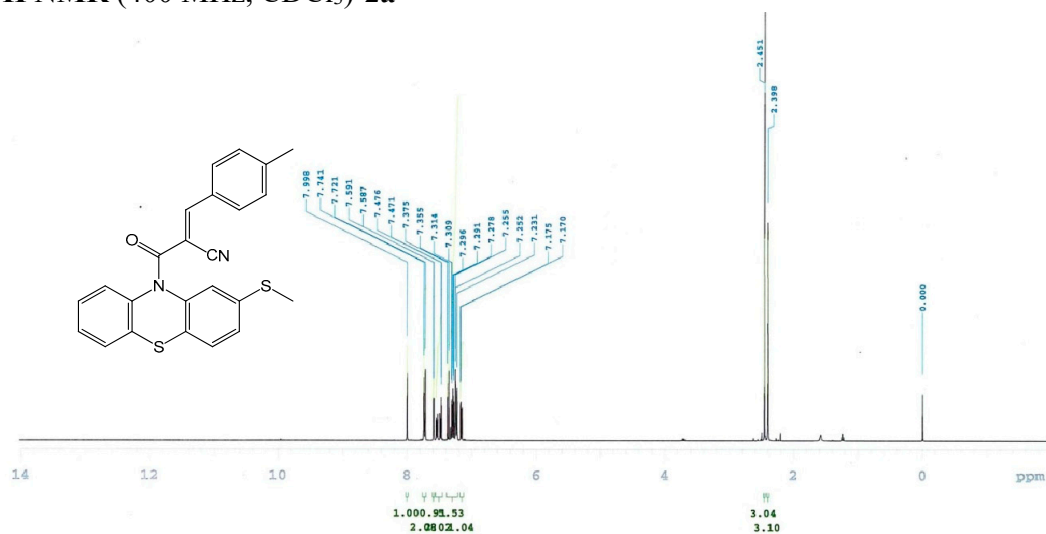
# **<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-1r**



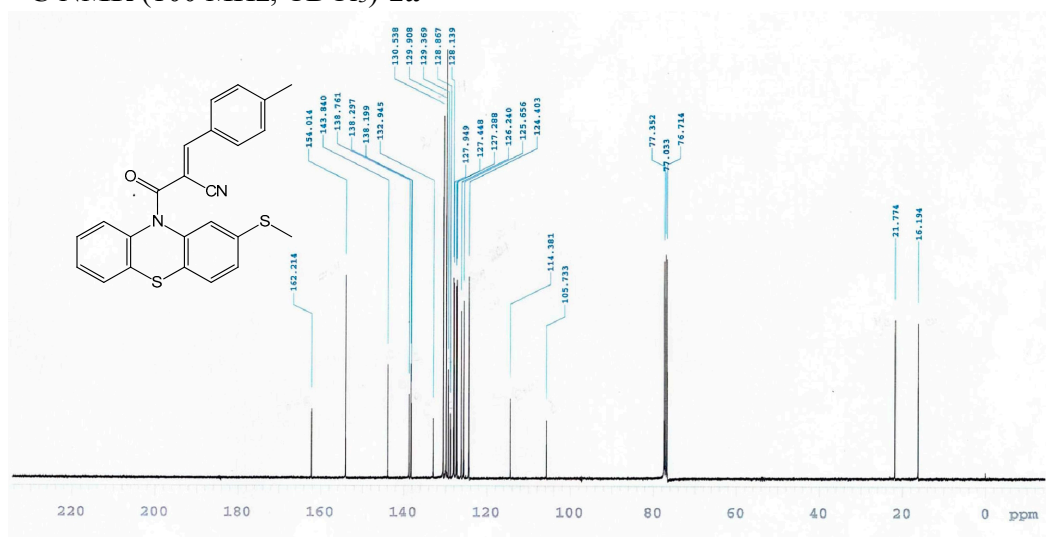
# **IR-1r**



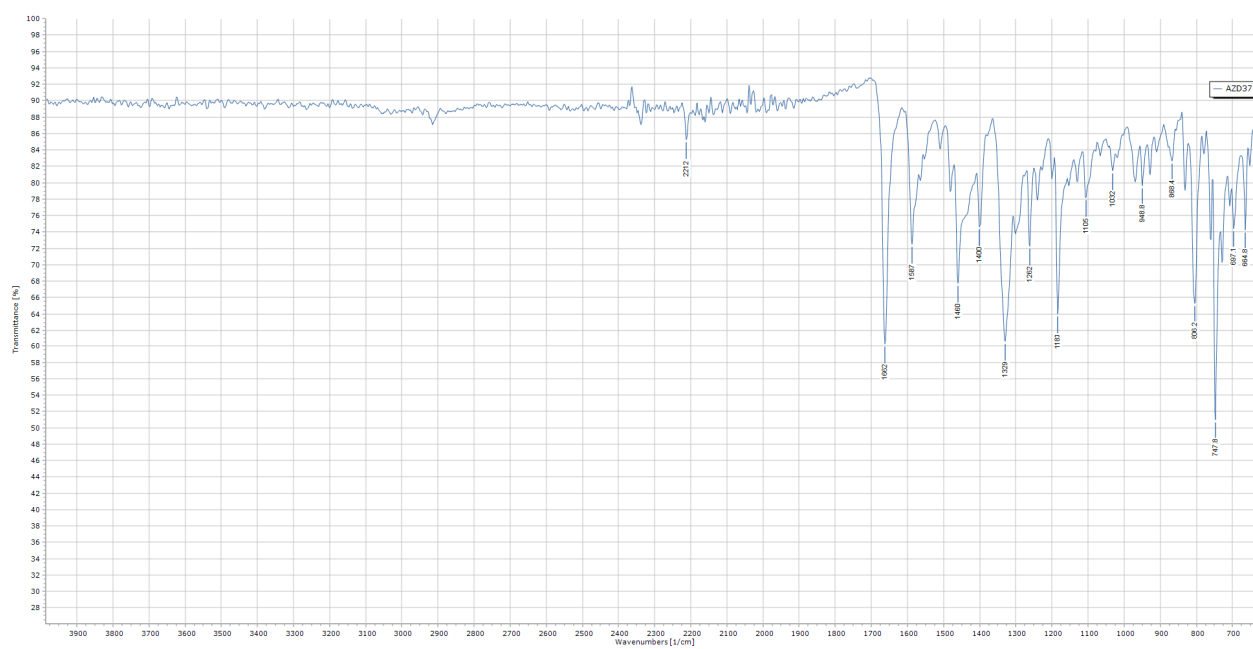
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)-2a**



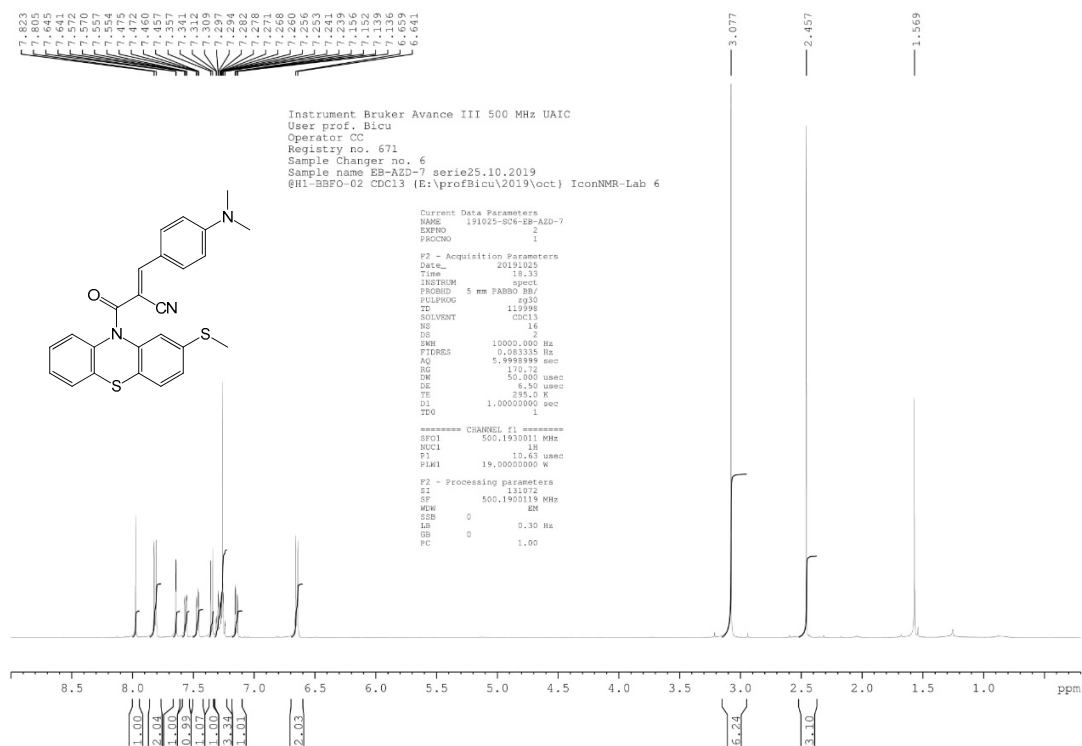
**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)-2a**



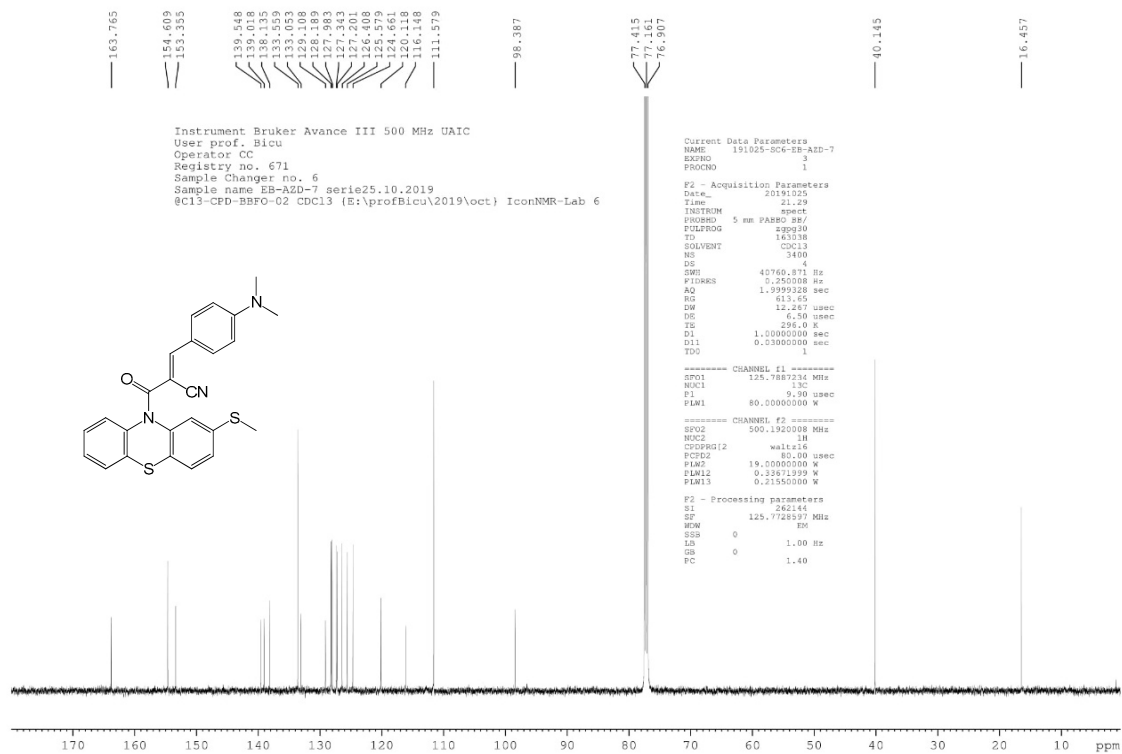
## IR-2a



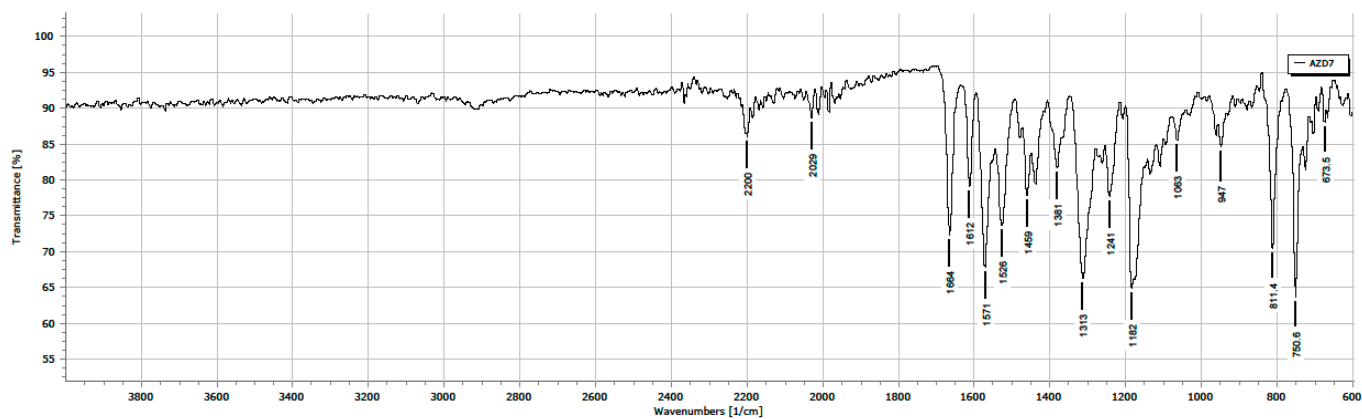
# <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)- **2b**



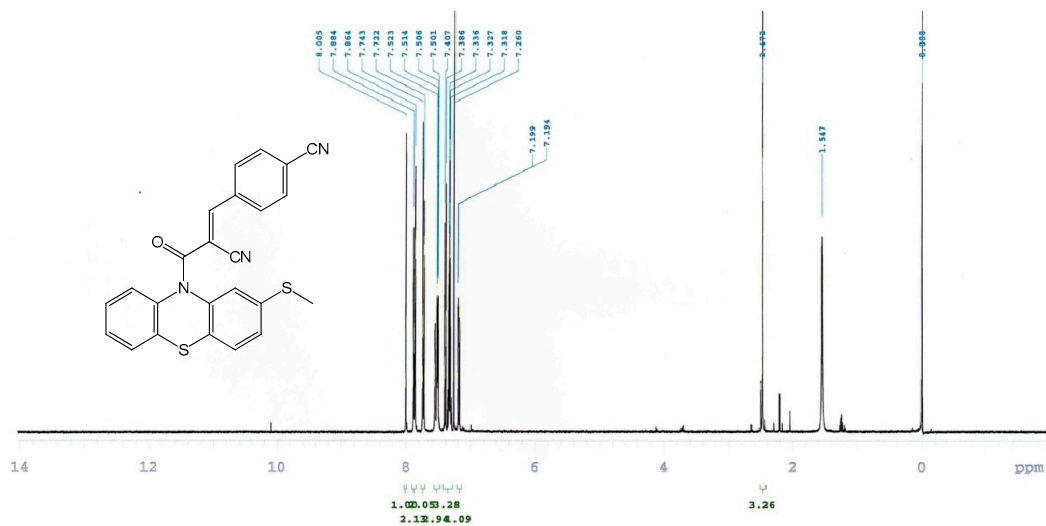
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)- **2b**



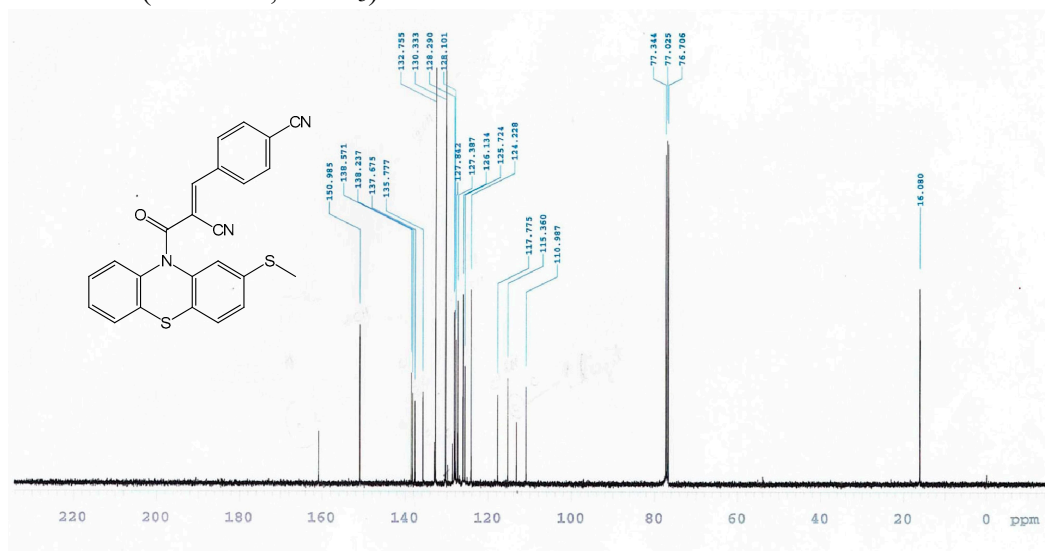
## IR-2b



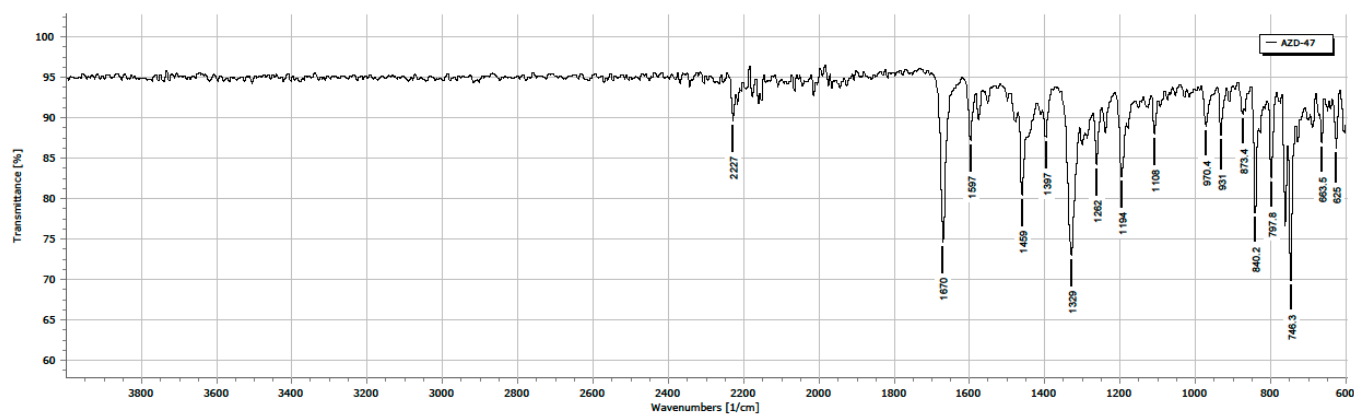
## <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)-2c



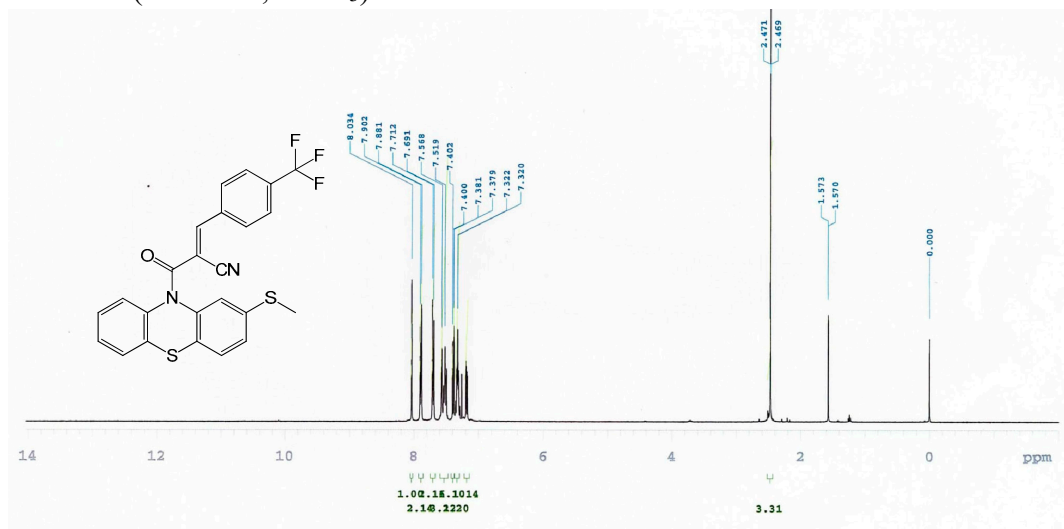
**$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )-2c**



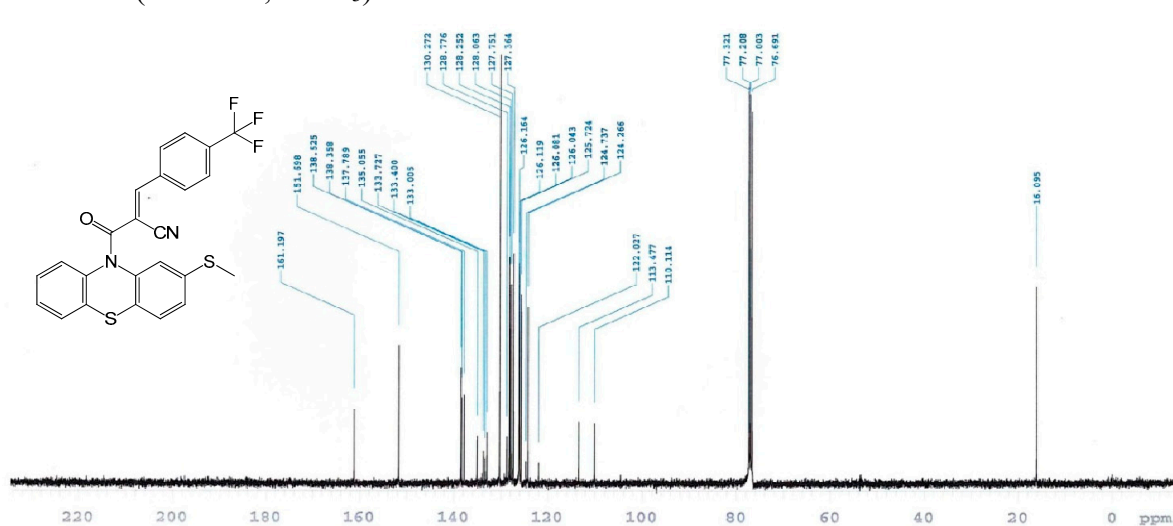
**IR-2c**



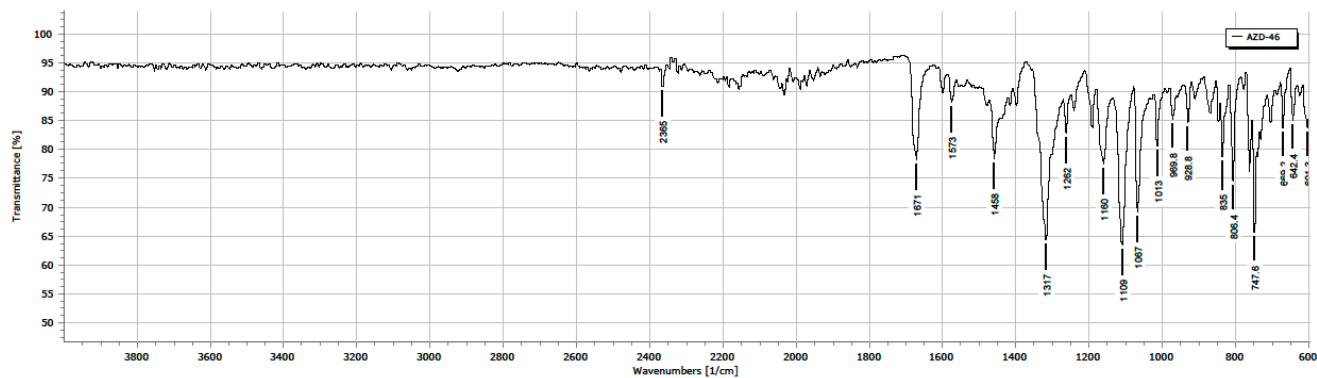
**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )-2d**



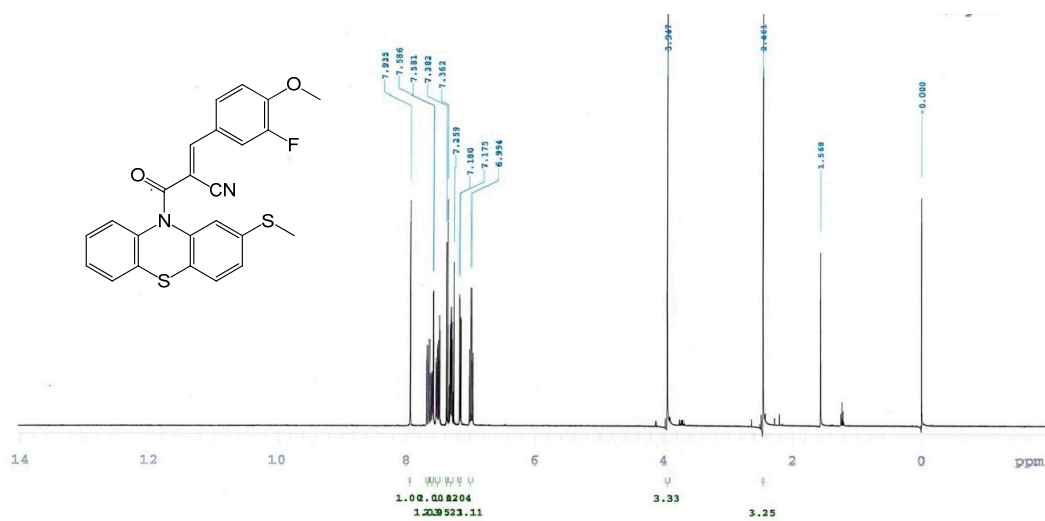
**$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )-2d**



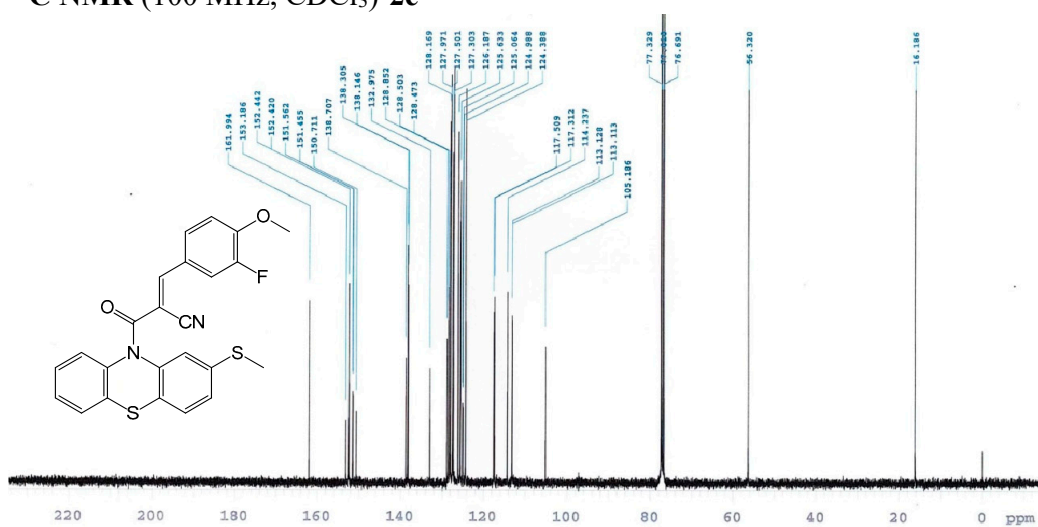
**IR-2d**



**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)-2e**

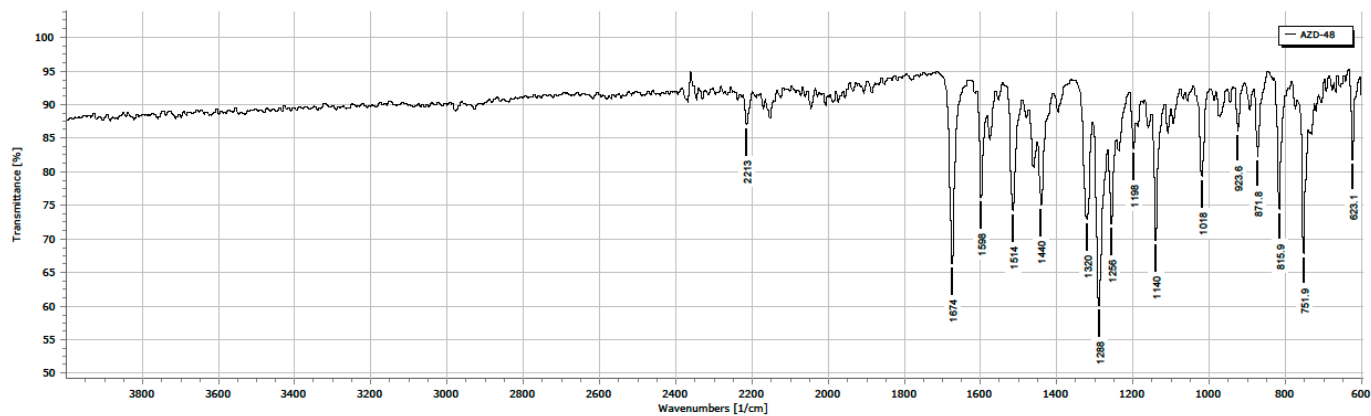


**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)-2e**



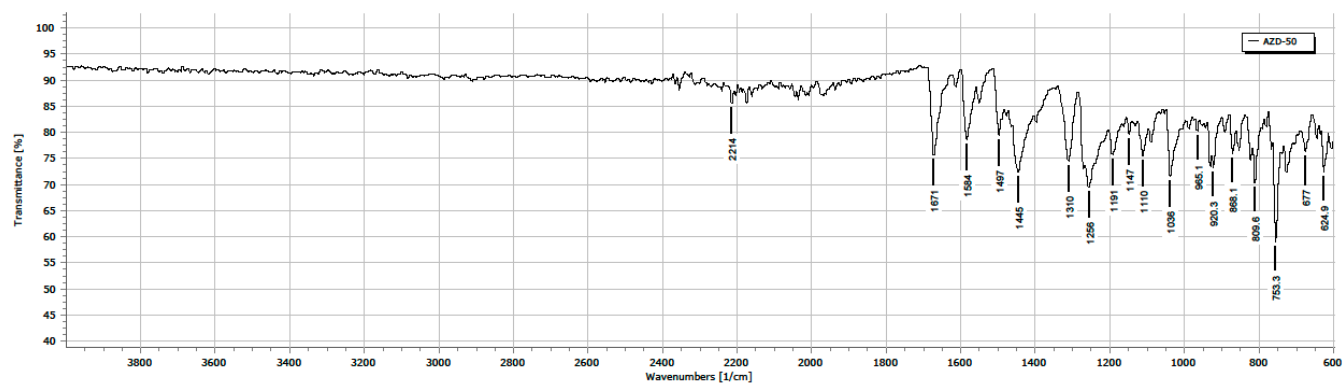


## IR-2e

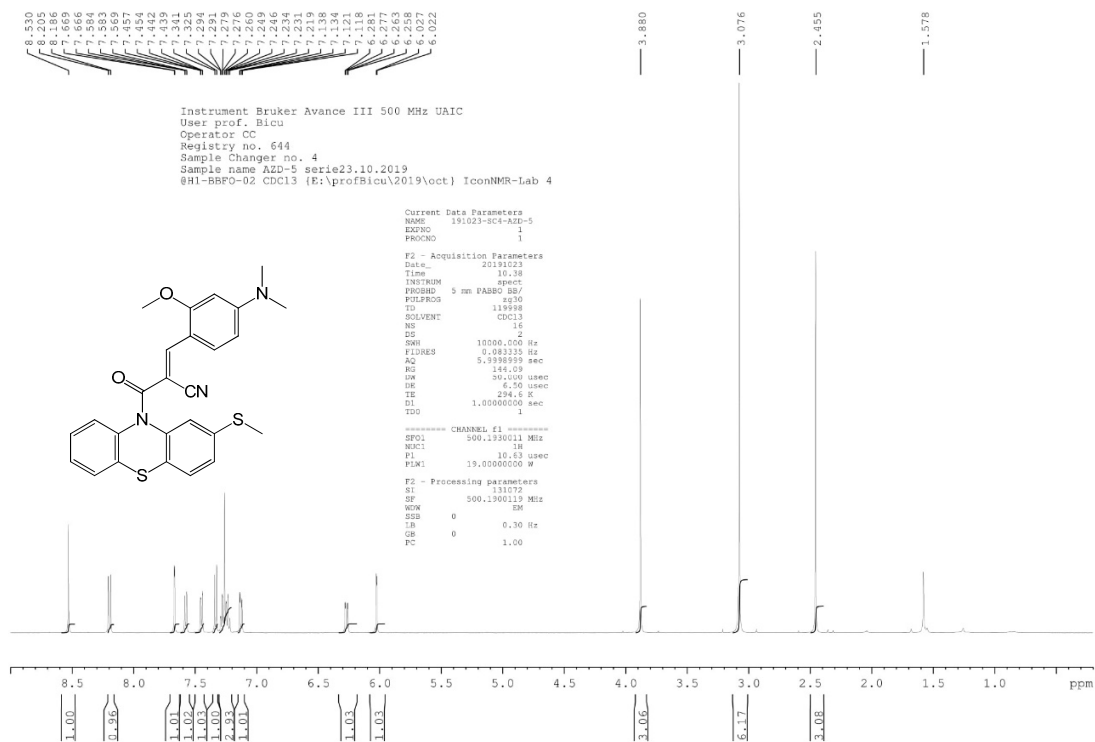




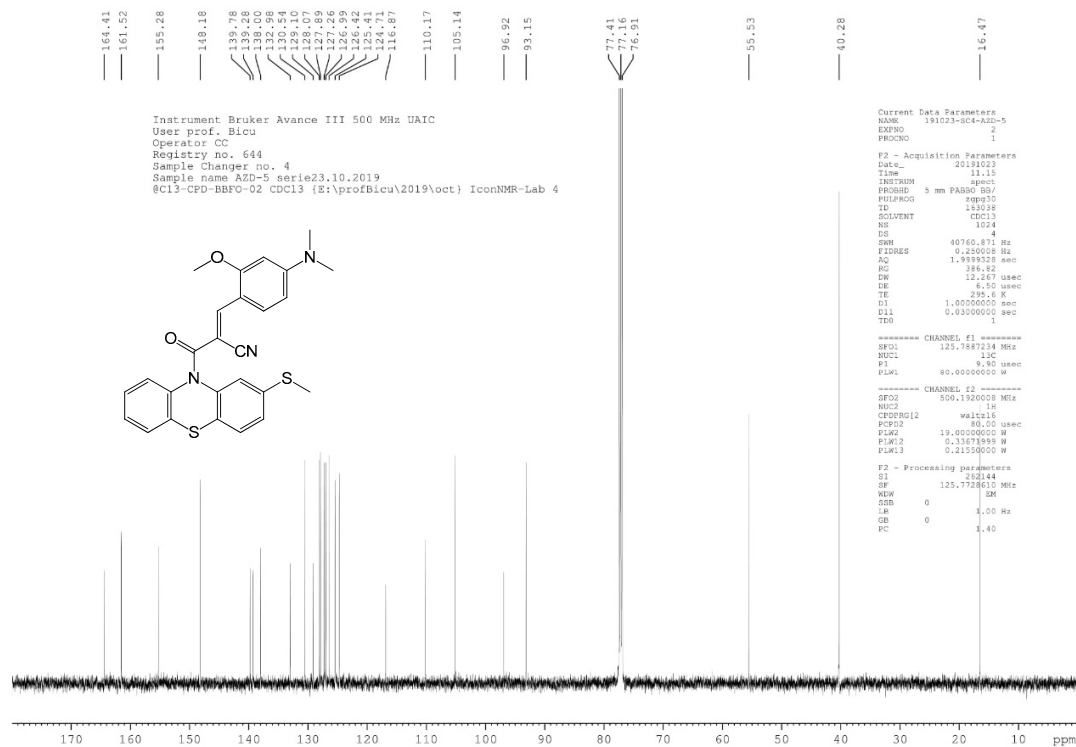
## IR-2f



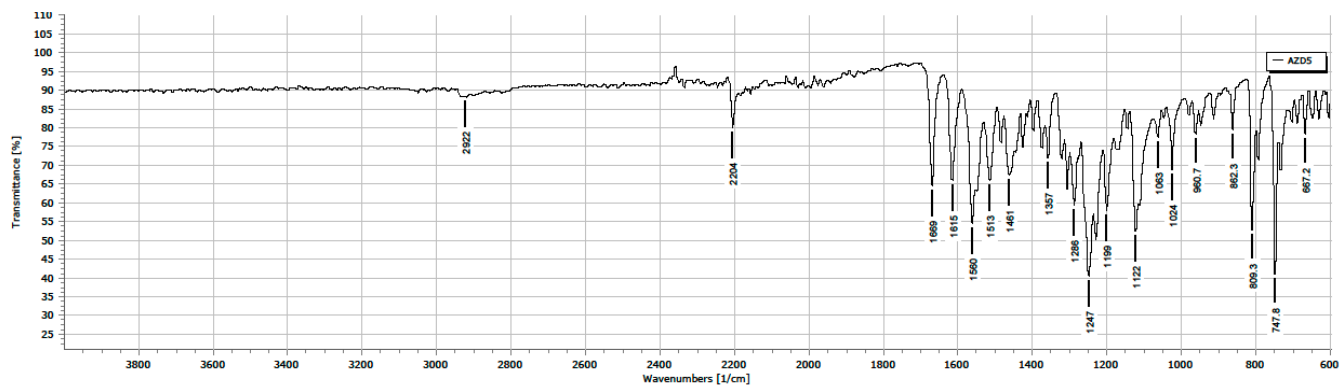
**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)- **2g**



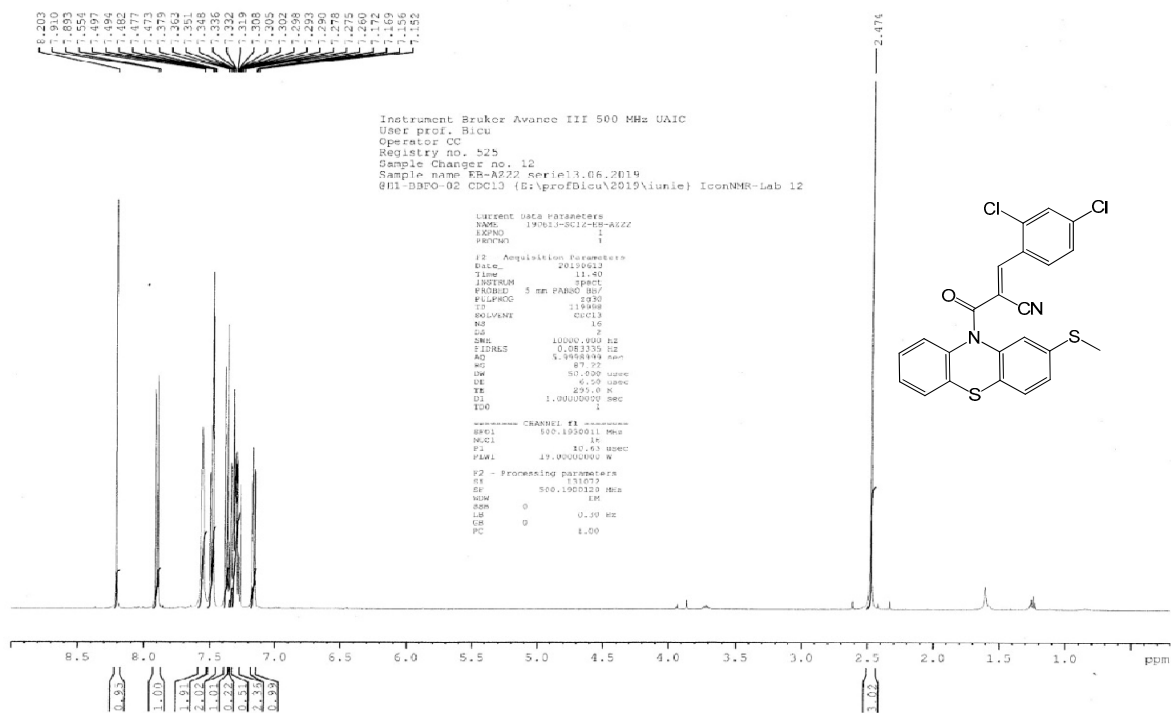
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-2g



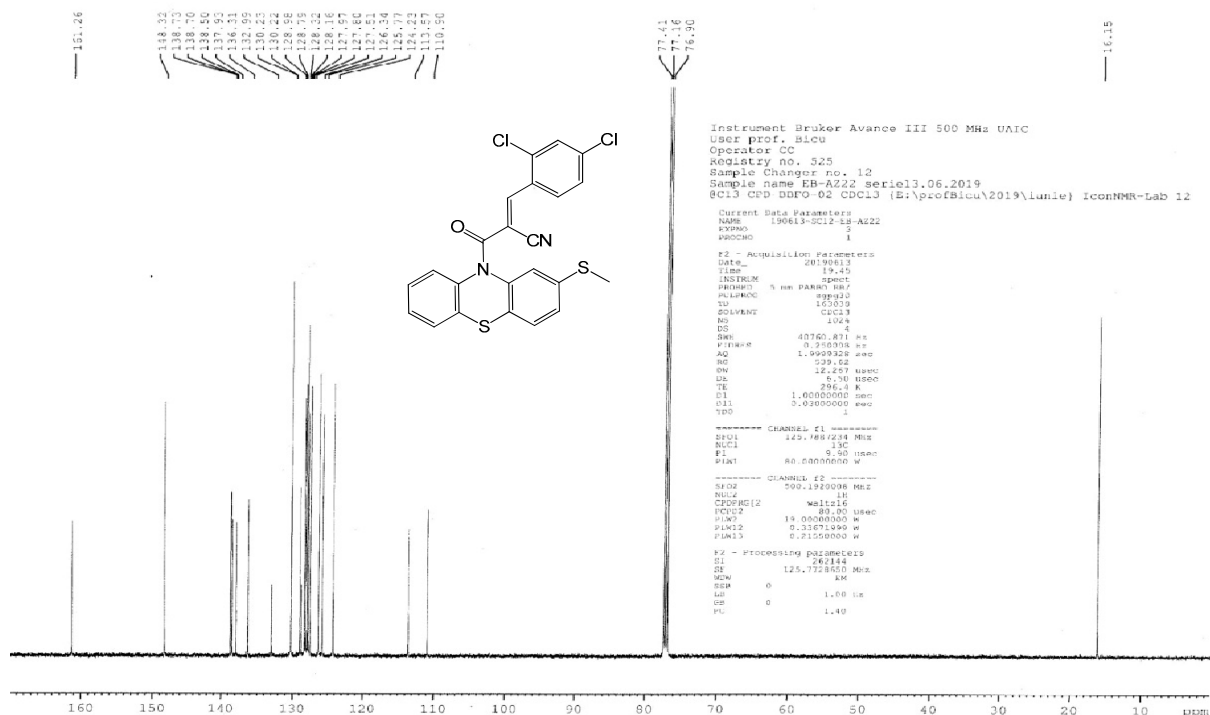
# IR-2g



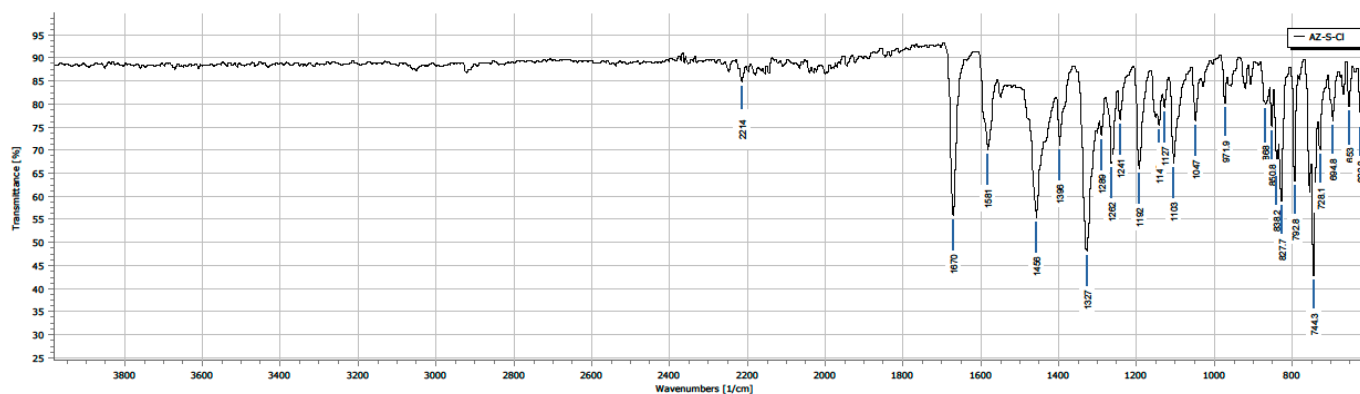
# <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-2h



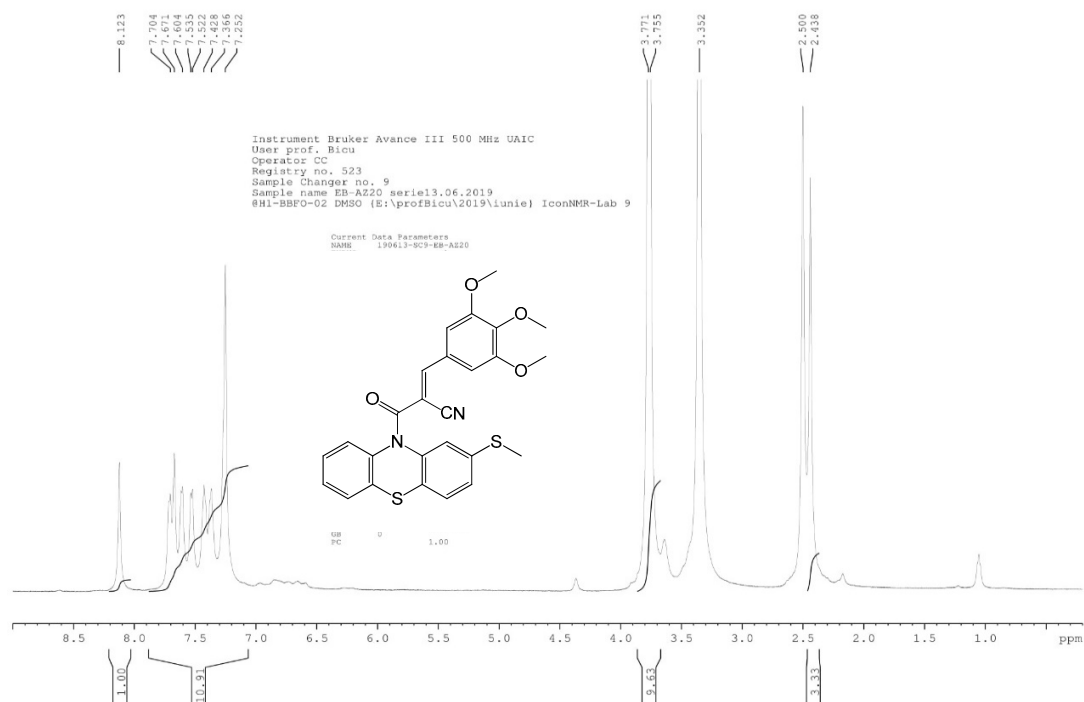
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-2h



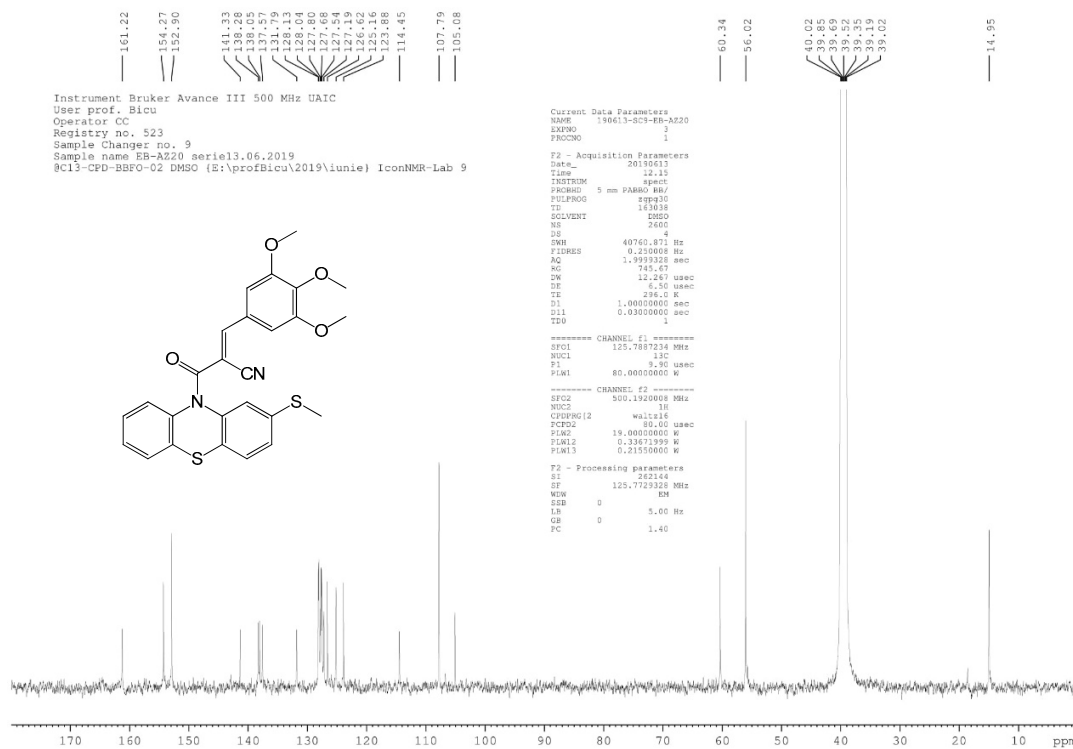
## IR-2h



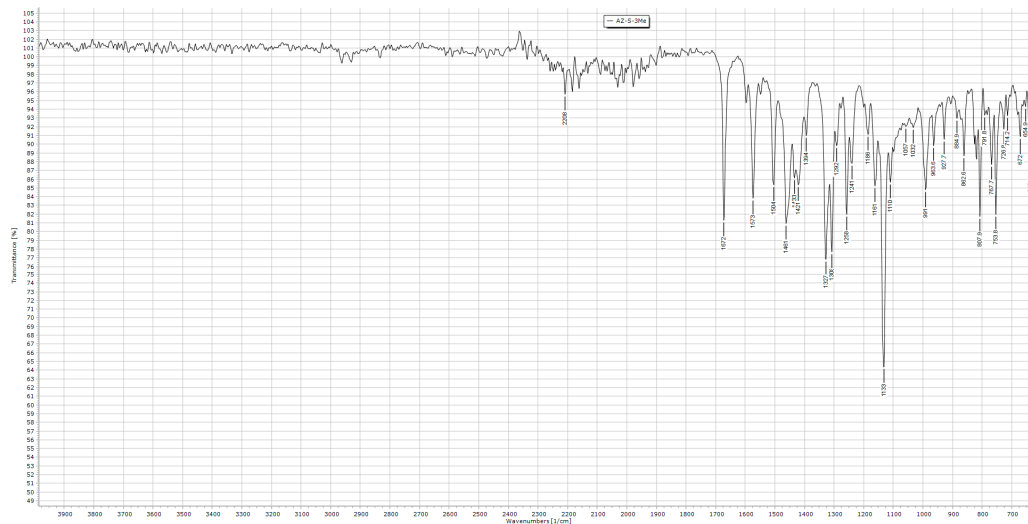
## <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-2i



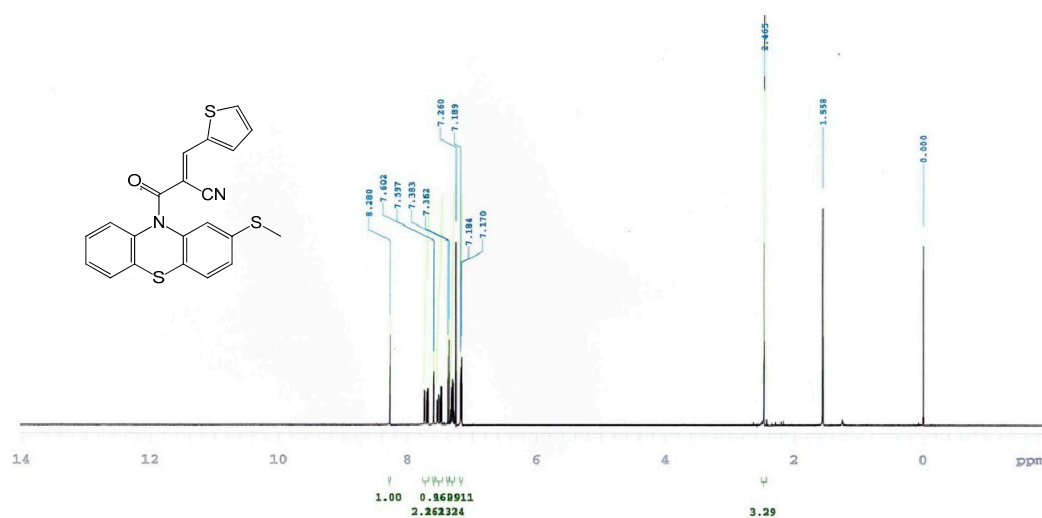
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-2i



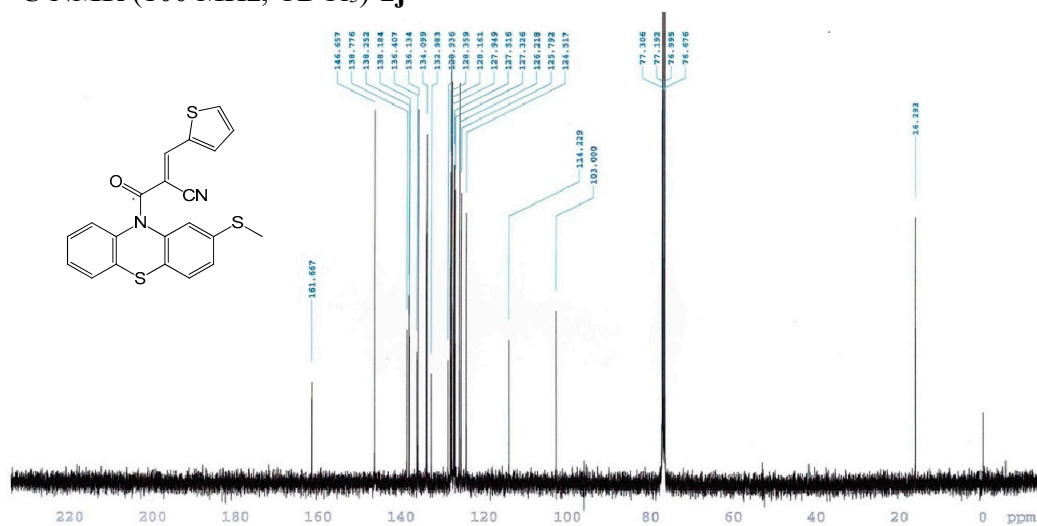
## IR-2i



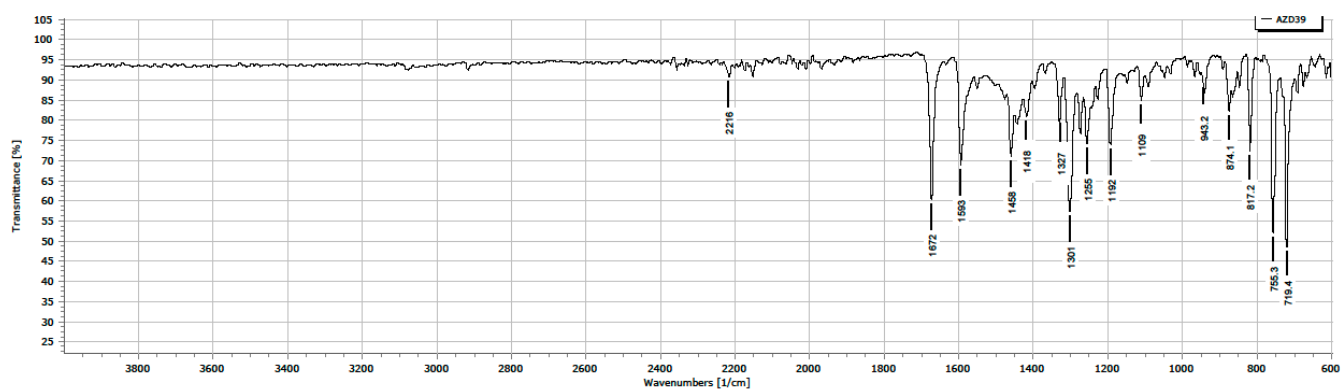
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)-2j**



**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)-2j**

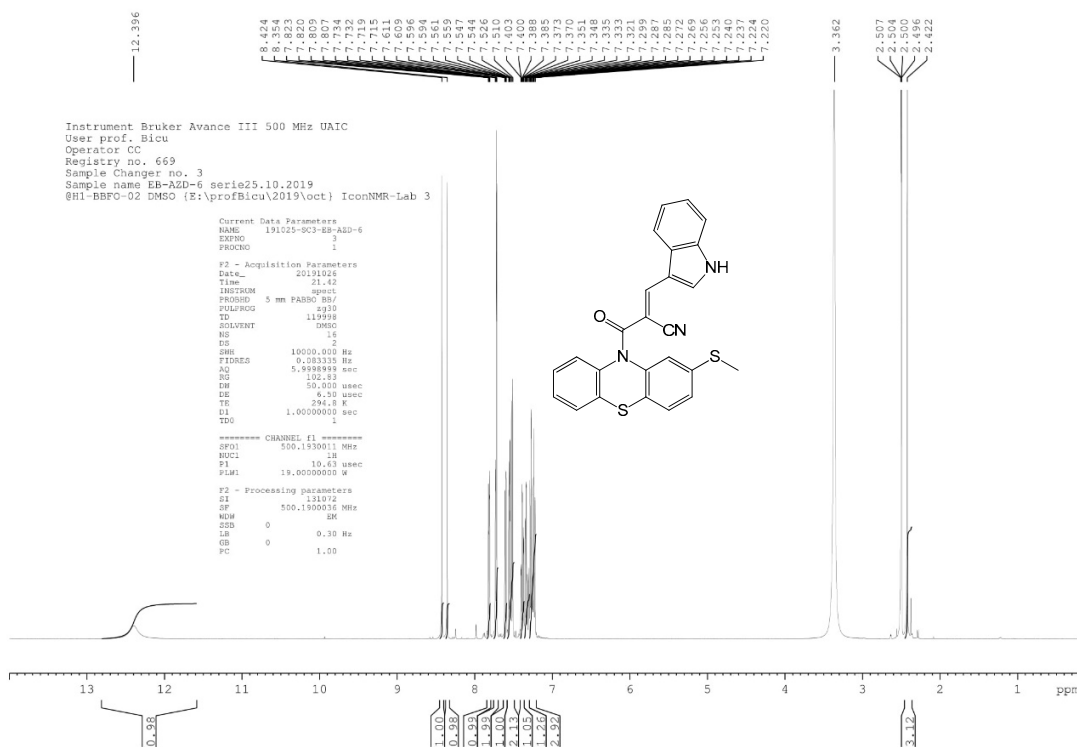


**IR-2j**

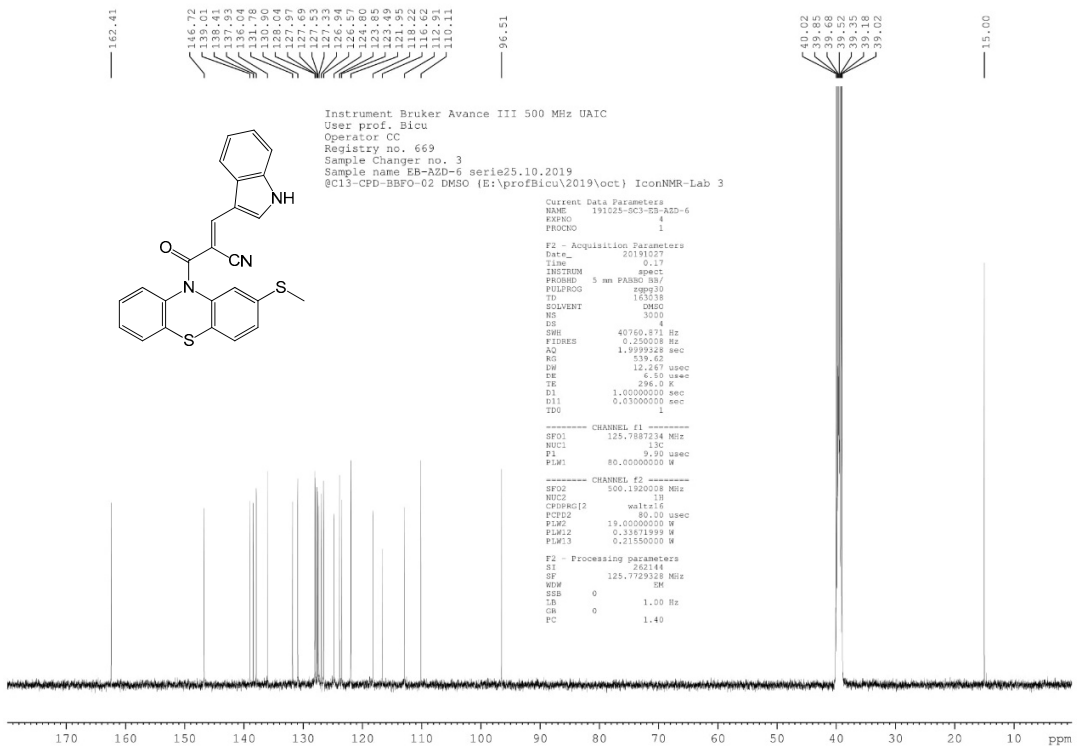


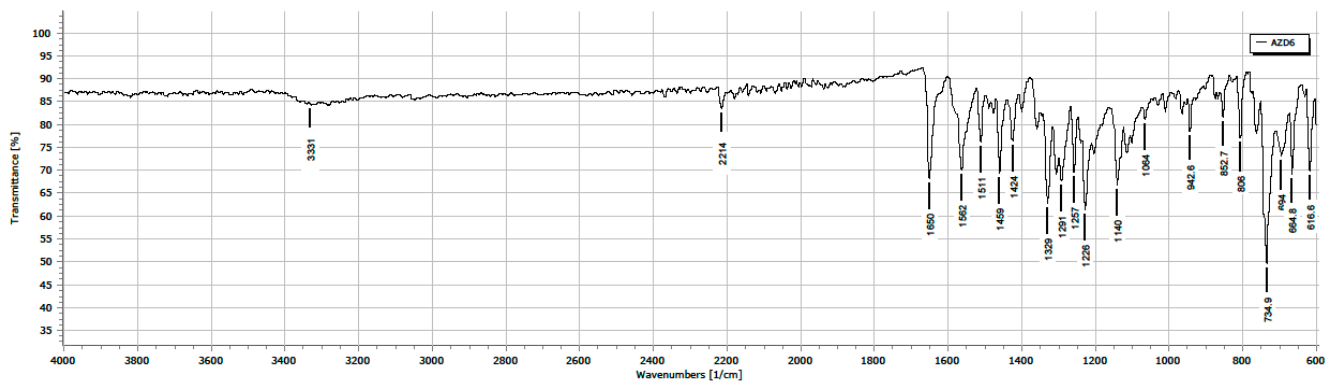


# <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)- 2k

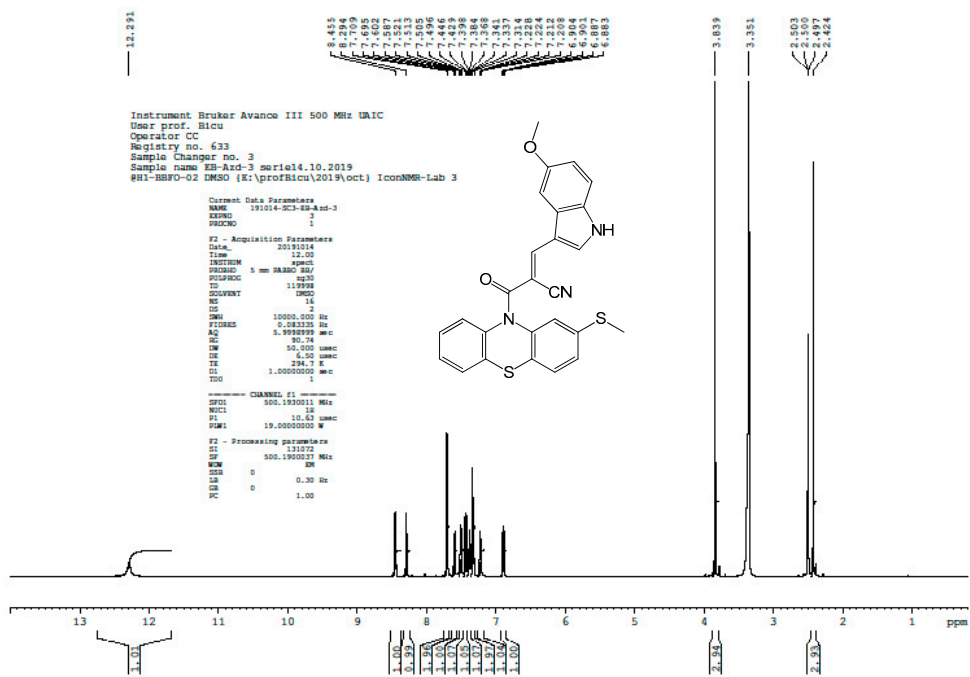


# <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>)-2k

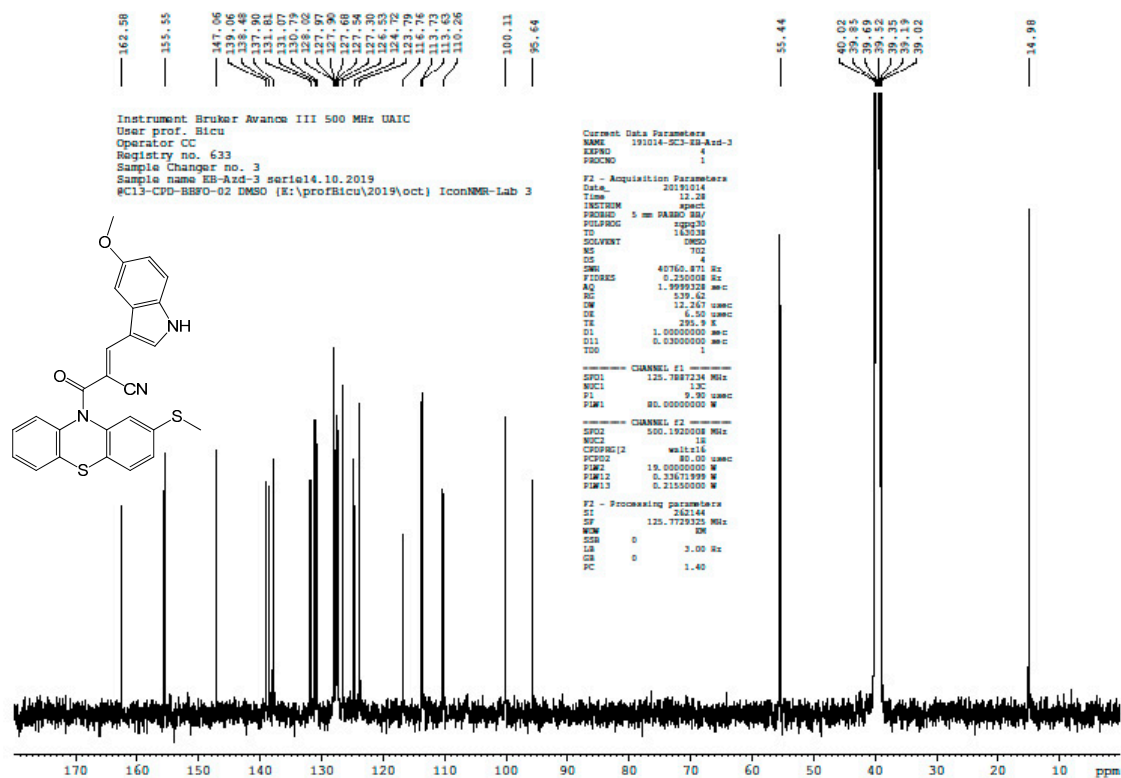


**IR-2k**

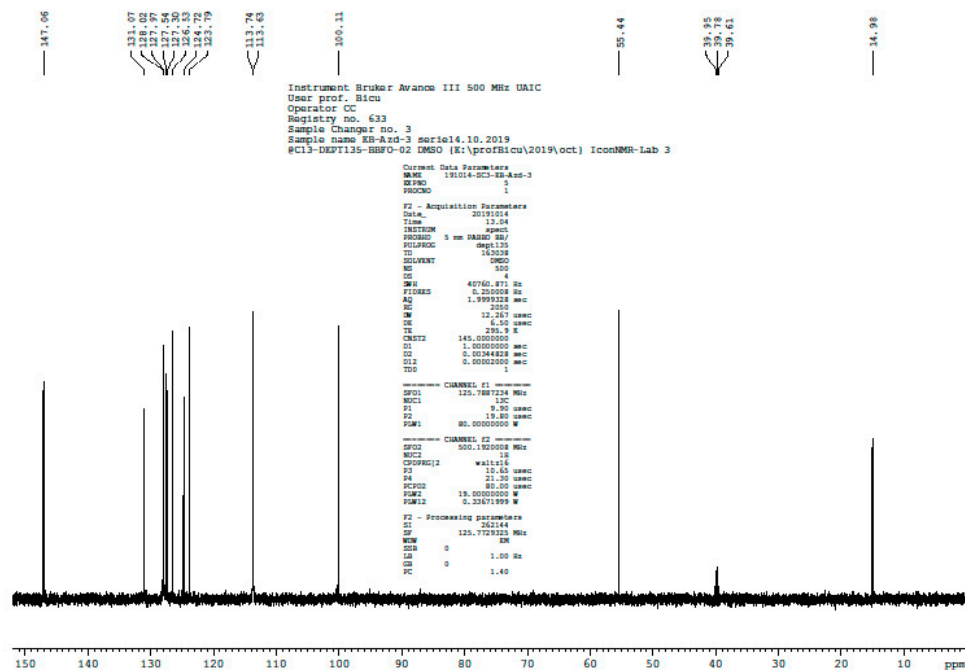
**<sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)- 2l**



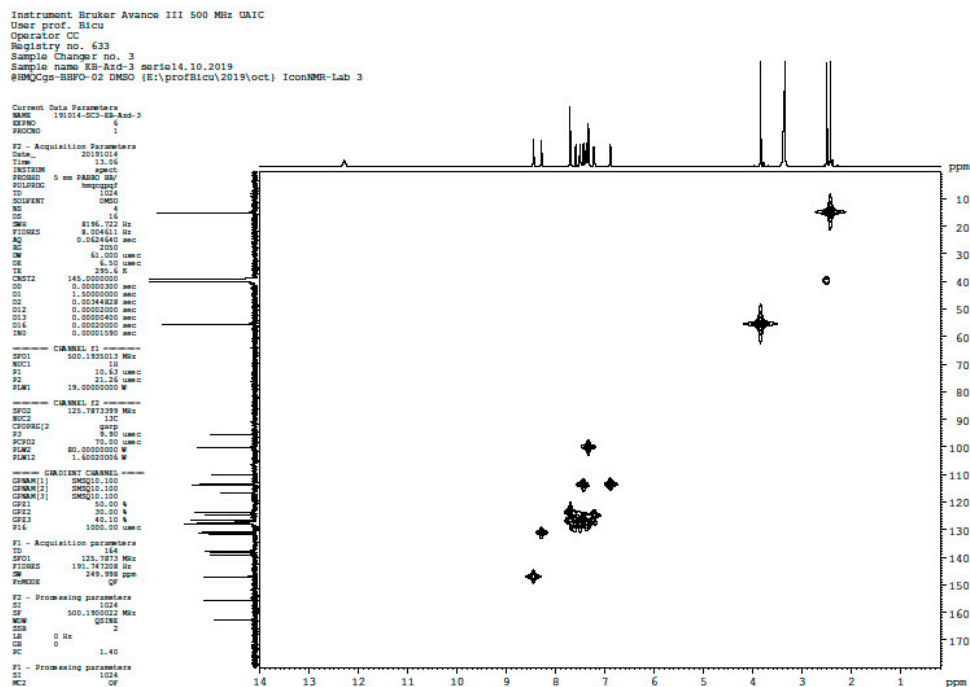
**$^{13}\text{C}$  NMR (125 MHz, DMSO- $d_6$ )-2I**



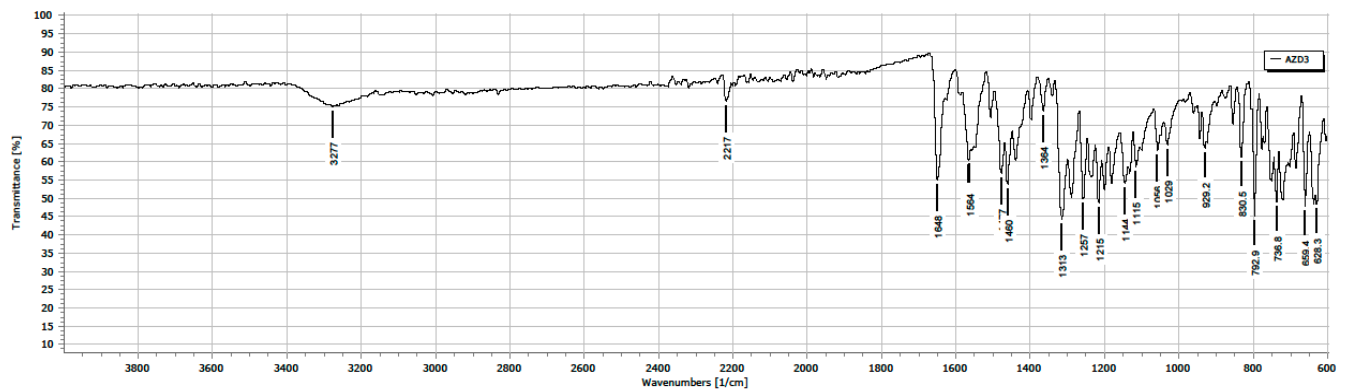
# <sup>13</sup>C-DEPT NMR (125 MHz, DMSO-*d*<sub>6</sub>)-2I



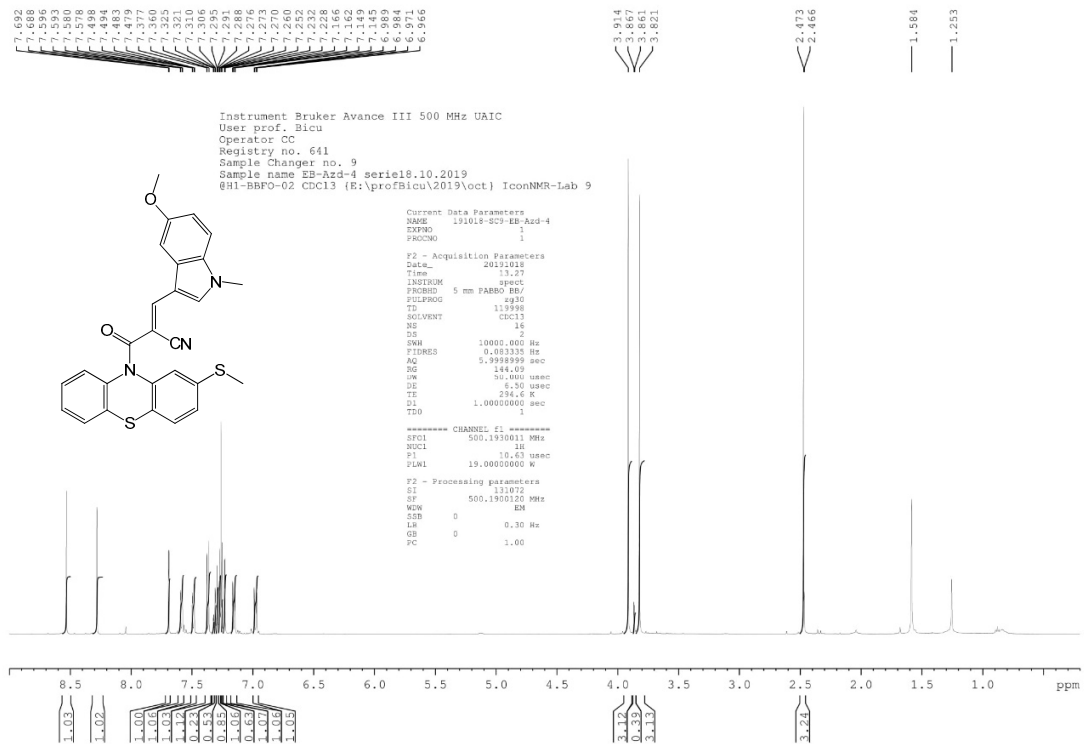
# HMQC NMR (500 MHz, DMSO-*d*<sub>6</sub>)-2I



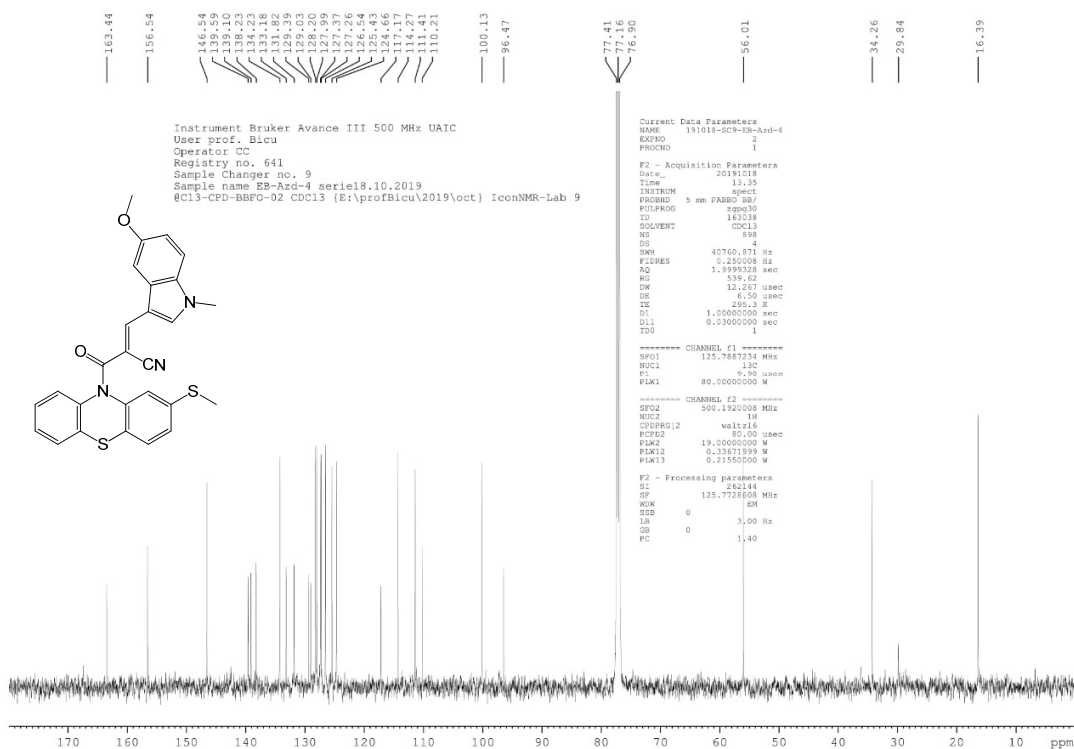
## IR-21



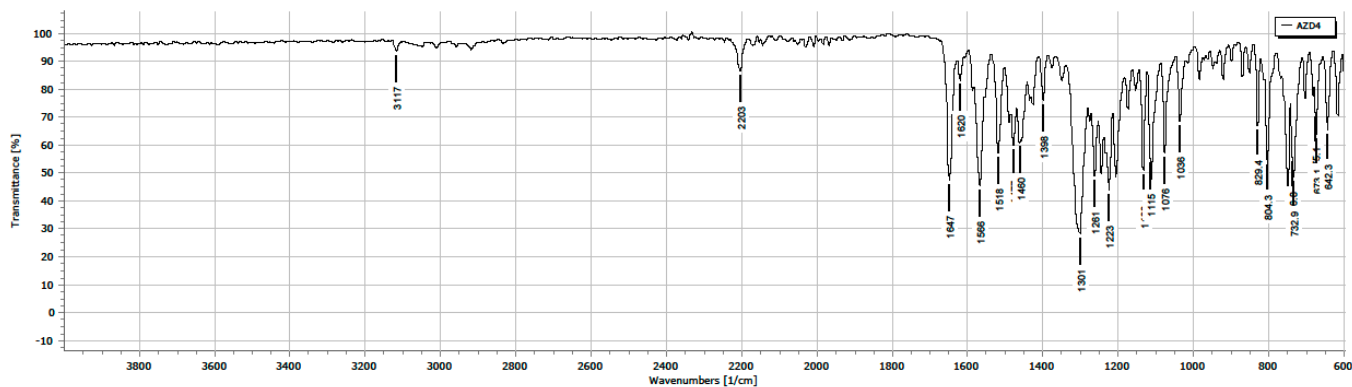
## <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)- 2m



# <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>)-2m



## IR-2m



Chemical structure of compound 15: COc1ccc2c(c1)c(c3ccccc3n2C(=O)c4ccc(C#N)cc4)S

<sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) of compound 15. The spectrum shows peaks from 1.5 to 8.5 ppm. Integration values are provided below the baseline: 1.00, 1.03, 1.08, 0.98, 1.03, 2.03, 2.03, 1.06, 1.08, 3.05, 3.09, and 2.495.

Chemical structure of compound 15 is shown on the right.

Cc1ccc2sc(n(c2c3ccccc3)C(=O)c4cncc5ccccc45)c1

**Instrument Bruker Avance III 500 MHz UAIC**

User prof. Bicu  
Operator CC  
Registry no. 788  
Sample Changer no. 10  
Sample name EB-AZD-15 serie25.11.2019  
@Cl3-CPD-BBFO-02 CDCl3 (E:\prof\Bicu\2019\nov) IconNMR-Lab 10

F2 - Acquisition Parameters	
Date_	20191125
Time	12.24
INSTRUM	spect
PQCHBG	5 mm PARBO BB
PULPROG	zgpg30
TD	16384
SOLVENT	CDCL3
NS	3024
DS	4
SWH	40760.871 Hz
FIDRES	0.230068 Hz
AQ	1.9999328 sec
RG	519.62
DW	15.267 usec
DE	6.50 usec
TE	300.2 K
D1	1.0000000 sec
d11	0.0300000 sec
TDO	1

----- CHANNEL f1 -----	
SFO1	125.7687234 MHz
NUC1	13C
P1	5.50 usec
PLA1	80.0000000 W

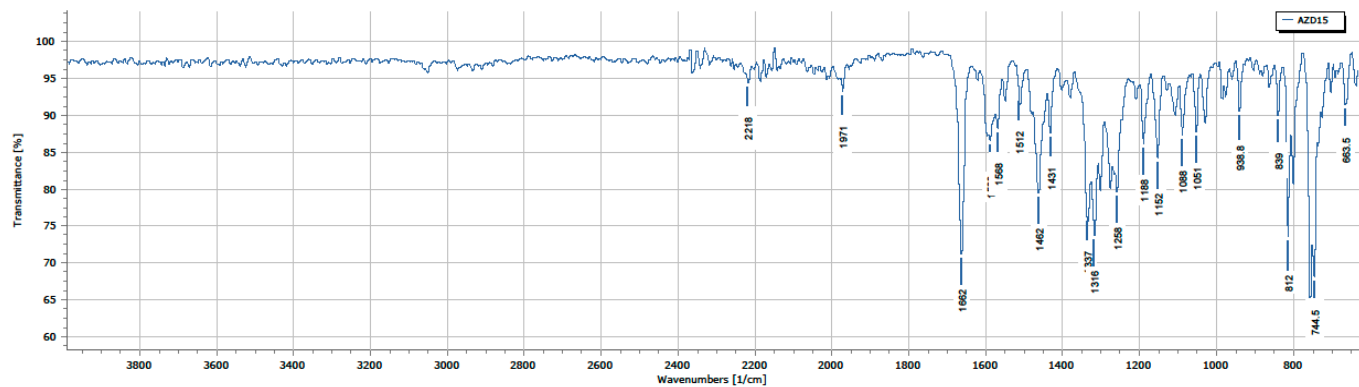
  

===== CHANNEL f2 =====	
SFO2	500.1920008 MHz
NUC2	1H
PCPRG12	waltz16
KPCPD	16.00 usec
PLM2	19.0000000 W
PLM12	0.33671999 W
PLM13	0.21350000 W

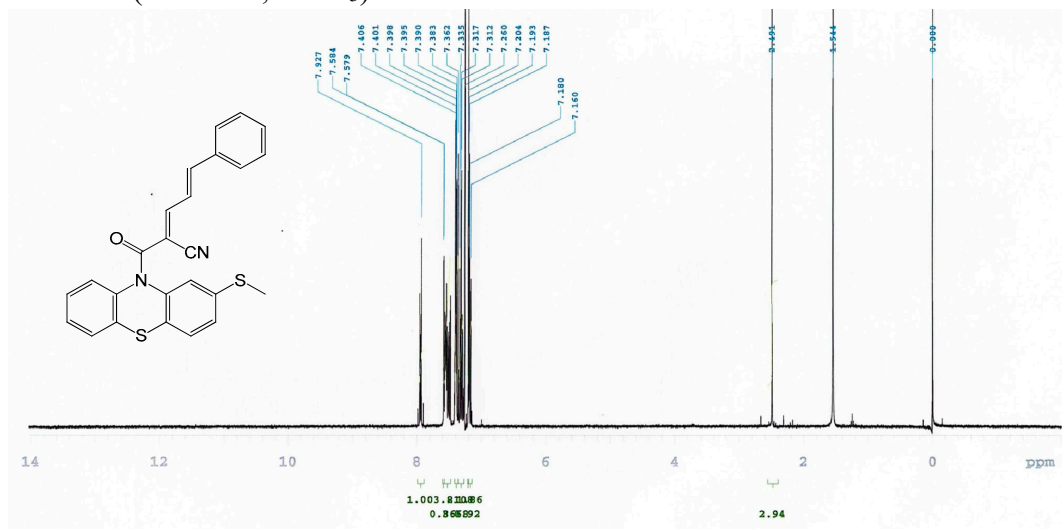
F2 - Processing parameters	
SF	262144
ST	125.7728616 MHz
MGN	EM
SGB	0
LH	1.00 Hz
GB	0
PC	1.60

IR-2n

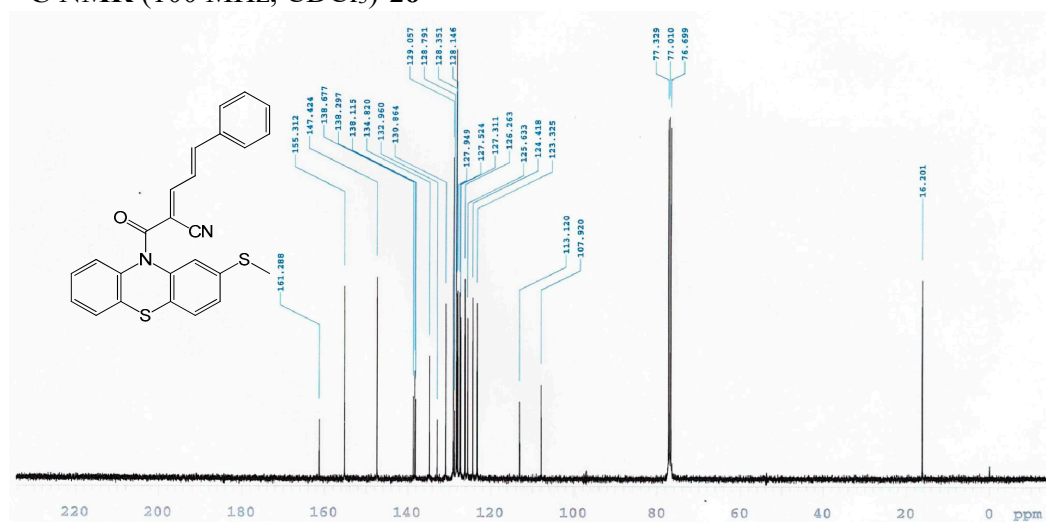




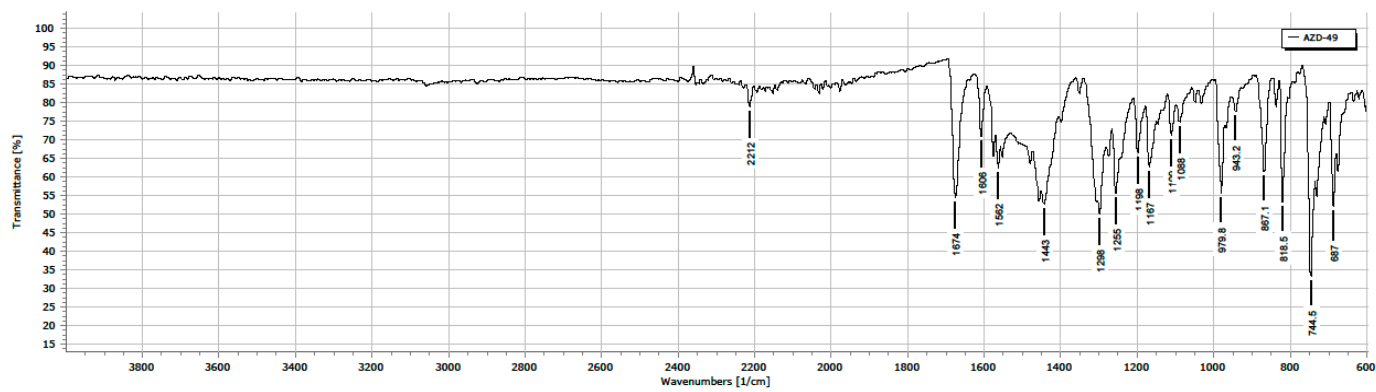
**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )-2o**



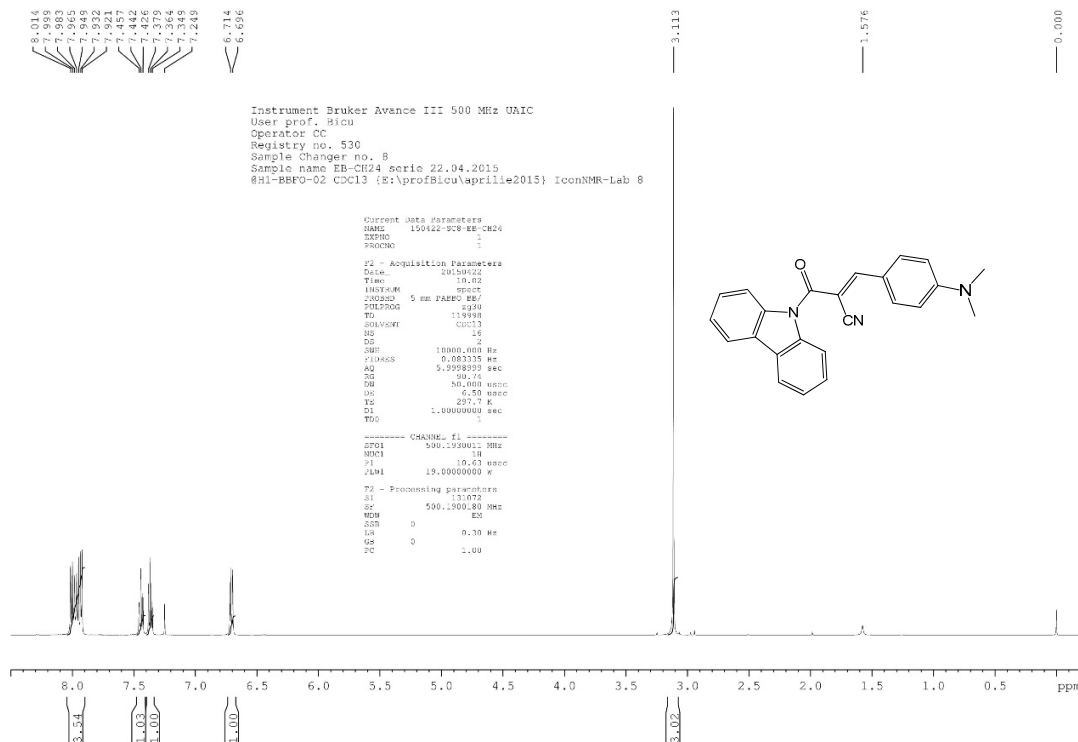
**$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )-2o**



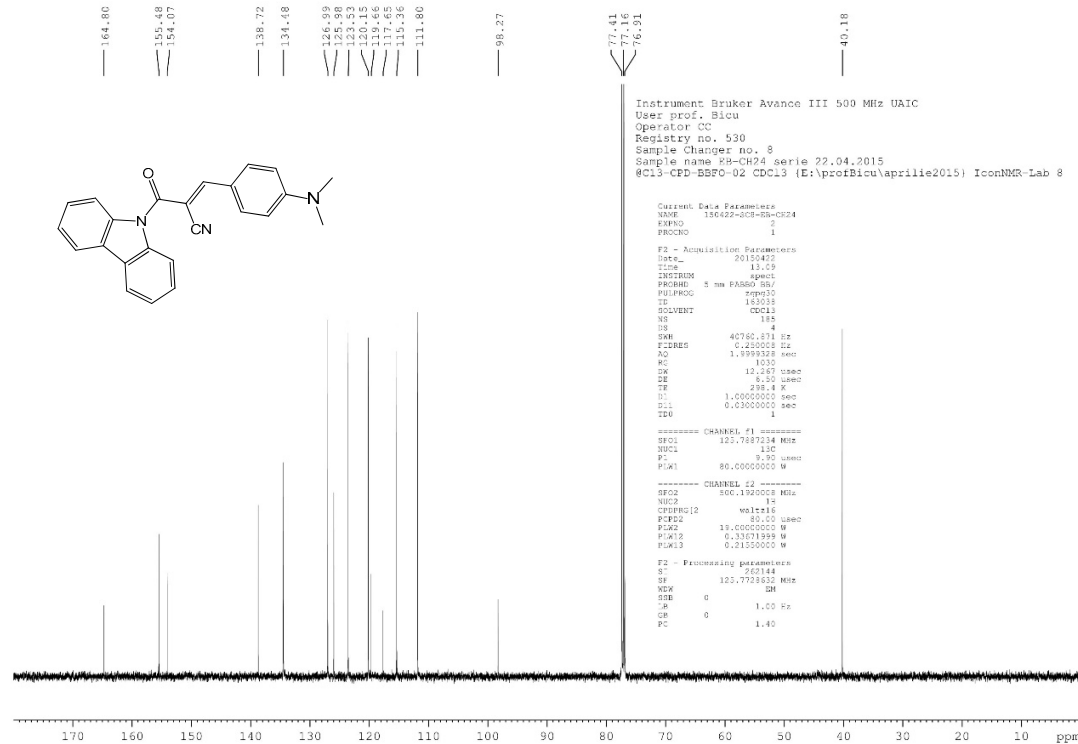
**IR-2o**



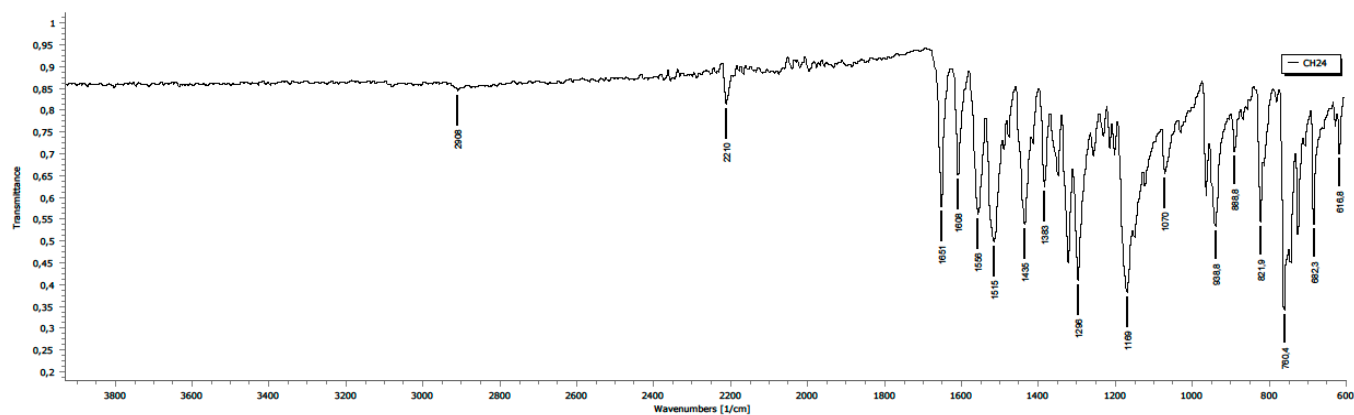
# <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)- **3a**



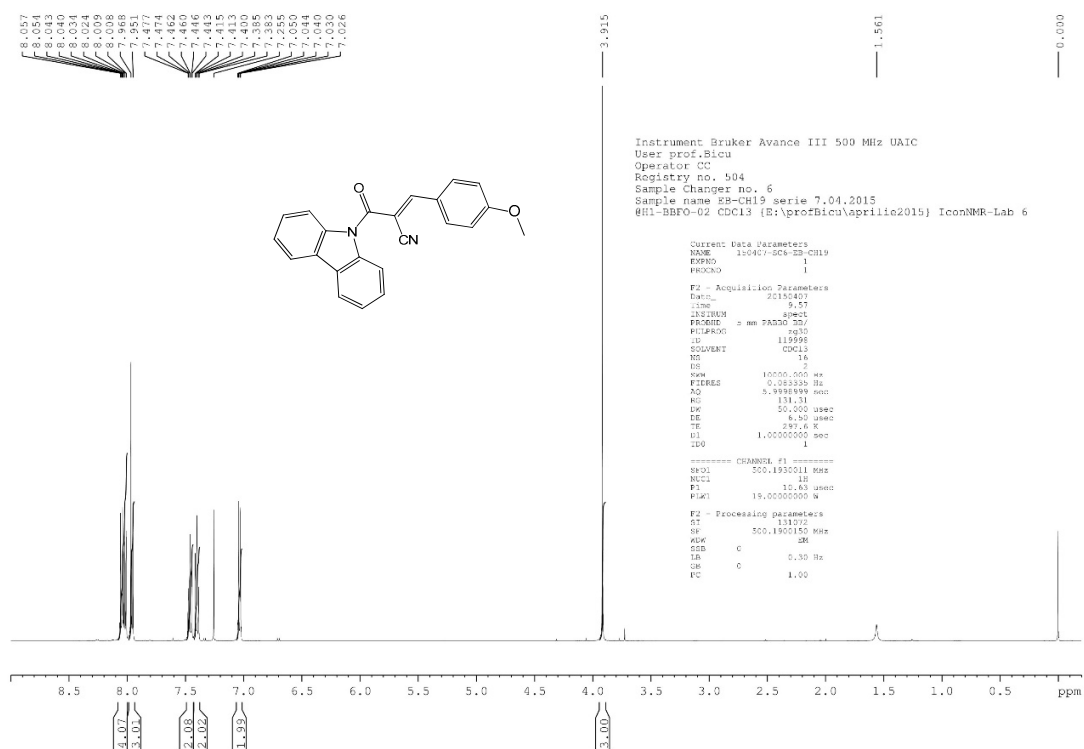
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)- **3a**



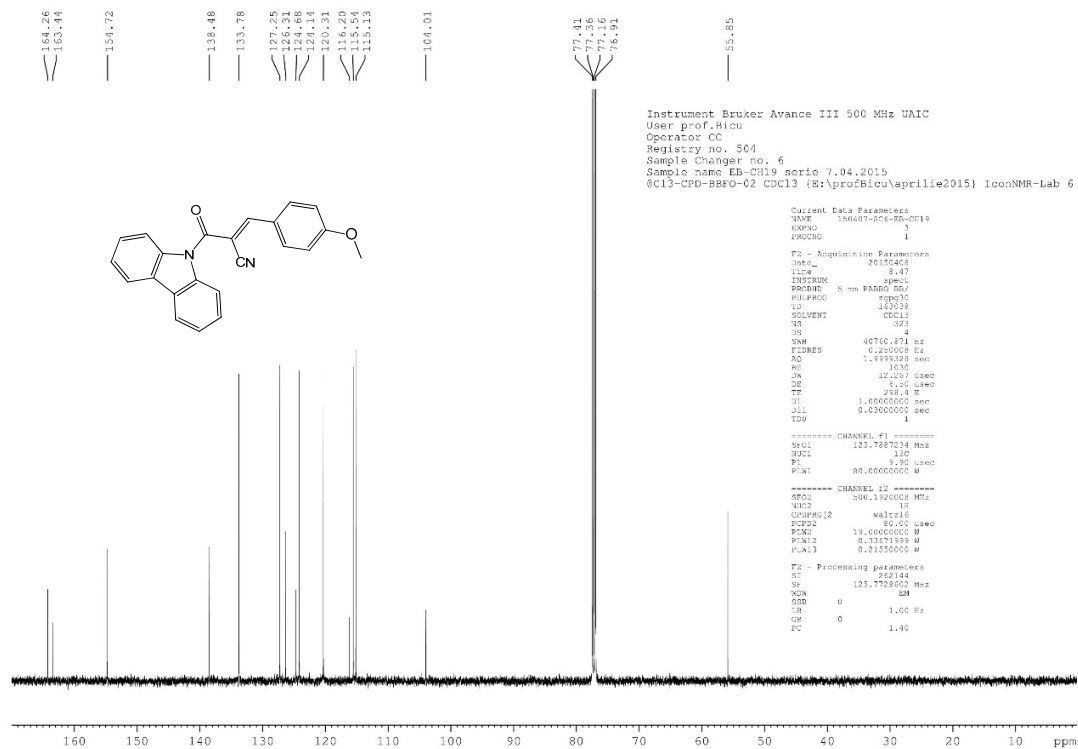
## IR-3a



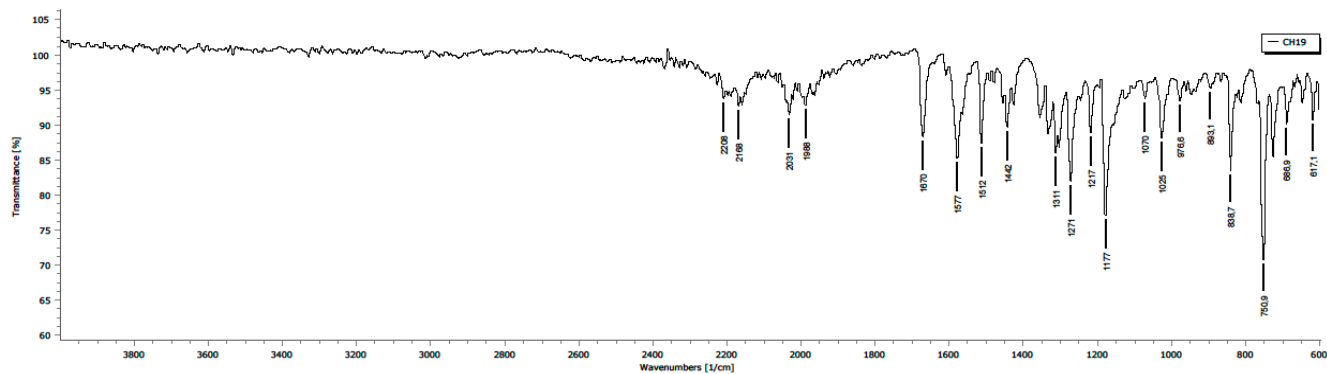
## <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-3b

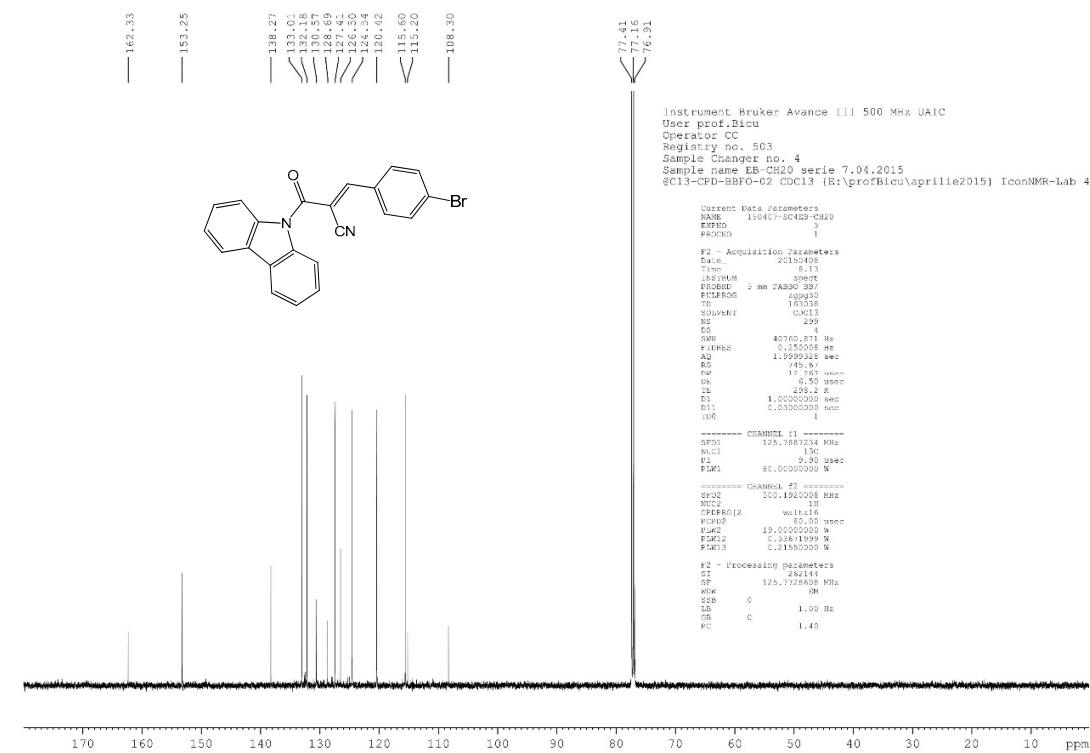
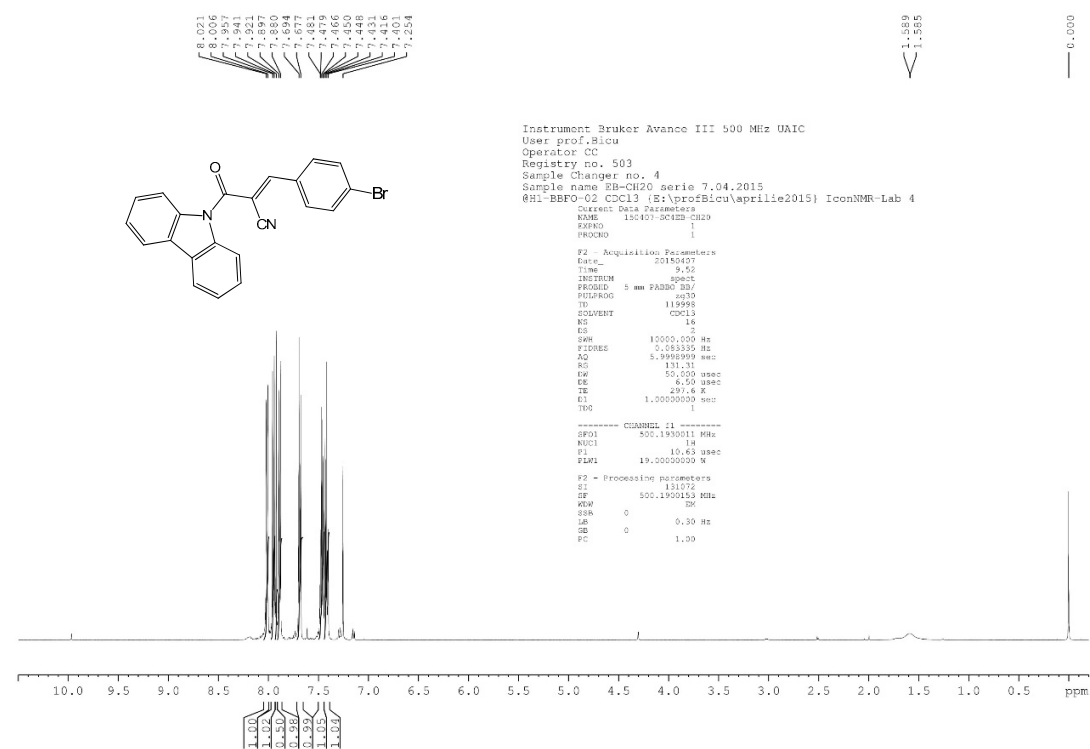


# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-3b

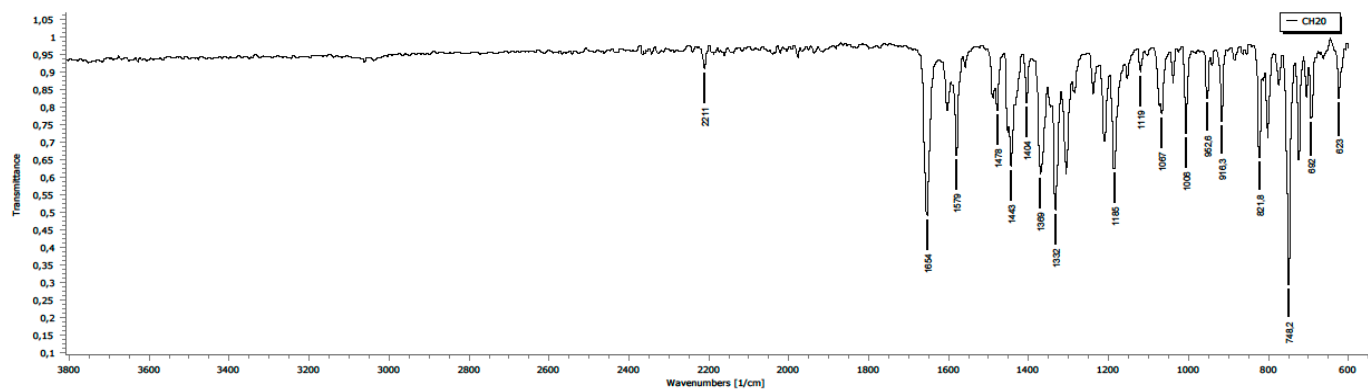


## IR-3b

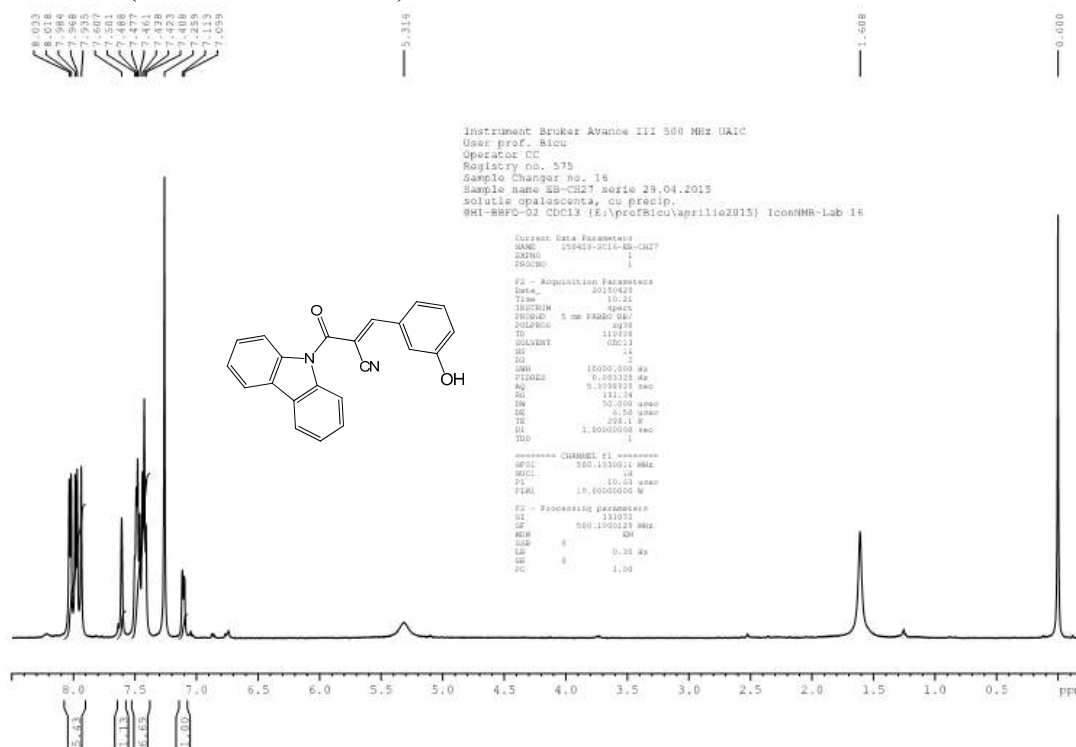




## IR-3c

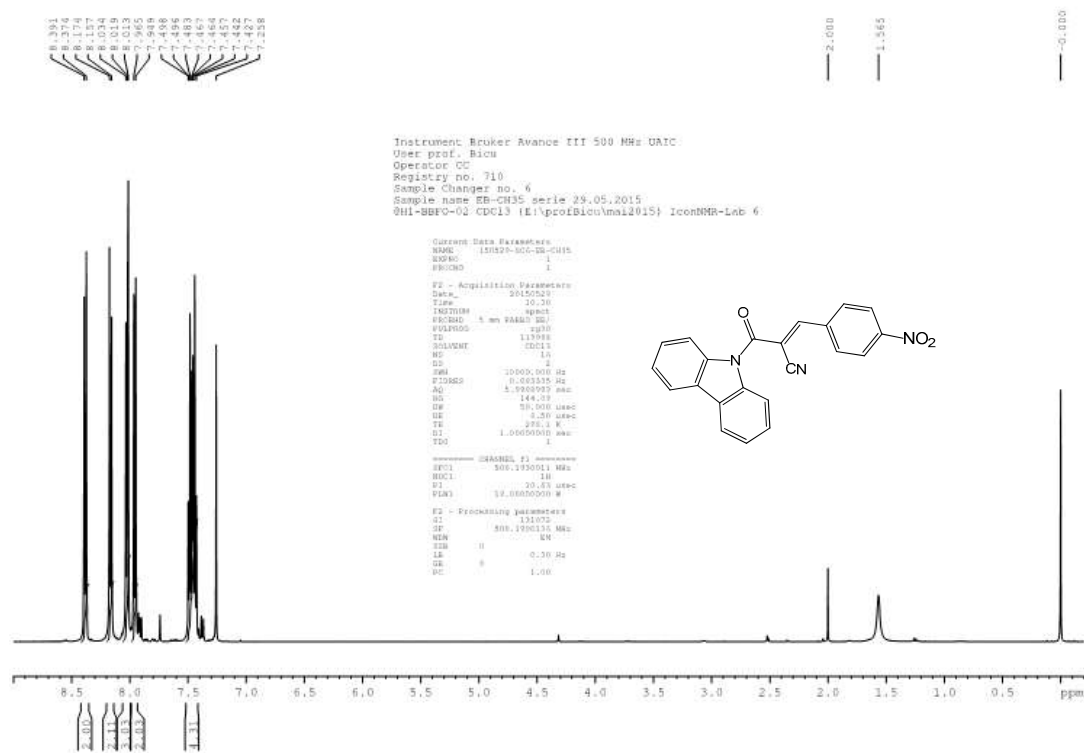


## <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)-3d

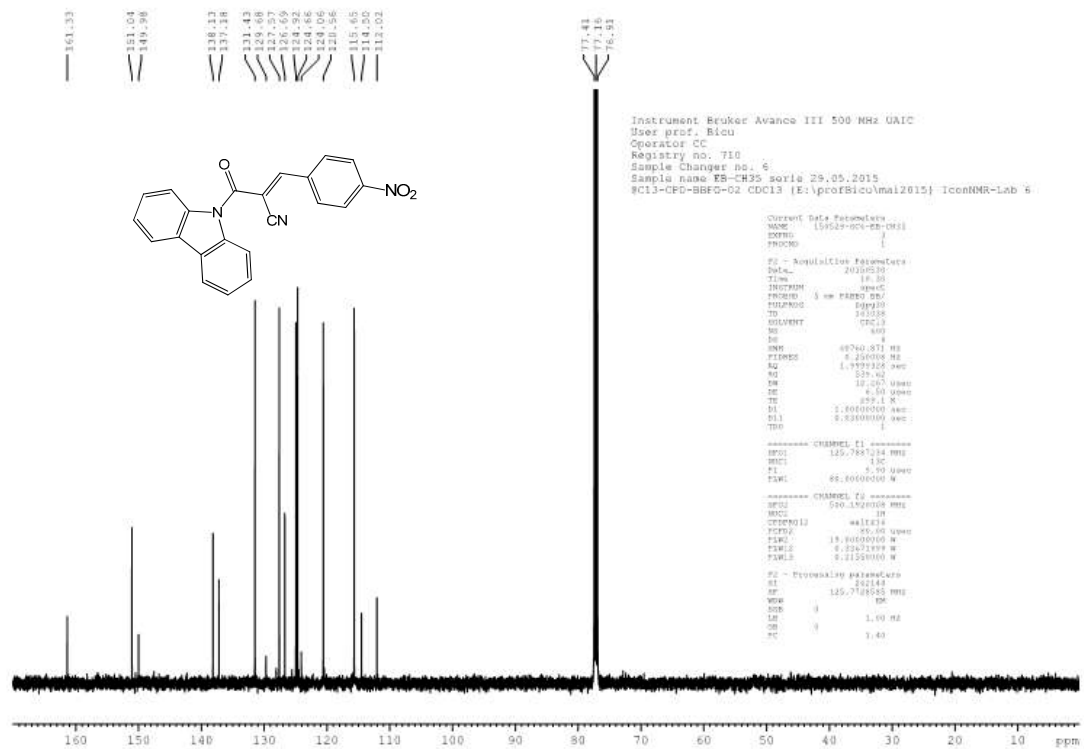


## <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>)-3d



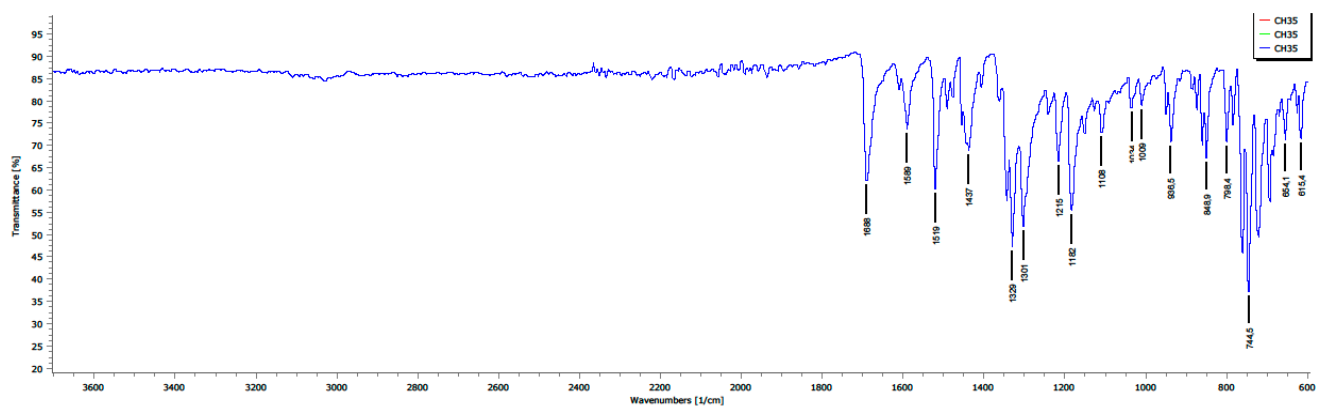


### <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-3e

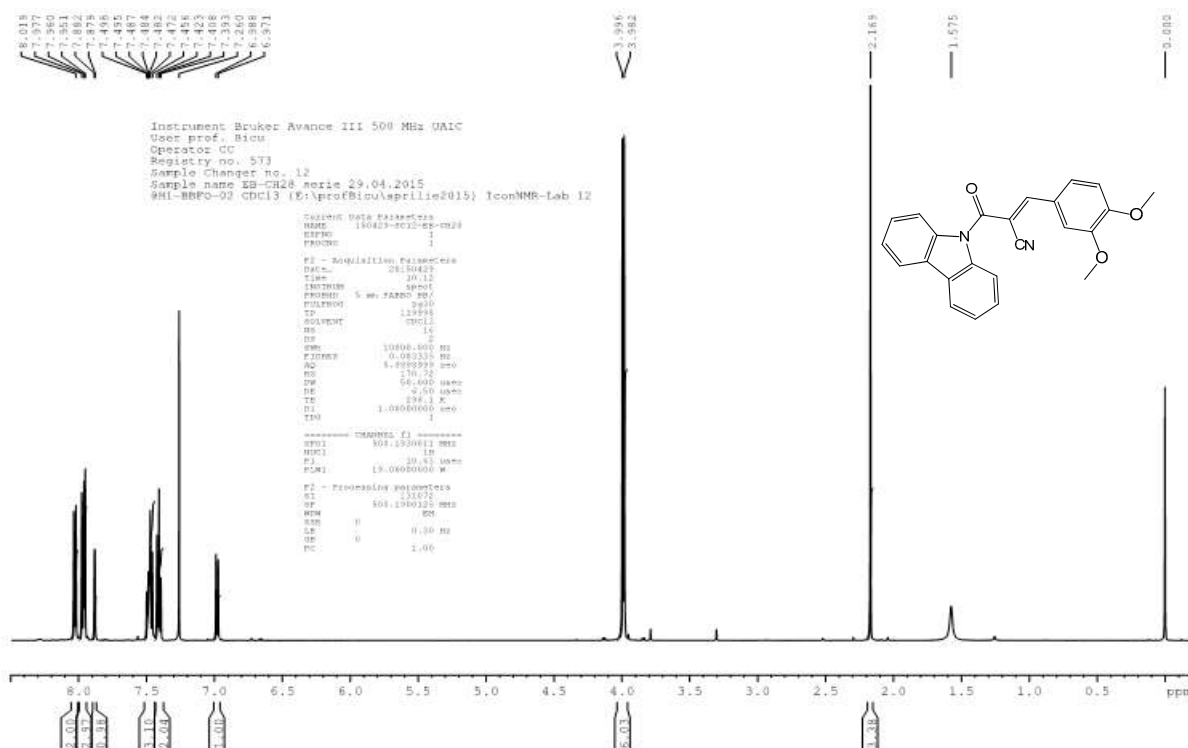




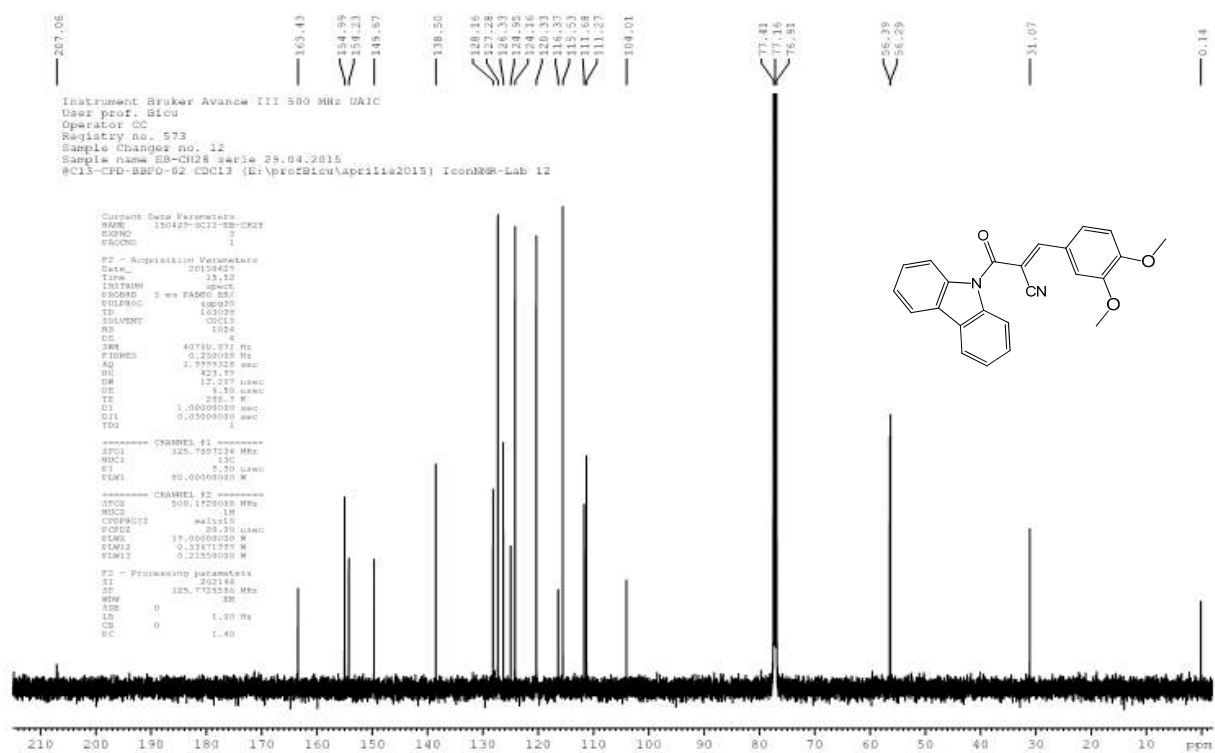
**IR-3e**



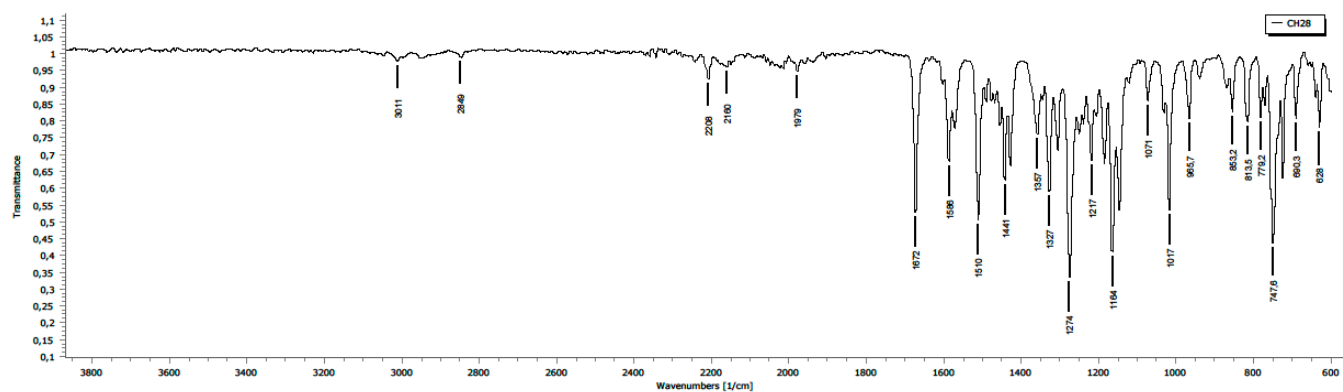
**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-3f**



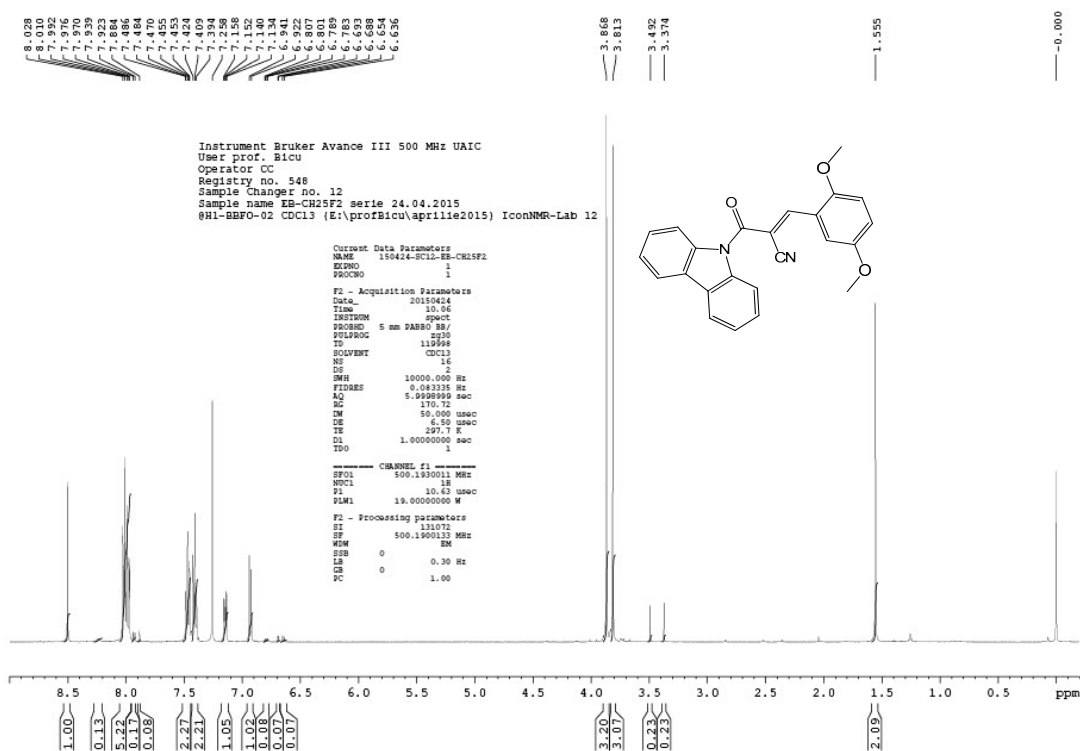
**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-3f**



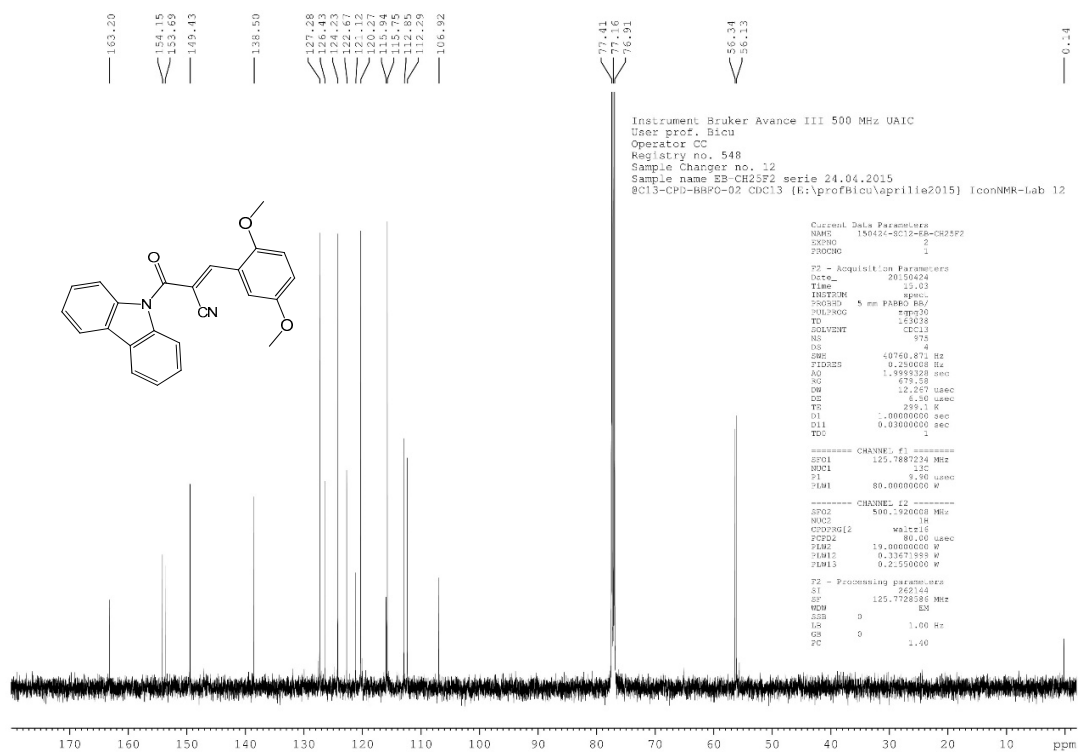
## IR-3f



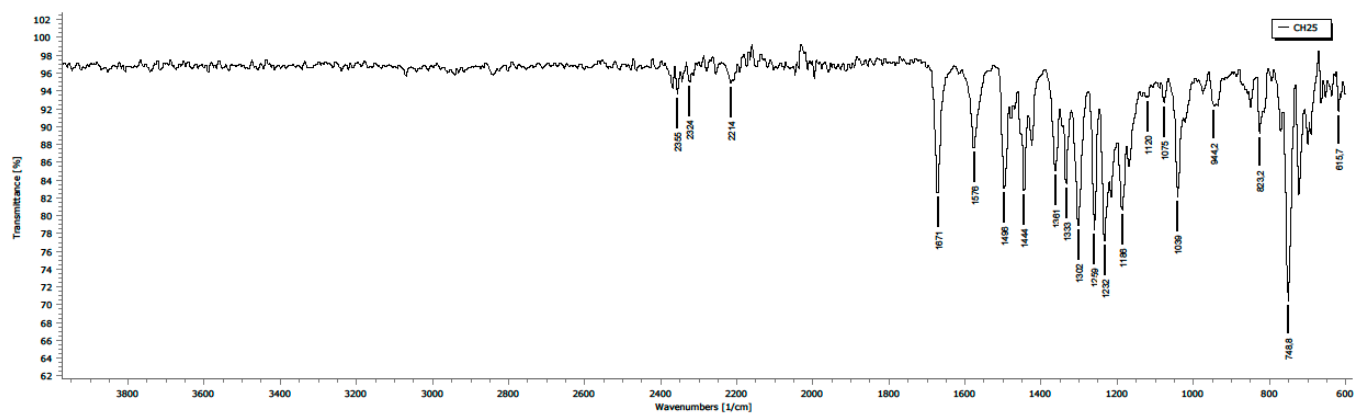
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-3g



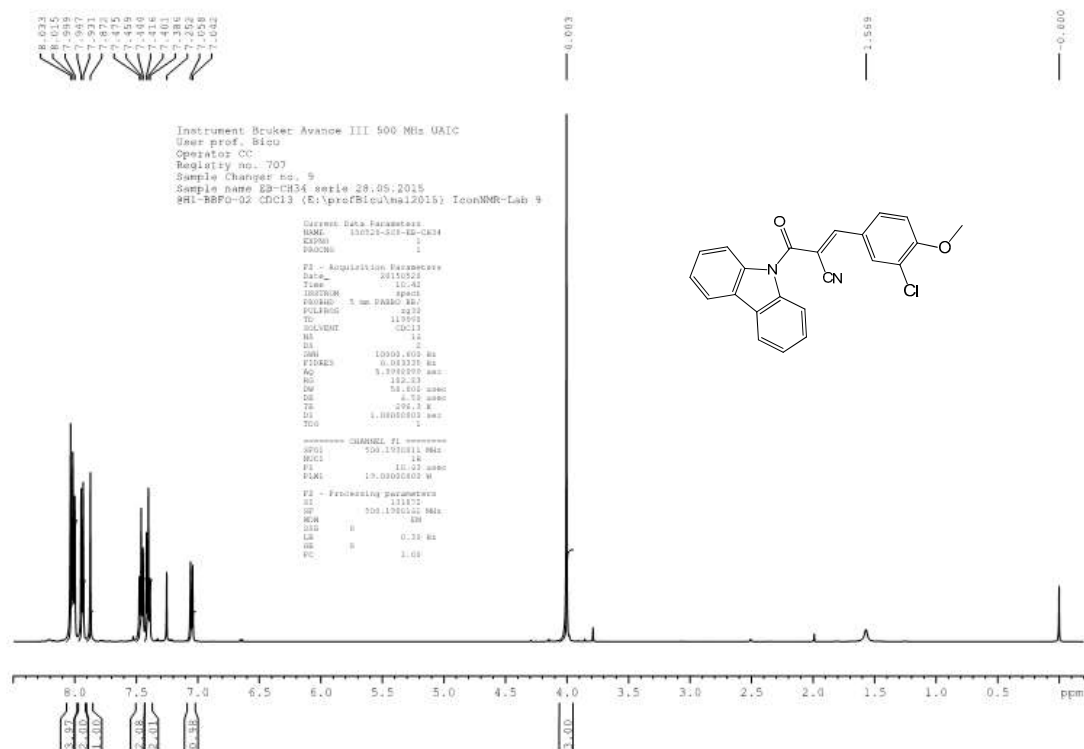
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-3g



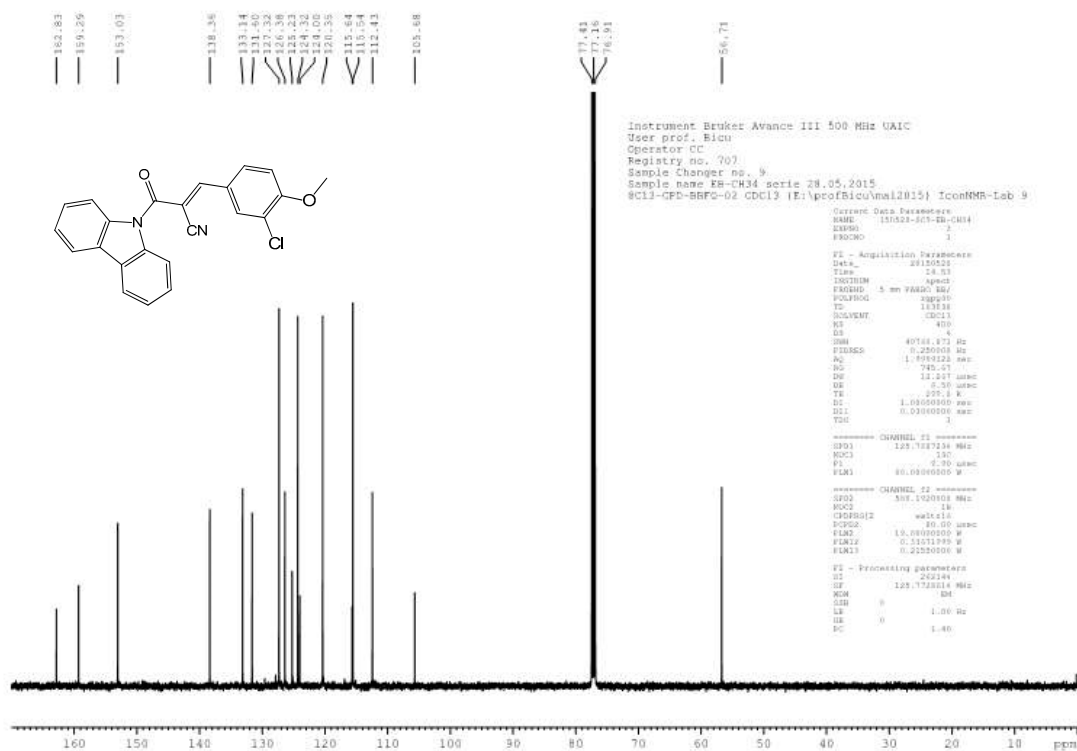
## IR-3g



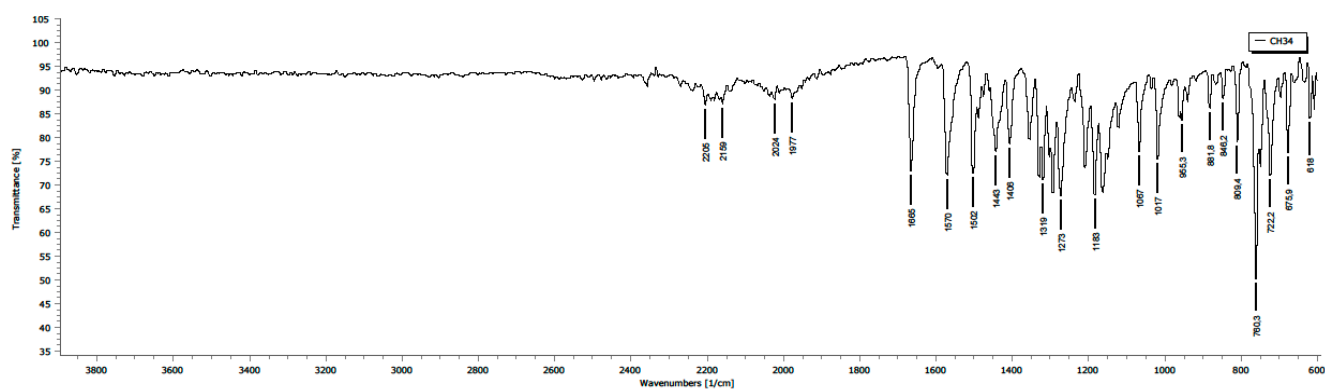
## <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-3h



## <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-3h



## IR-3h



Chemical structure of 8H-CH32: COc1ccc(cc1)/C=C/C(=O)N2c3ccccc3c4ccccc24

<sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) data:

Chemical Shift (ppm)	Integration
7.900	1.00
7.815	1.00
7.711	1.00
7.505	1.00
7.488	1.00
7.298	1.00
7.281	1.00
7.265	1.00
7.247	1.00
7.233	1.00
7.211	1.00
7.196	1.00
7.179	1.00
7.162	1.00
7.146	1.00
7.129	1.00
7.113	1.00
7.096	1.00
7.079	1.00
7.063	1.00
3.800	3.00

Instrument: Bruker Avance III 500 MHz UAIC  
 User: prof. Biça  
 Operator: CC  
 Registry no.: 705  
 Sample Changer no.: 5  
 Sample name: 8H-CH32 serie 28.05.2015  
 8H-CH32 (CDCl<sub>3</sub>) (E:prof.Bica\mai2015) IconNMR-Lab 5

Experimental Data Parameters:  
 NAME: 150129-001-8H-CH32  
 EXPNO: 1  
 PROCNO: 1  
 F2 - Acquisition Parameters:  
 Date\_: 23/10/2015  
 Time: 10.35  
 INSTRUM: spect  
 PULPROG: zgpg30  
 F4 - 5 mm PABBO 800  
 TD: 65536  
 TE: 300.2  
 SOLVENT: CDCl3  
 NS: 16  
 DS: 2  
 SWH: 10000.500 KHz  
 FIDRES: 0.002335 Hz  
 AQ: 1.1994999 sec  
 RG: 144.00  
 DQ: 55.001 usec  
 DE: 6.50 usec  
 TE: 299.2 K  
 SI: 1.00000000 sec  
 TDO: 1  
 CHANNEL f1:   
 NUC1: 13C 101.251 MHz  
 P1: 18  
 PL1: 0.00420 sec  
 PRG2: 19.00000000 sec  
 F2 - Processing parameters:  
 SI: 133472  
 SF: 500.1301115 MHz  
 GR: 324  
 LB: 0  
 GB: 0.35 Hz  
 RB: 0  
 PC: 1.00

Chemical structure of the sample is displayed above the spectrum.

**1H NMR Spectrum (500 MHz, DMSO-d6):**

**Chemical Structure:** COc1ccc(cc1)/C=C/C(=O)N2c3ccccc3c4ccccc24

**1H NMR Data:**

Chemical Shift (ppm)	Integration
7.70 (d, 2H)	1.00
7.50 (d, 2H)	1.00
7.30 (d, 2H)	1.00
7.10 (d, 2H)	1.00
6.90 (d, 2H)	1.00
6.70 (d, 2H)	1.00
6.50 (d, 2H)	1.00
6.30 (d, 2H)	1.00
6.10 (d, 2H)	1.00
5.90 (d, 2H)	1.00
5.70 (d, 2H)	1.00
5.50 (d, 2H)	1.00
5.30 (d, 2H)	1.00
5.10 (d, 2H)	1.00
4.90 (d, 2H)	1.00
4.70 (d, 2H)	1.00
4.50 (d, 2H)	1.00
4.30 (d, 2H)	1.00
4.10 (d, 2H)	1.00
3.90 (d, 2H)	1.00
3.70 (d, 2H)	1.00
3.50 (d, 2H)	1.00
3.30 (d, 2H)	1.00
3.10 (d, 2H)	1.00
2.90 (d, 2H)	1.00
2.70 (d, 2H)	1.00
2.50 (d, 2H)	1.00
2.30 (d, 2H)	1.00
2.10 (d, 2H)	1.00
1.90 (d, 2H)	1.00
1.70 (d, 2H)	1.00
1.50 (d, 2H)	1.00
1.30 (d, 2H)	1.00
1.10 (d, 2H)	1.00
0.90 (d, 2H)	1.00
0.70 (d, 2H)	1.00
0.50 (d, 2H)	1.00
0.30 (d, 2H)	1.00
0.10 (d, 2H)	1.00

**13C NMR Spectrum (125 MHz, DMSO-d6):**

**13C NMR Data:**

Chemical Shift (ppm)
160.0
155.0
150.0
145.0
140.0
135.0
130.0
125.0
120.0
115.0
110.0
105.0
100.0
95.0
90.0
85.0
80.0
75.0
70.0
65.0
60.0
55.0
50.0
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0

**Acquisition Parameters:**

- NAME: 130517-015-EB-CH3
- PROCNO: 1
- FE - Acquisition Parameters
- DATE\_: 20150520
- TIME: 14.11
- INSTRUM: spect
- PROBHD: 5 mm PABBO 400
- PULPROG: zgpg30
- TD: 131072
- SOLVENT: DMSO-d6
- NS: 512
- DS: 4
- SWH: 40740.171 Hz
- F2HREF: 0.25000000 Hz
- AQ: 1.8994332 sec
- RG: 675.00
- DE: 12.047 mm
- TE: 300.2 K
- DT: 0.00001000 sec
- D11: 0.10000000 sec
- TD0: 1

**Channel f1:**

- NUC1: 13C
- PC1: 0.00000000 M
- PLW1: 0.00000000 M

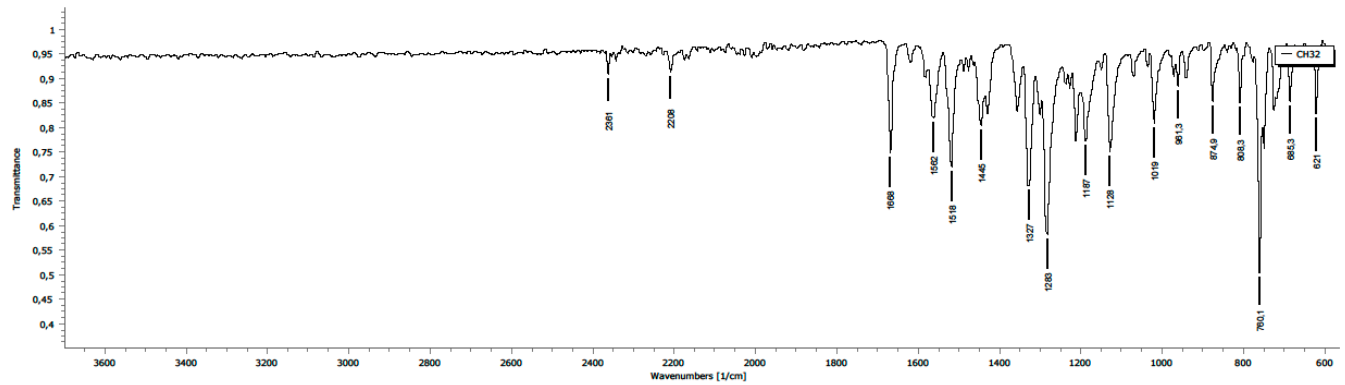
**Channel f2:**

- NUC2: 1H
- PC2: 0.00000000 M
- PLW2: 0.00000000 M
- PLW3: 0.00000000 M
- PLW4: 0.00000000 M
- PLW5: 0.00000000 M

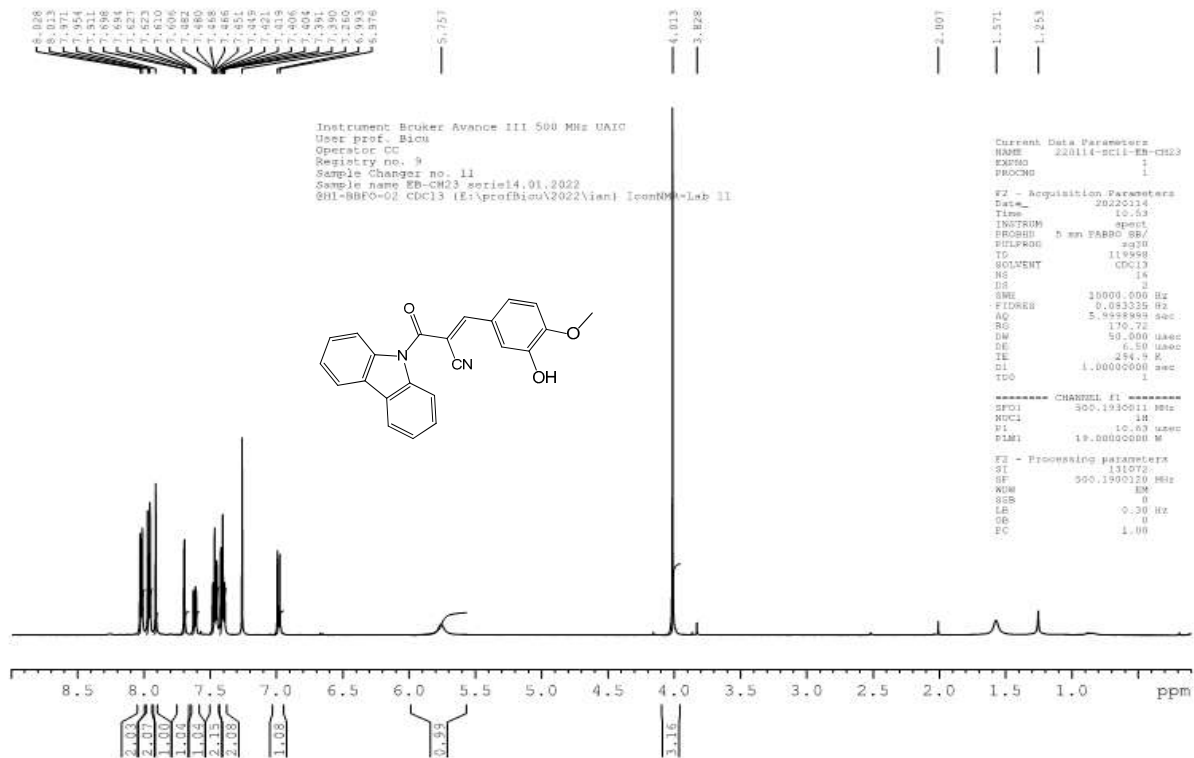
**Processing parameters:**

- SI: 32768
- SF: 125.7603690 MHz
- WDW: EM
- SSB: 0
- LB: 1.00 Hz
- GB: 0
- PC: 1.00

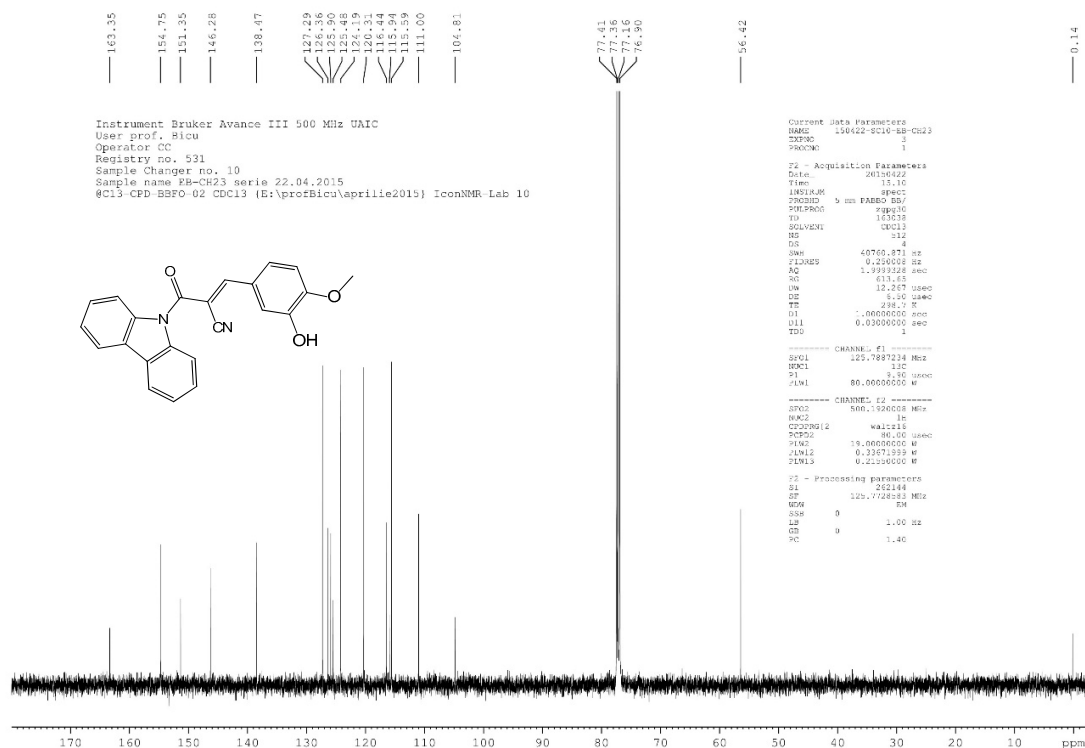
## IR-3i



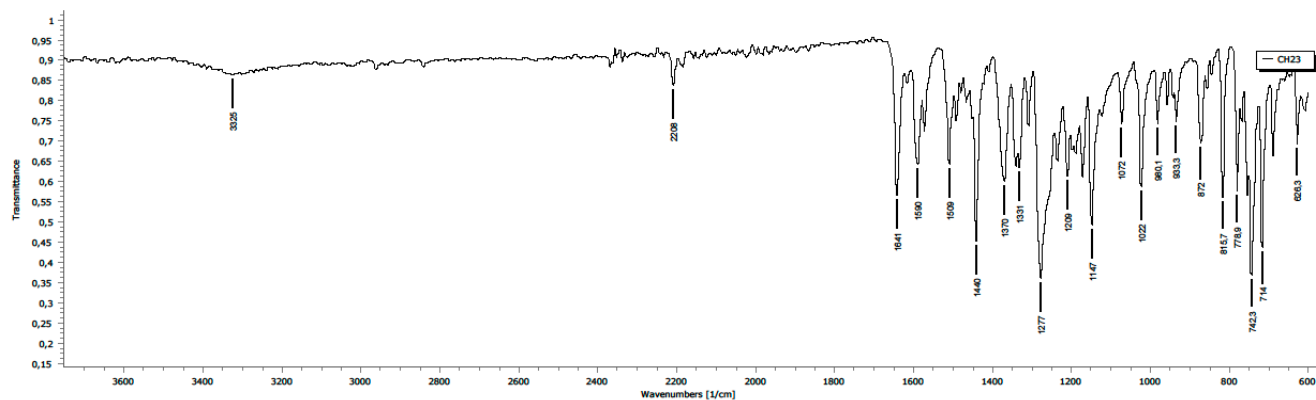
## <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-3j



# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-3j

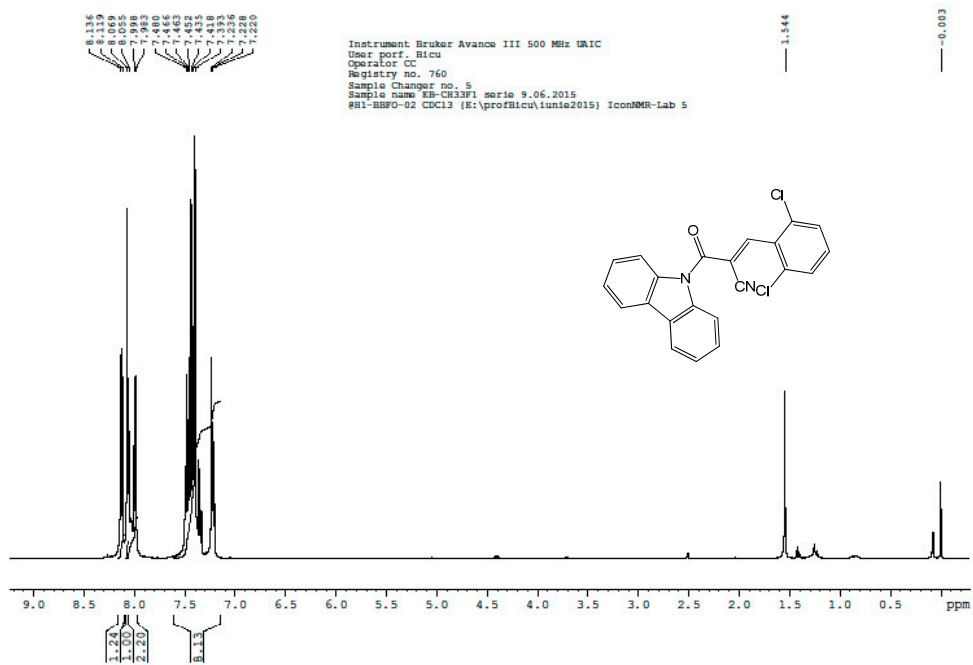


## IR-3j

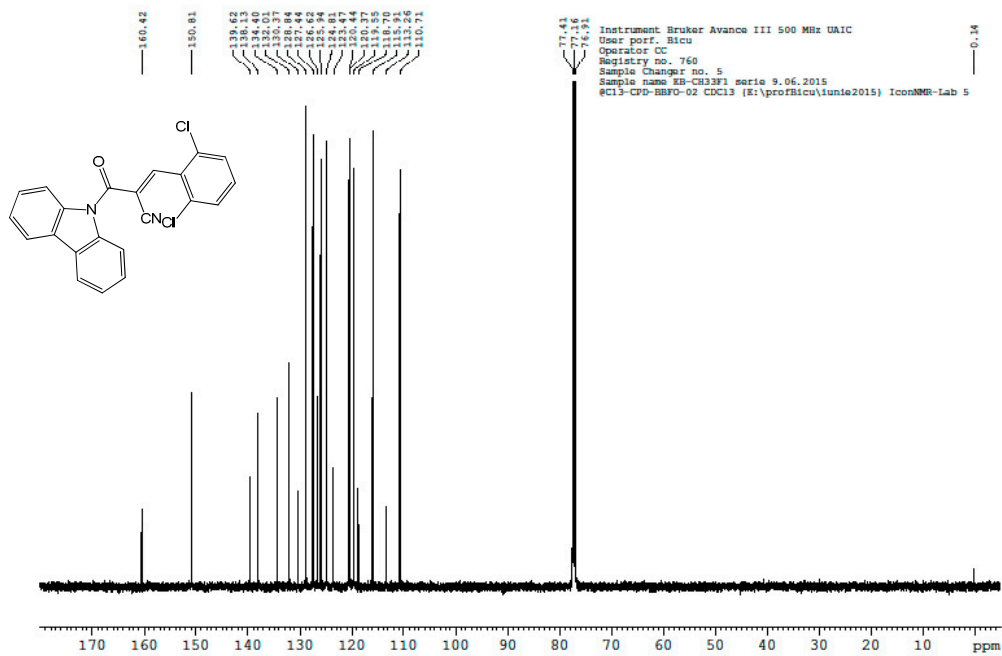




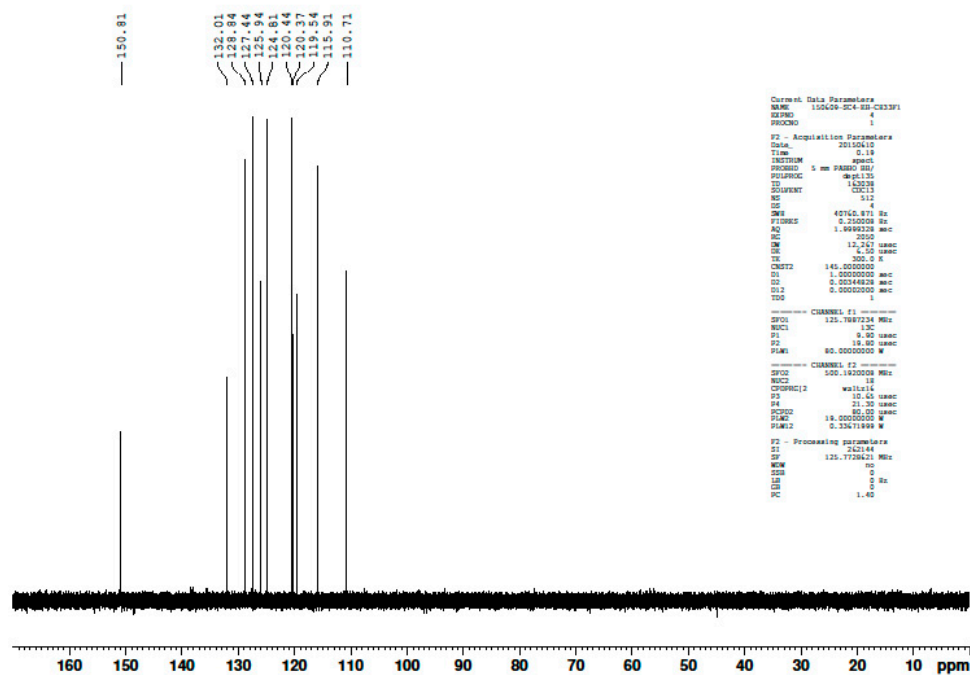
**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-3k**



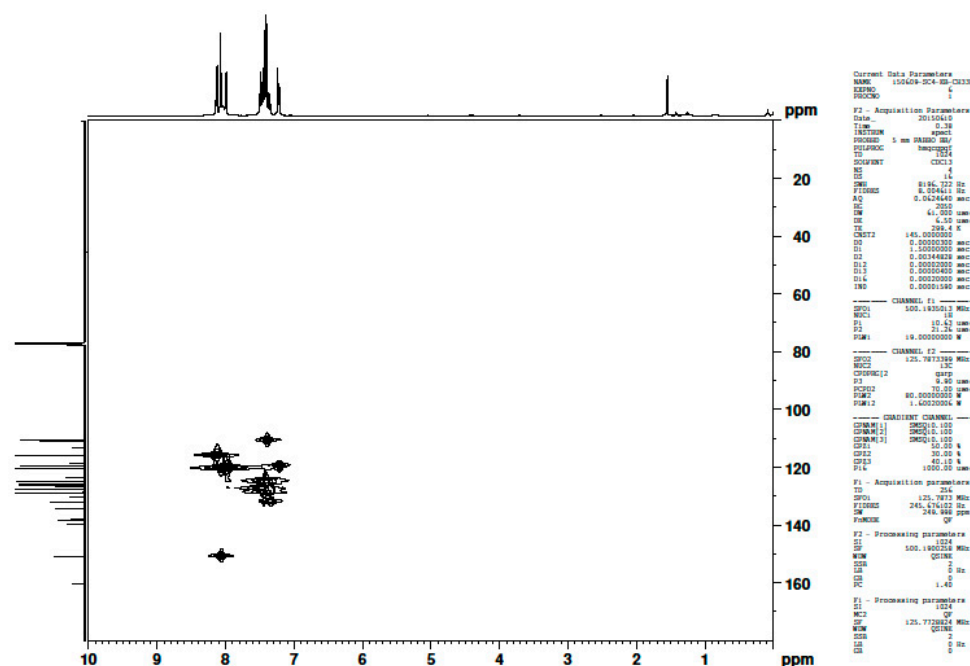
**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-3k**

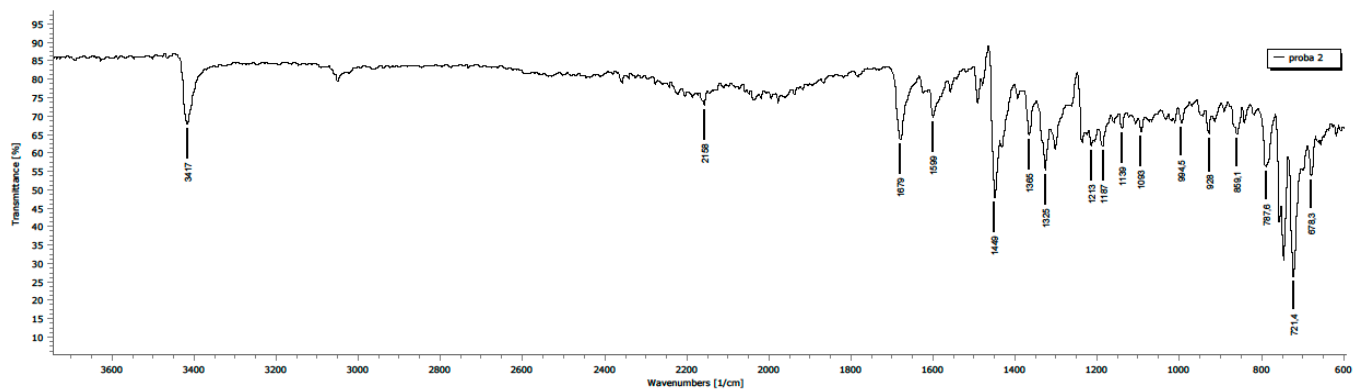


# <sup>13</sup>C-DEPT NMR (125 MHz, CDCl<sub>3</sub>)-3k

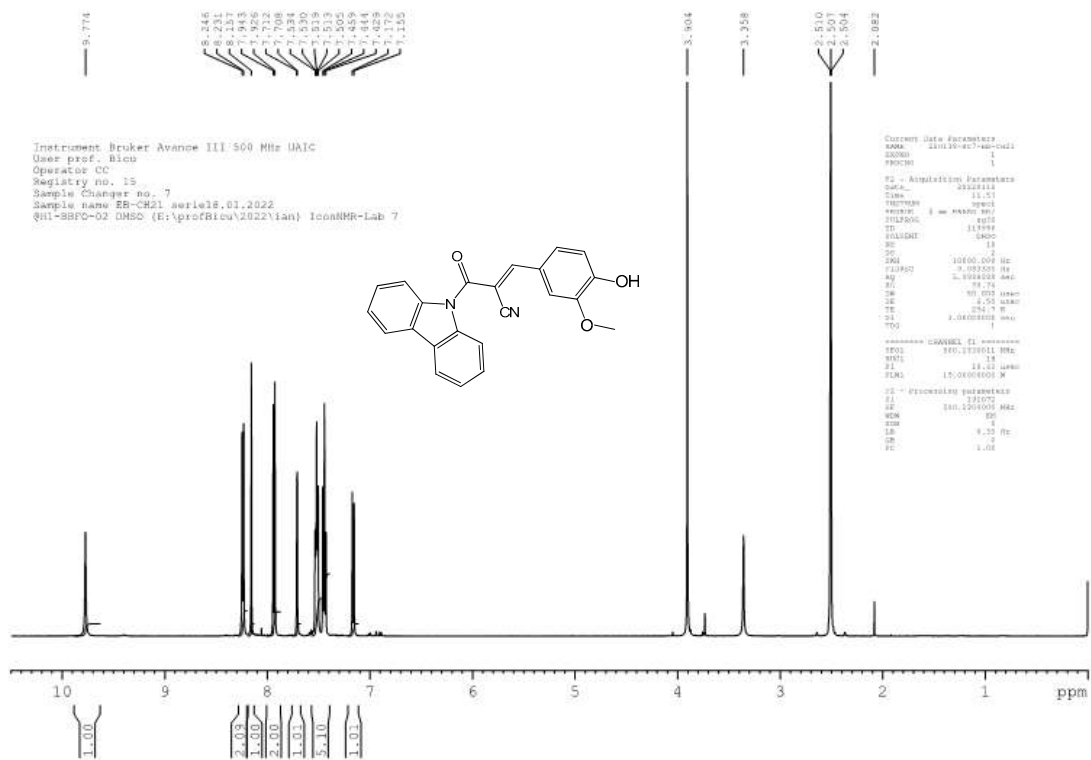


# HMQC NMR (500 MHz, CDCl<sub>3</sub>)-3k

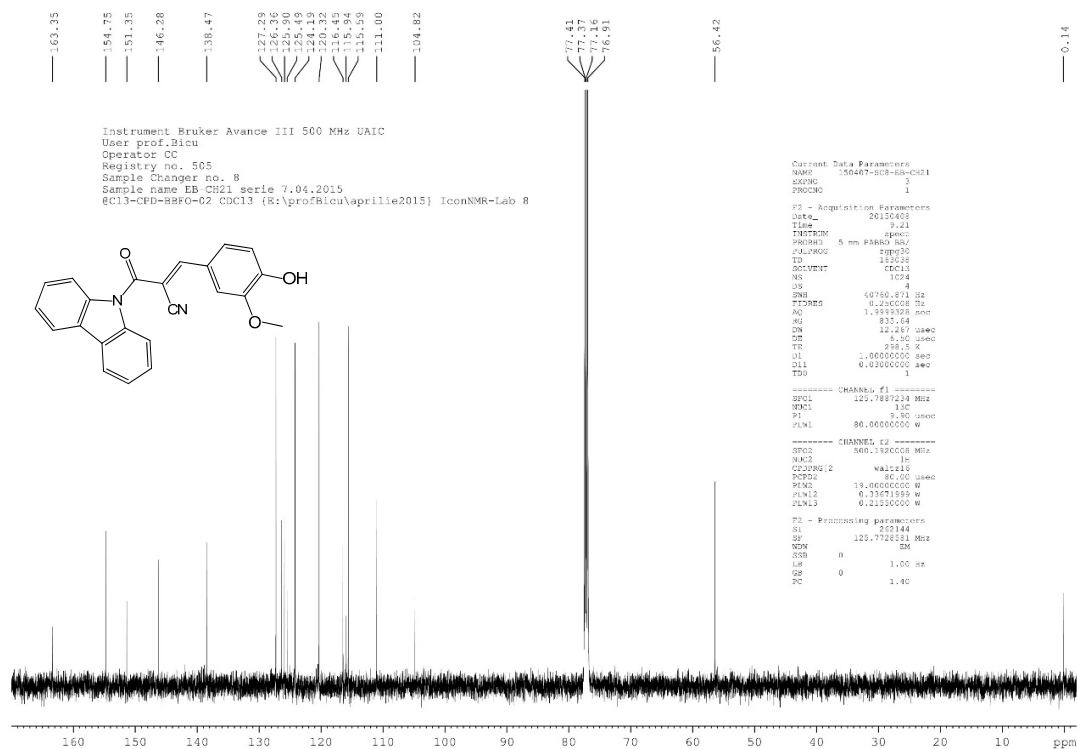


**IR-3k**

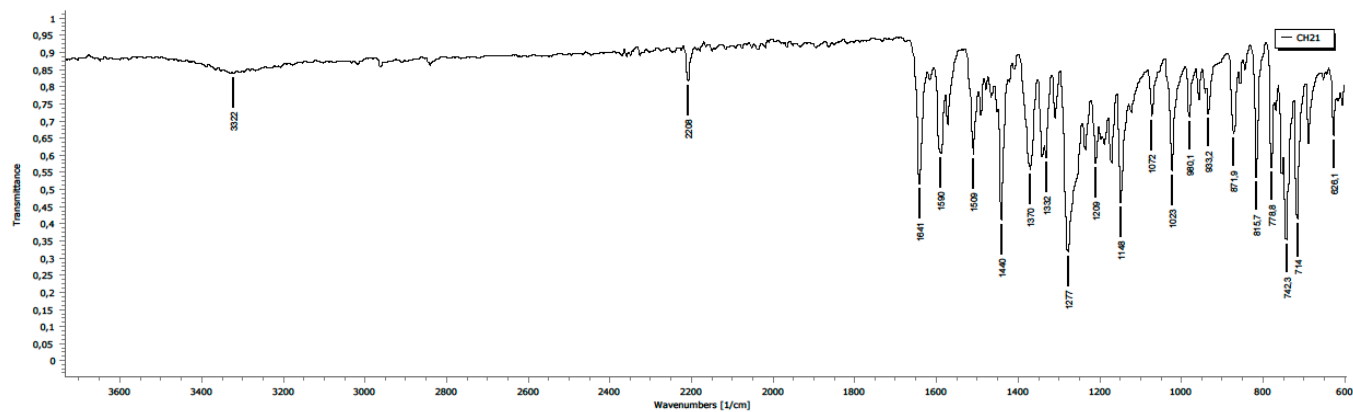
**<sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)-3I**



# <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>)- 3I



## IR-3I



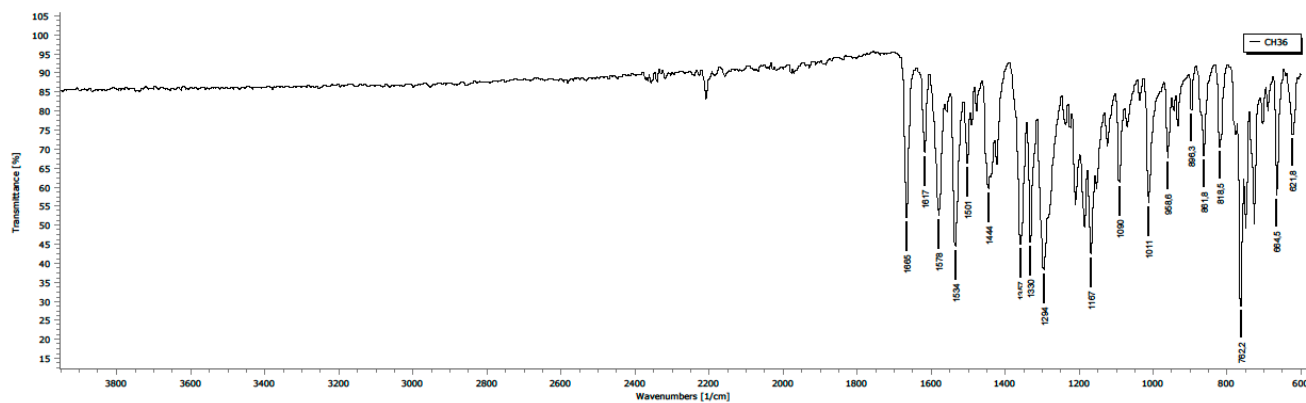
[illegible]

Chemical structure of compound 15d: COc1ccc(cc1)/C=C/C(C#N)C(=O)n2c3ccccc3cc2

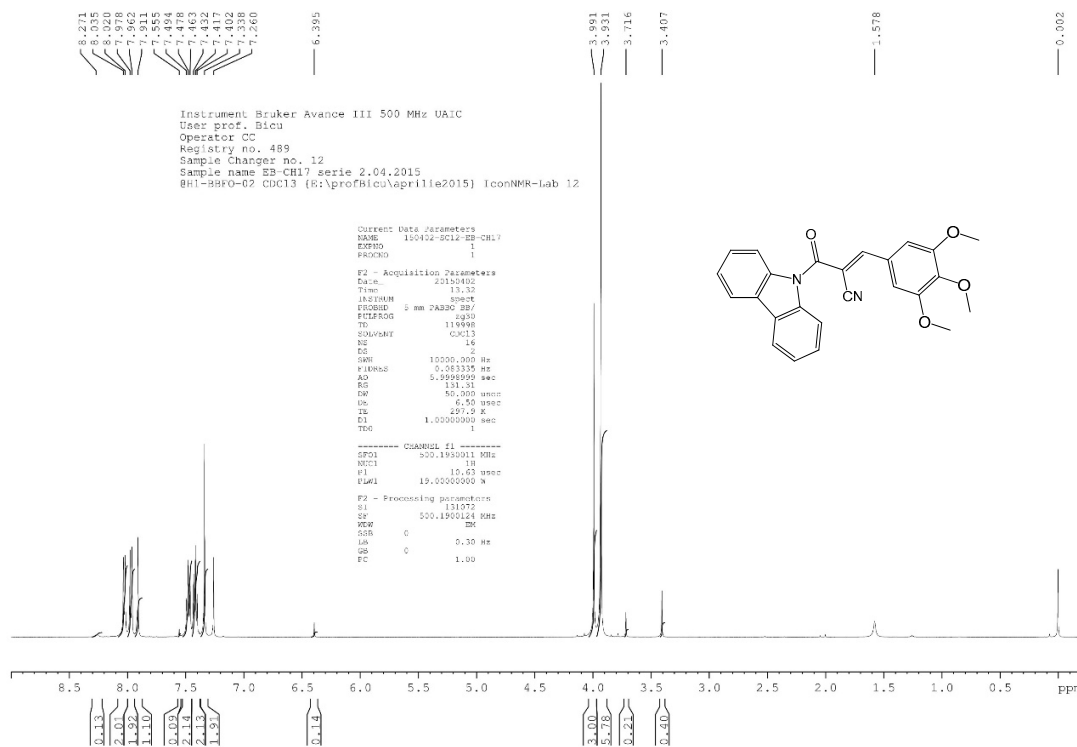
<sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) of compound 15d. The spectrum shows peaks from 1.4 to 8.2 ppm. The chemical structure of 15d is shown above the spectrum.

Peak list (ppm): 8.16, 7.74, 7.69, 7.30, 6.90, 6.82, 6.74, 6.66, 6.58, 6.50, 6.42, 6.34, 6.26, 6.18, 6.10, 6.02, 5.94, 5.86, 5.78, 5.70, 5.62, 5.54, 5.46, 5.38, 5.30, 5.22, 5.14, 5.06, 4.98, 4.90, 4.82, 4.74, 4.66, 4.58, 4.50, 4.42, 4.34, 4.26, 4.18, 4.10, 4.02, 3.94, 3.86, 3.78, 3.70, 3.62, 3.54, 3.46, 3.38, 3.30, 3.22, 3.14, 3.06, 2.98, 2.90, 2.82, 2.74, 2.66, 2.58, 2.50, 2.42, 2.34, 2.26, 2.18, 2.10, 2.02, 1.94, 1.86, 1.78, 1.70, 1.62, 1.54, 1.46, 1.38, 1.30, 1.22, 1.14, 1.06, 1.02, 1.00, 0.98, 0.96, 0.94, 0.92, 0.90, 0.88, 0.86, 0.84, 0.82, 0.80, 0.78, 0.76, 0.74, 0.72, 0.70, 0.68, 0.66, 0.64, 0.62, 0.60, 0.58, 0.56, 0.54, 0.52, 0.50, 0.48, 0.46, 0.44, 0.42, 0.40, 0.38, 0.36, 0.34, 0.32, 0.30, 0.28, 0.26, 0.24, 0.22, 0.20, 0.18, 0.16, 0.14, 0.12, 0.10, 0.08, 0.06, 0.04, 0.02, 0.00.

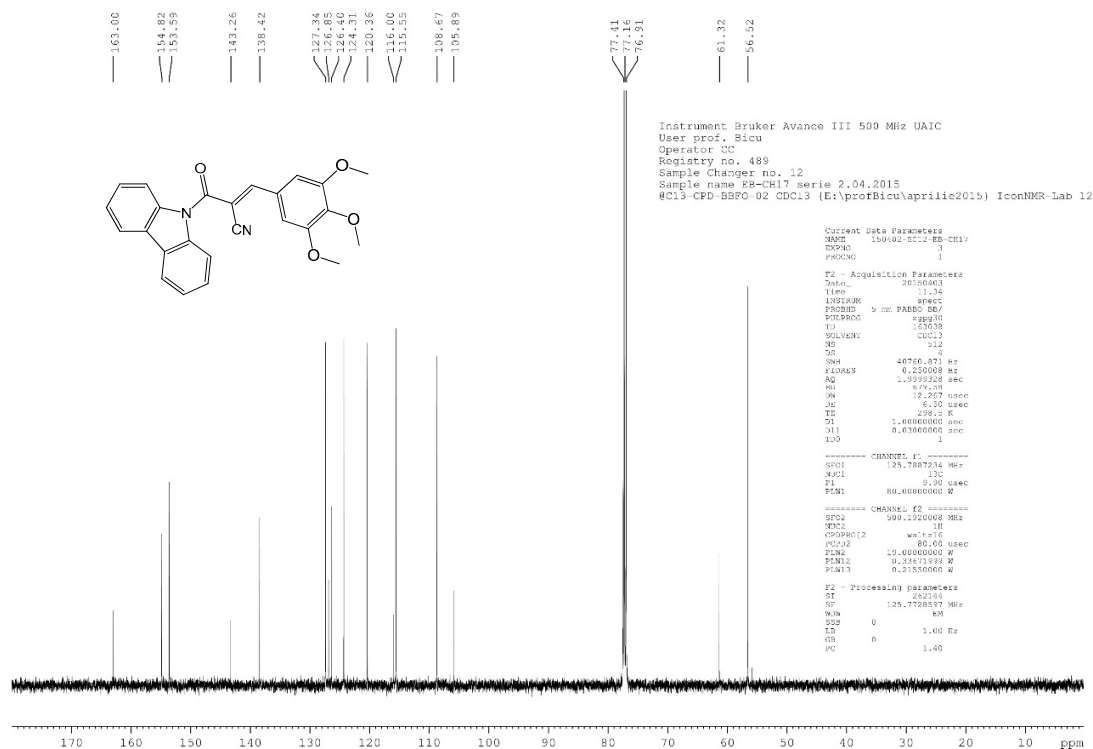
## IR-3m



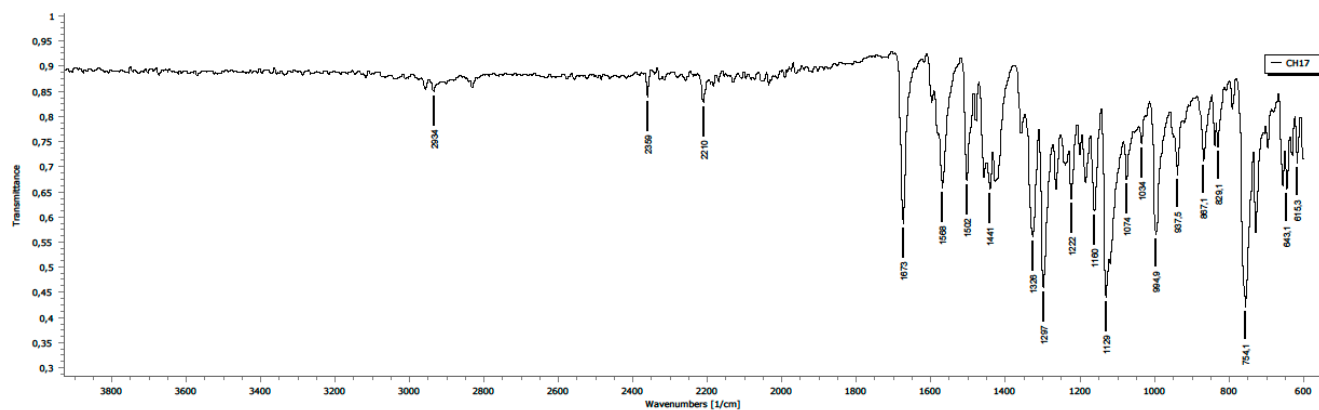
## <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-3n



# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)- **3n**



## IR-**3n**



Chemical structure of compound 5: COc1ccc2c(c1)c[nH]2C=C(C#N)C(=O)N3c4ccccc4c5ccccc35

<sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) data:

Chemical Shift (ppm)	Integration
9.50	1.00
8.50	2.15
8.00	2.00
7.50	4.47
7.00	5.16
6.50	2.00
6.00	1.00
5.50	1.00
5.00	1.00
4.50	1.00
4.00	3.79
3.50	1.00
3.00	1.00
2.50	1.00
2.00	1.00
1.50	1.00
1.00	1.00
0.50	1.00
0.00	1.00

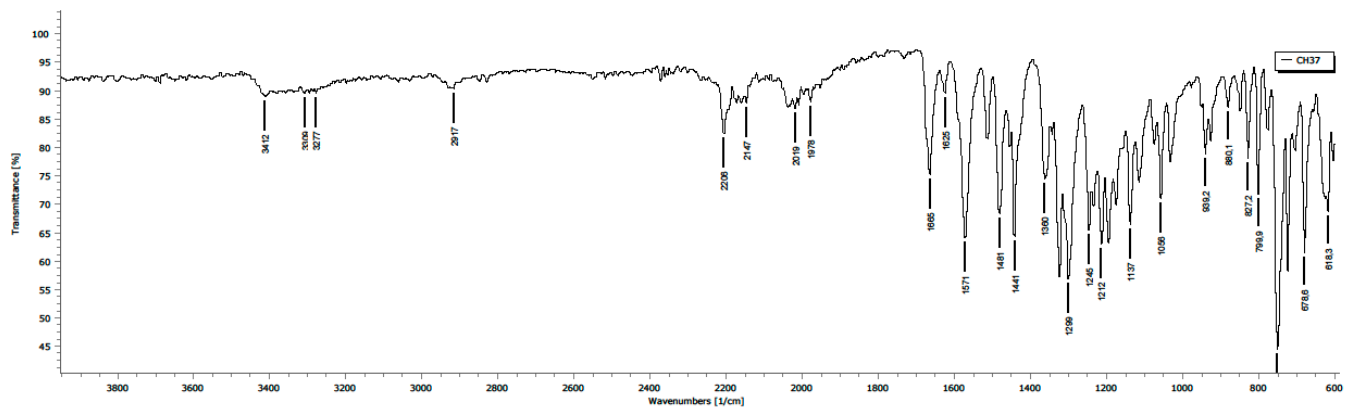
Chemical structure of 9c13-CPD-BBFO-02:

COc1ccc2c(c1)c[nH]2C=C(C#N)C(=O)N3c4ccccc4c5ccccc35

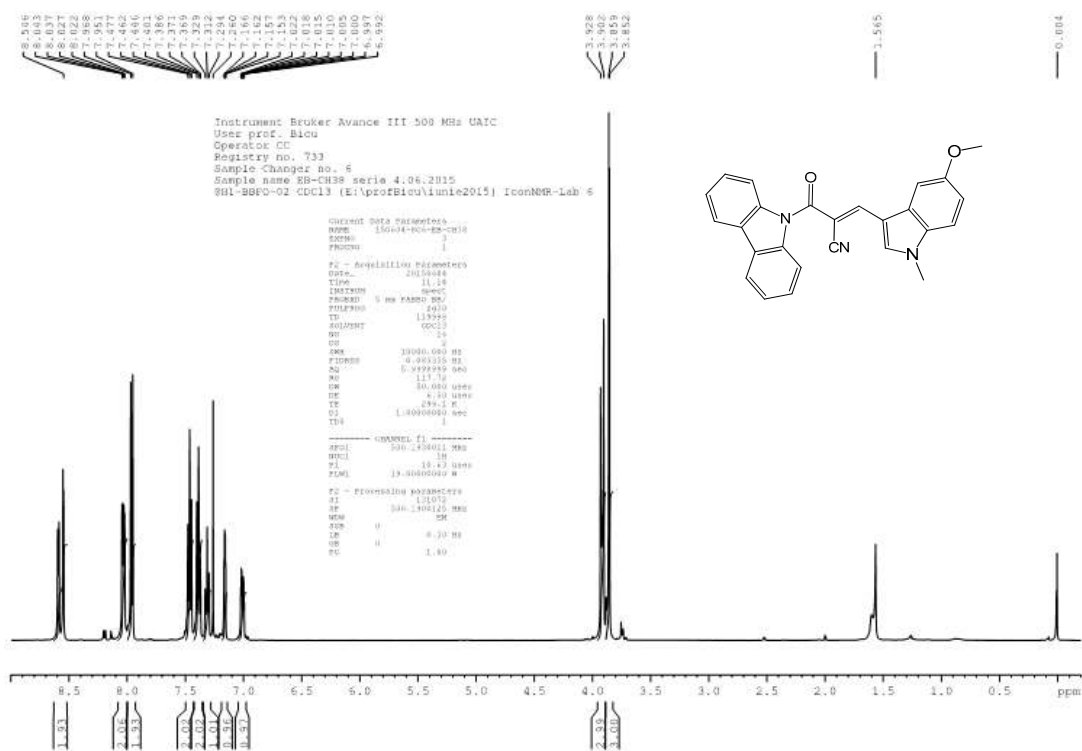
<sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) data:

Chemical Shift (ppm)	Integration
7.65	1.00
7.62	1.00
7.59	1.00
7.56	1.00
7.53	1.00
7.50	1.00
7.47	1.00
7.44	1.00
7.41	1.00
7.38	1.00
7.35	1.00
7.32	1.00
7.29	1.00
7.26	1.00
7.23	1.00
7.20	1.00
7.17	1.00
7.14	1.00
7.11	1.00
7.08	1.00
7.05	1.00
7.02	1.00
6.99	1.00
6.96	1.00
6.93	1.00
6.90	1.00
6.87	1.00
6.84	1.00
6.81	1.00
6.78	1.00
6.75	1.00
6.72	1.00
6.69	1.00
6.66	1.00
6.63	1.00
6.60	1.00
6.57	1.00
6.54	1.00
6.51	1.00
6.48	1.00
6.45	1.00
6.42	1.00
6.39	1.00
6.36	1.00
6.33	1.00
6.30	1.00
6.27	1.00
6.24	1.00
6.21	1.00
6.18	1.00
6.15	1.00
6.12	1.00
6.09	1.00
6.06	1.00
6.03	1.00
6.00	1.00
5.97	1.00
5.94	1.00
5.91	1.00
5.88	1.00
5.85	1.00
5.82	1.00
5.79	1.00
5.76	1.00
5.73	1.00
5.70	1.00
5.67	1.00
5.64	1.00
5.61	1.00
5.58	1.00
5.55	1.00
5.52	1.00
5.49	1.00
5.46	1.00
5.43	1.00
5.40	1.00
5.37	1.00
5.34	1.00
5.31	1.00
5.28	1.00
5.25	1.00
5.22	1.00
5.19	1.00
5.16	1.00
5.13	1.00
5.10	1.00
5.07	1.00
5.04	1.00
5.01	1.00
4.98	1.00
4.95	1.00
4.92	1.00
4.89	1.00
4.86	1.00
4.83	1.00
4.80	1.00
4.77	1.00
4.74	1.00
4.71	1.00
4.68	1.00
4.65	1.00
4.62	1.00
4.59	1.00
4.56	1.00
4.53	1.00
4.50	1.00
4.47	1.00
4.44	1.00
4.41	1.00
4.38	1.00
4.35	1.00
4.32	1.00
4.29	1.00
4.26	1.00
4.23	1.00
4.20	1.00
4.17	1.00
4.14	1.00
4.11	1.00
4.08	1.00
4.05	1.00
4.02	1.00
3.99	1.00
3.96	1.00
3.93	1.00
3.90	1.00
3.87	1.00
3.84	1.00
3.81	1.00
3.78	1.00
3.75	1.00
3.72	1.00
3.69	1.00
3.66	1.00
3.63	1.00
3.60	1.00
3.57	1.00
3.54	1.00
3.51	1.00
3.48	1.00
3.45	1.00
3.42	1.

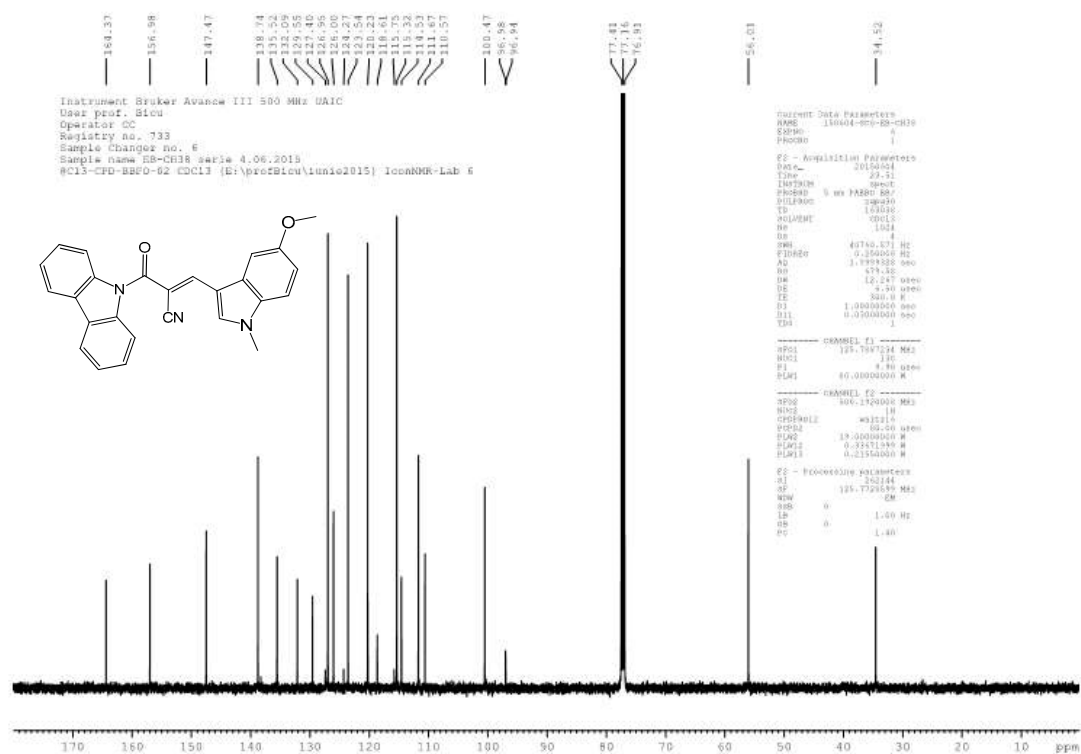


**IR-30**

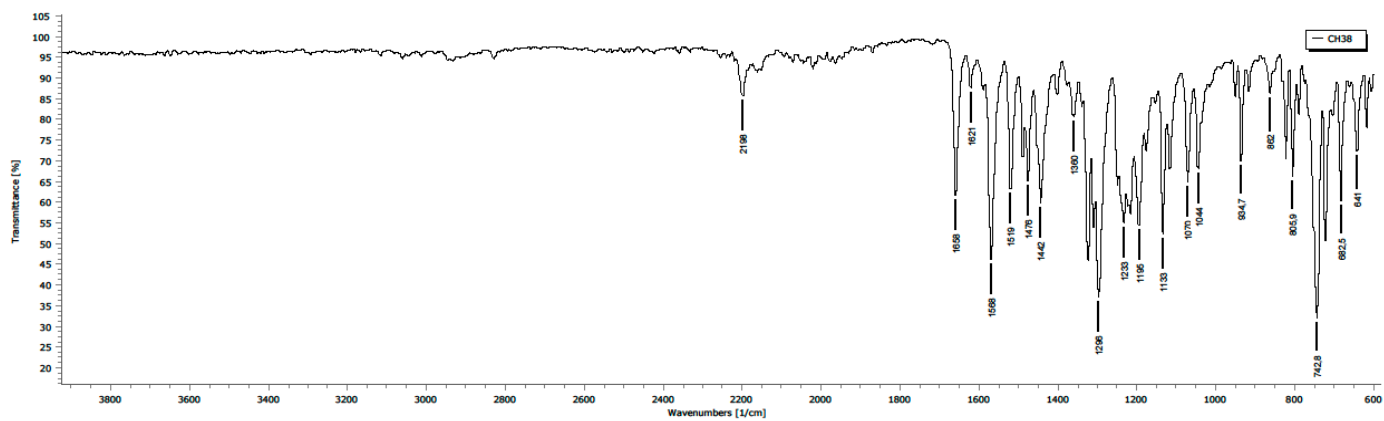
**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-3p**



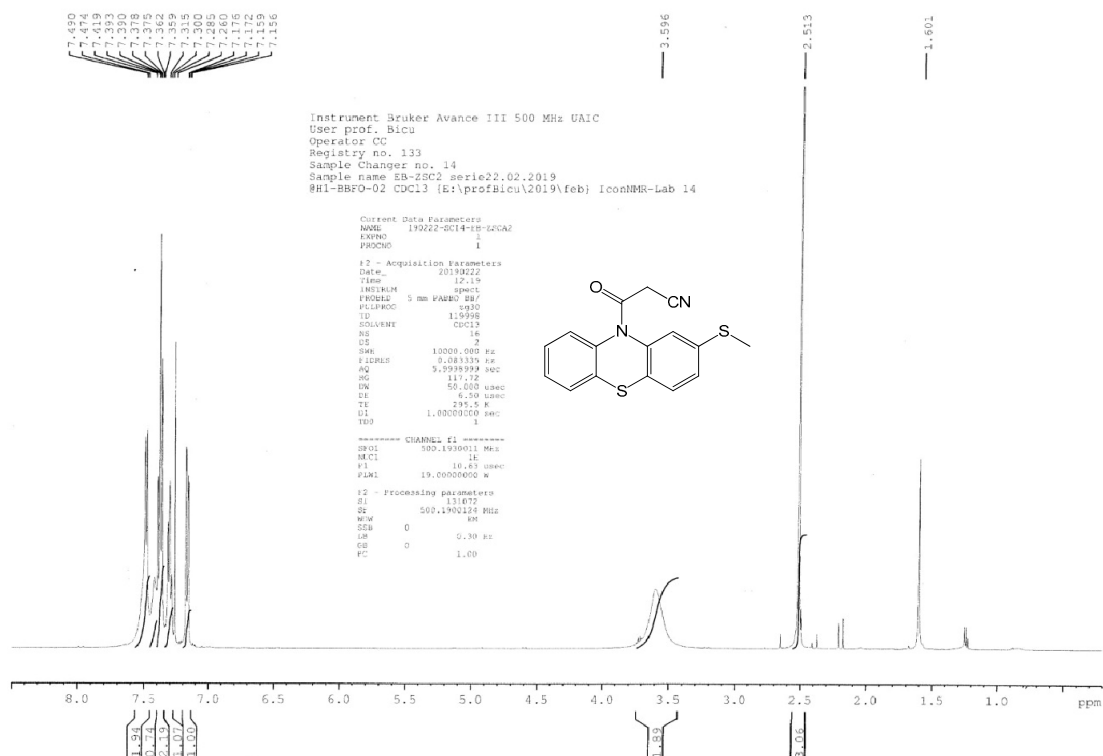
# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-3p



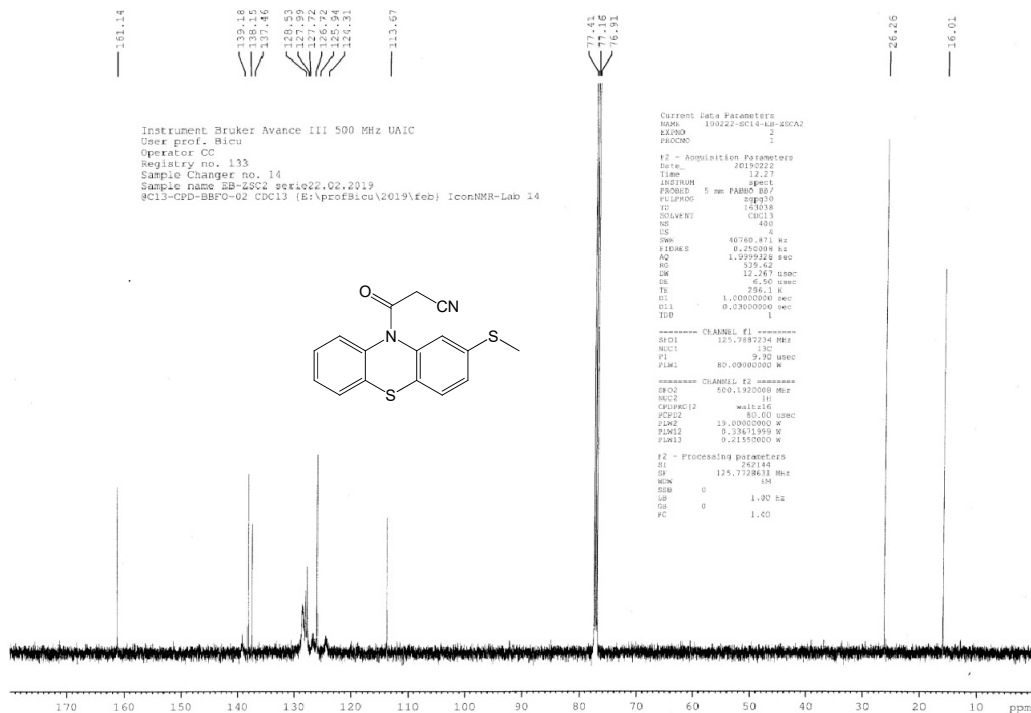
# IR-3p



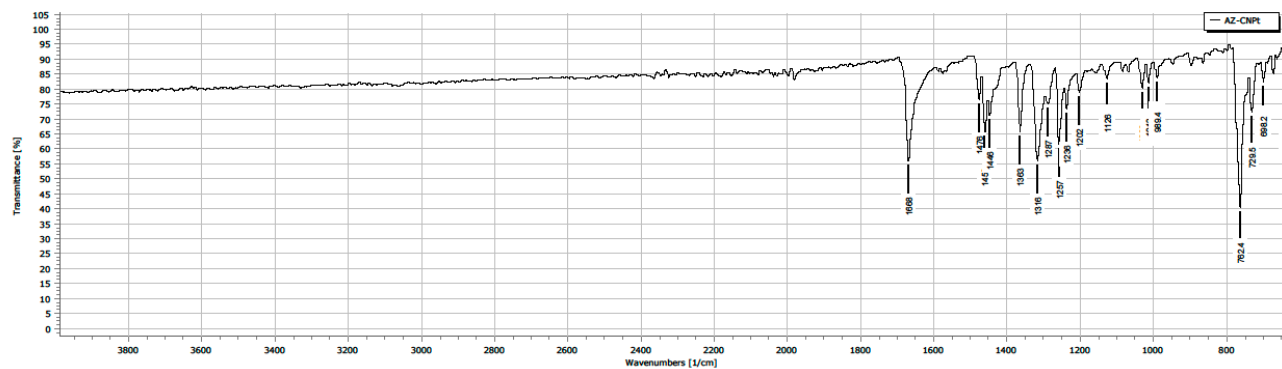
# <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)-4b



# <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)-4b

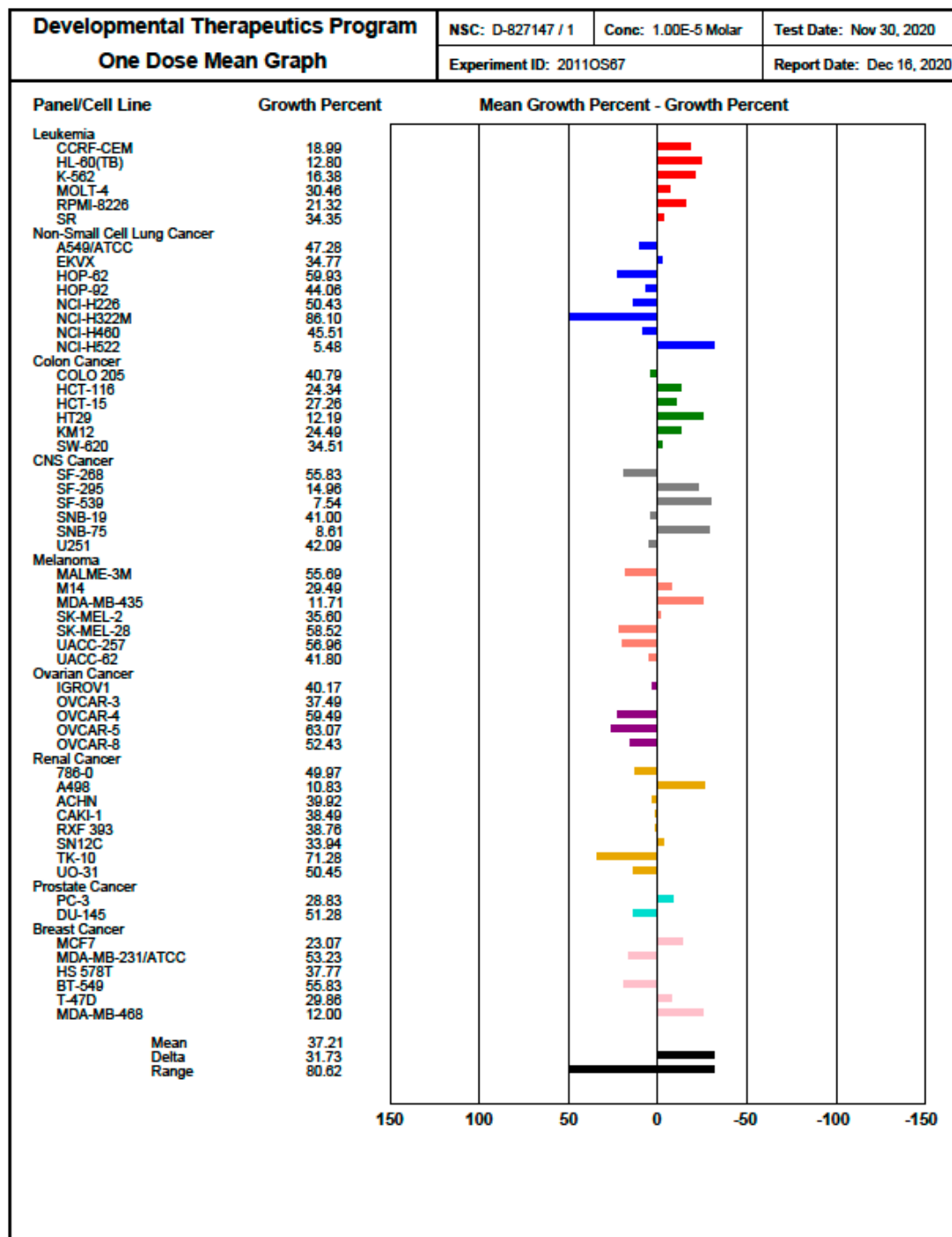


## IR-4b

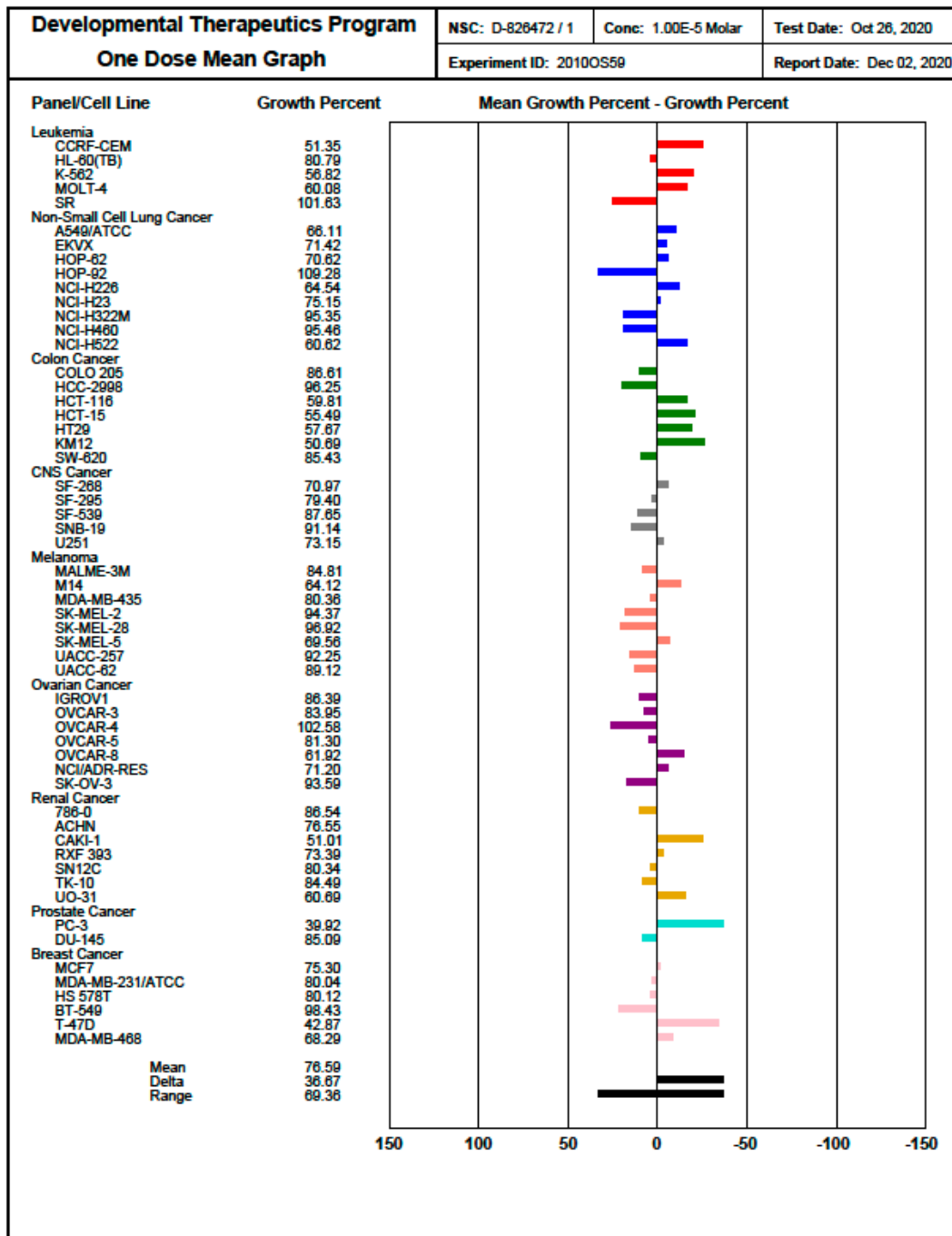


# One-dose full graphs obtained on NCI-60 cancer cell lines panel

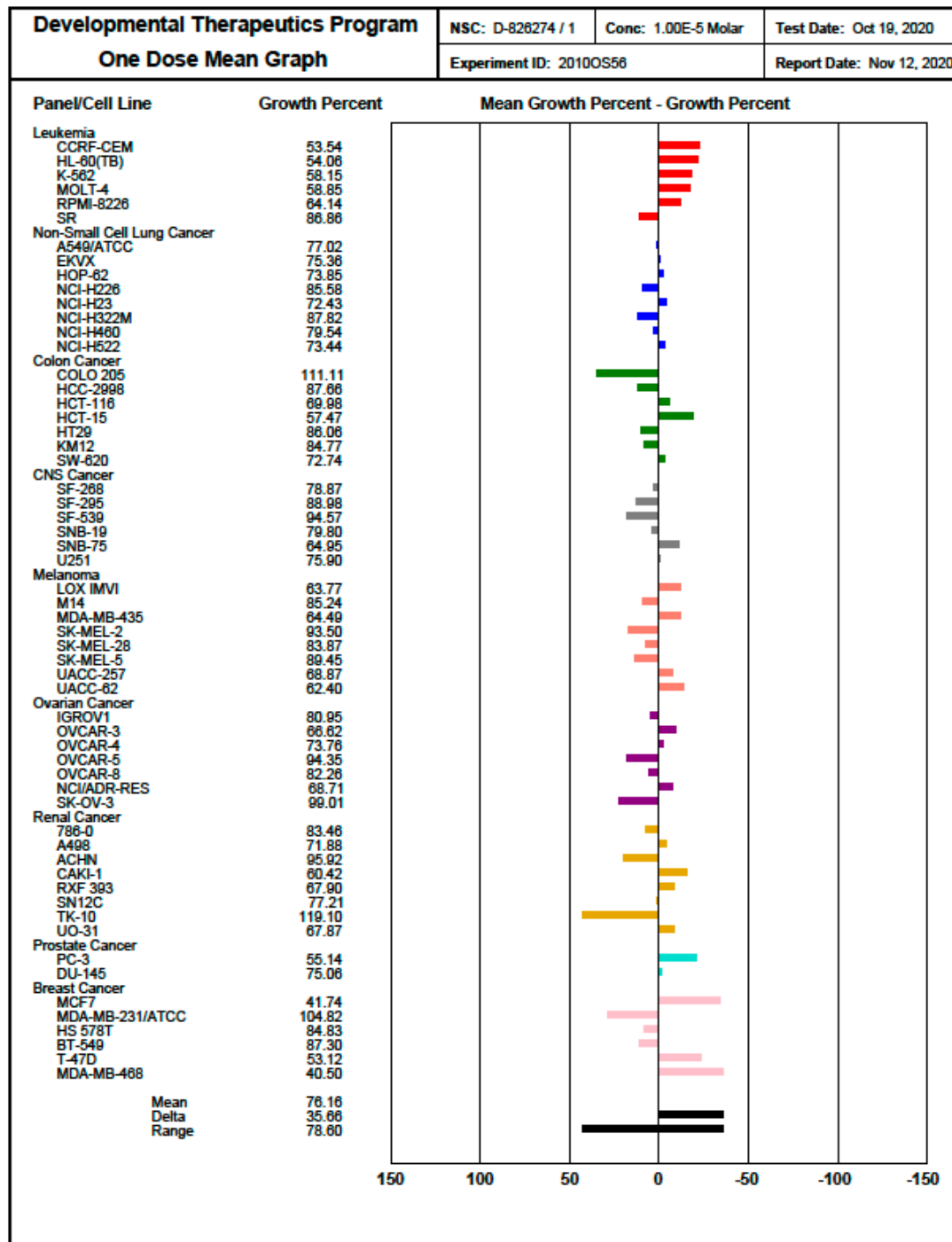
## Compound 2k

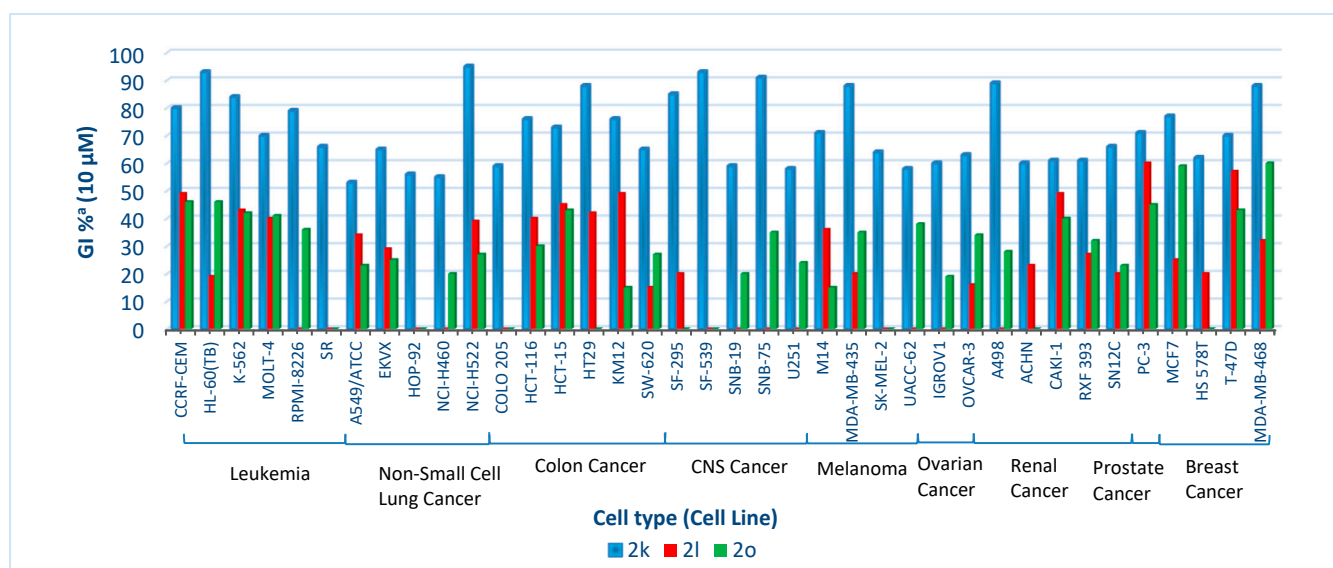


## Compound 21



## Compound 2o



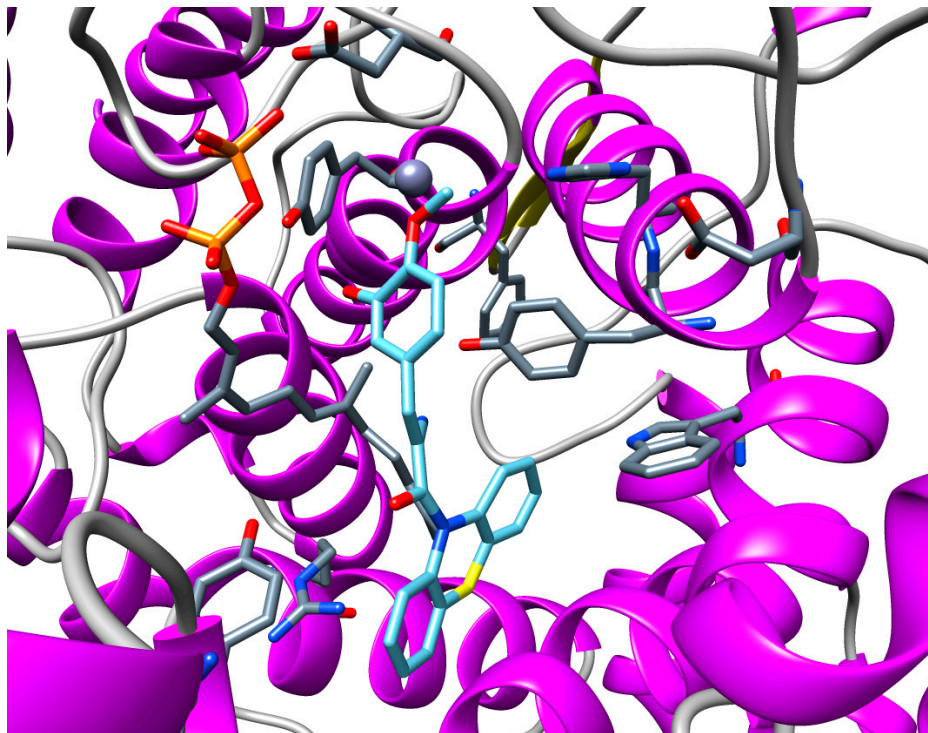


**Figure S1.** Results of the *in vitro* human cancer cell growth inhibition for selected compounds 2k, 2l and 2o.

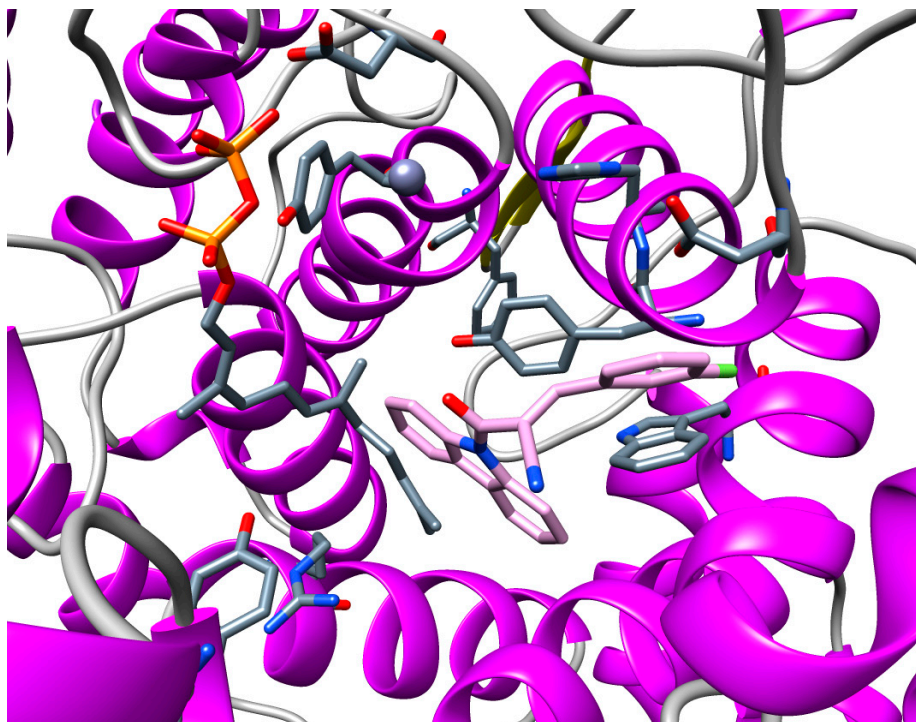


## Docking FTase

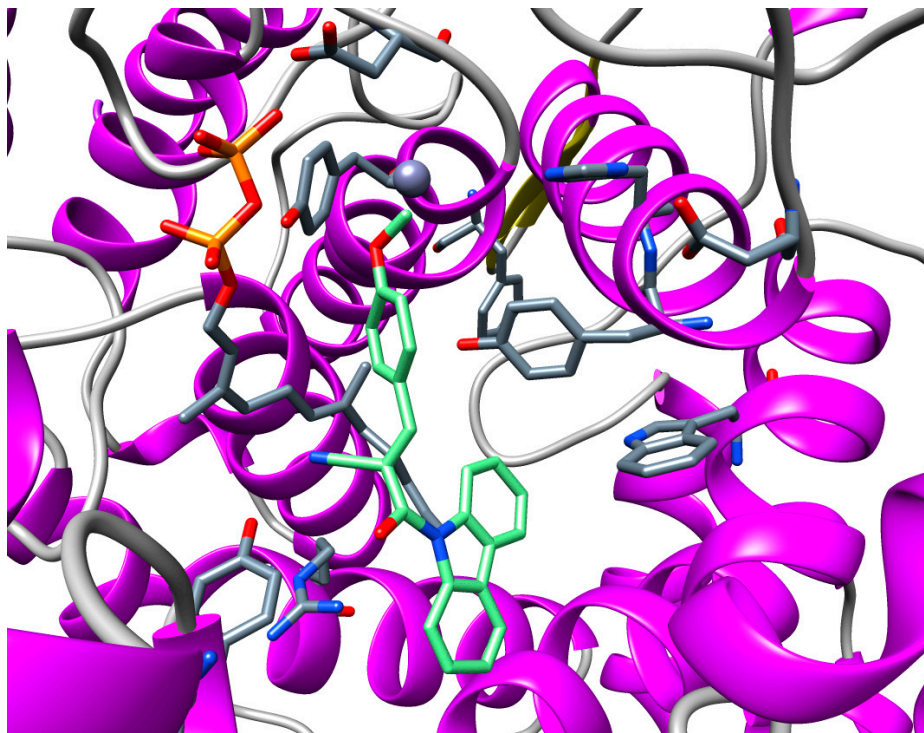
**Compound 11**



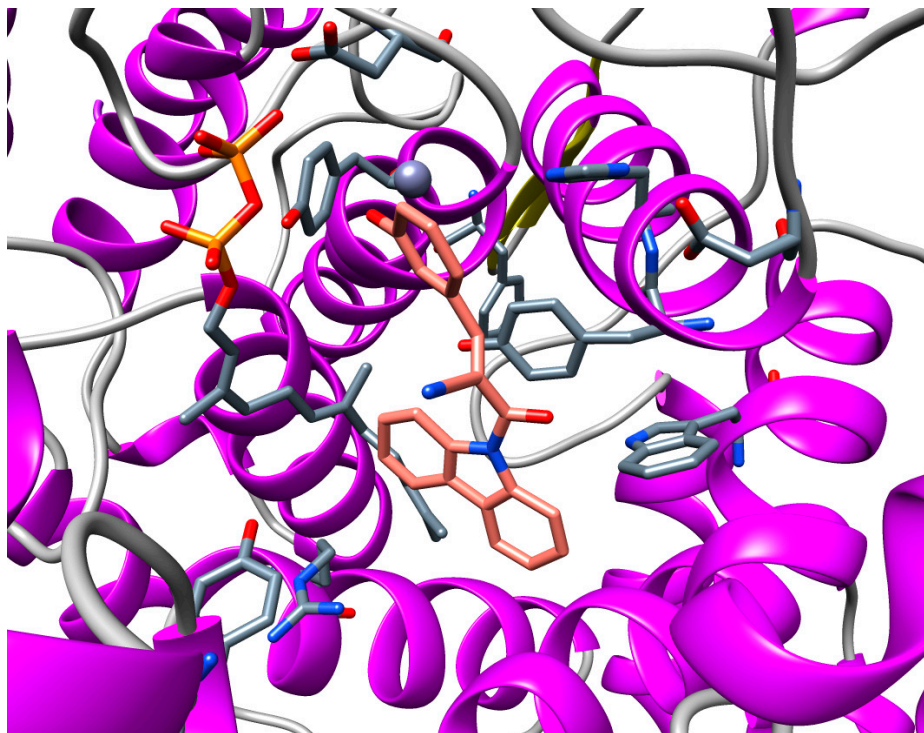
**Compound 3a**



**Compound 3b**

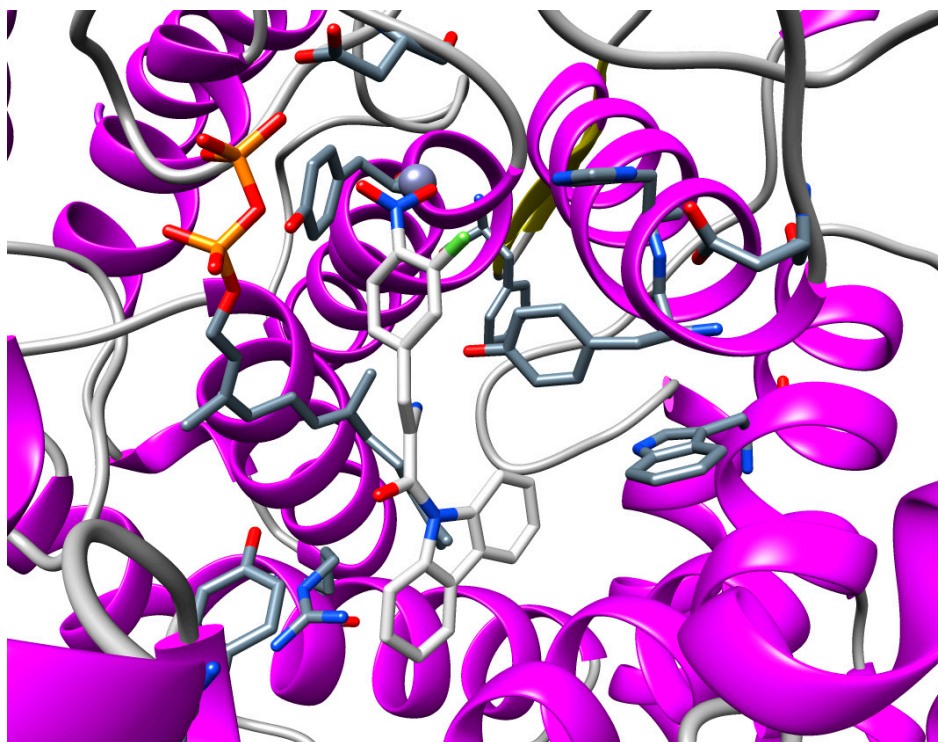


**Compound 3d**

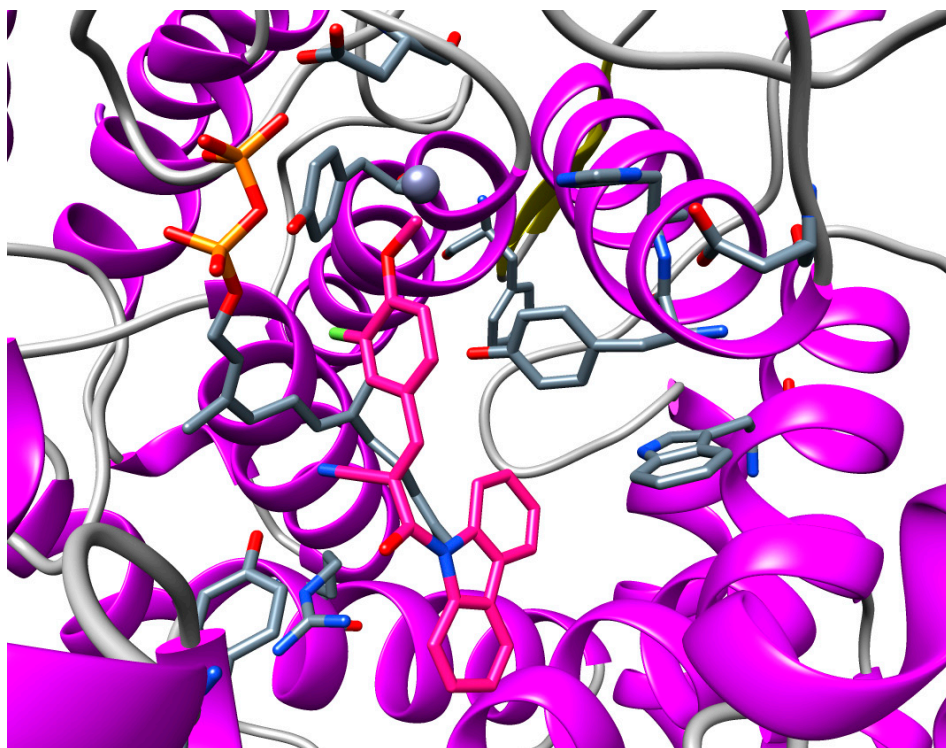




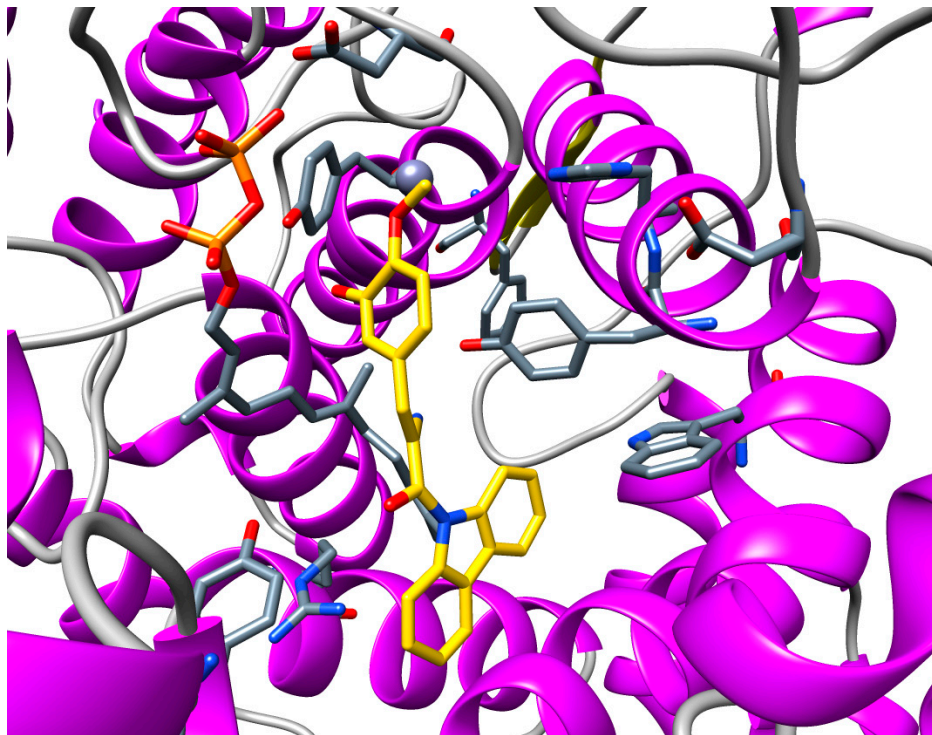
**Compound 3e**



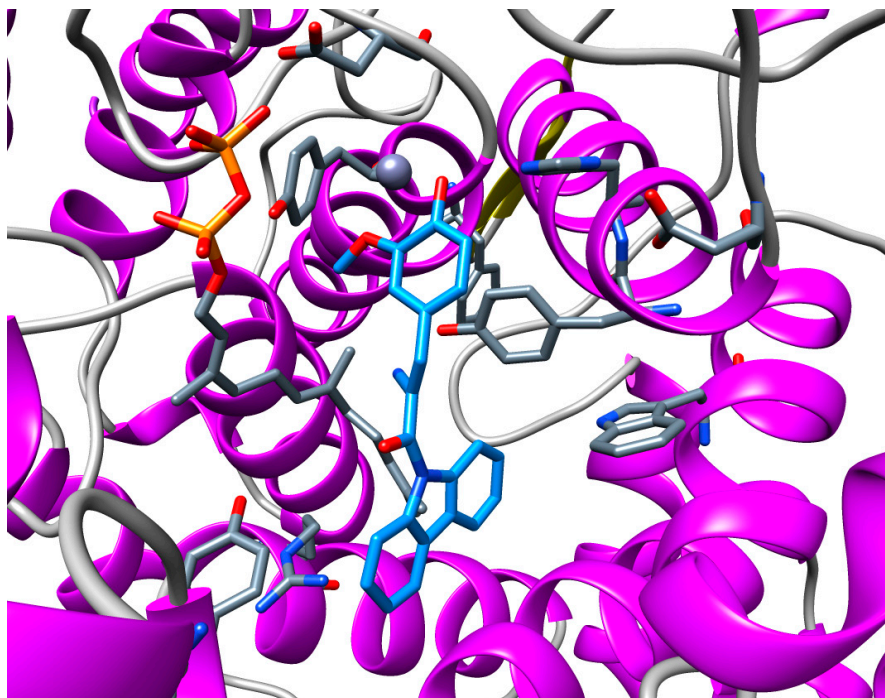
**Compound 3i**



**Compound 3j**

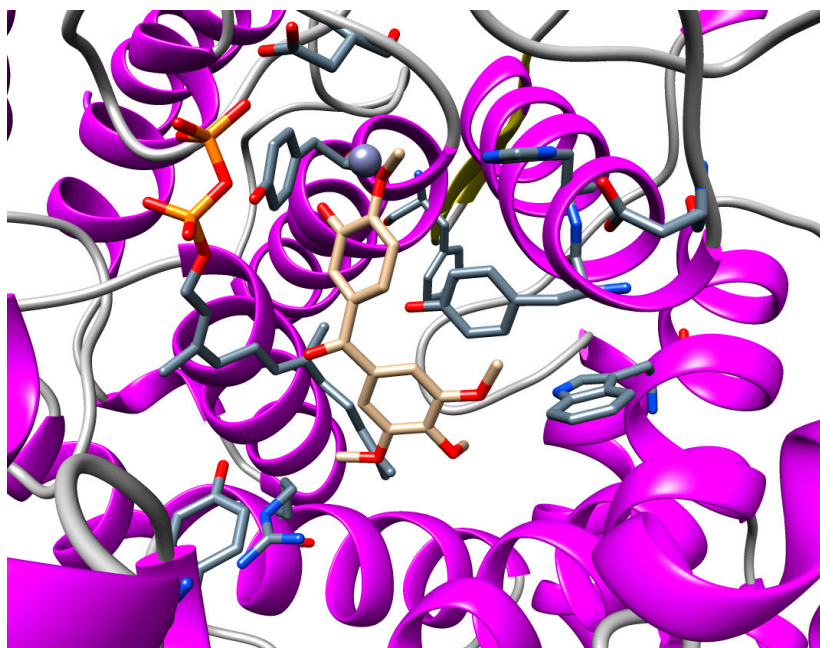


**Compound 3l**



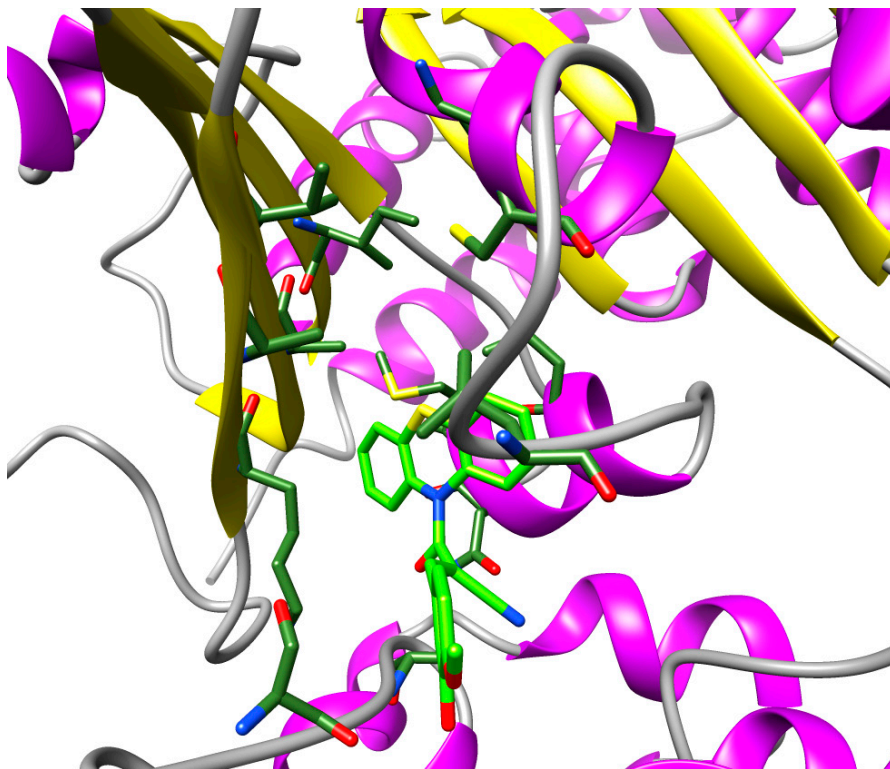


### Phenstatin

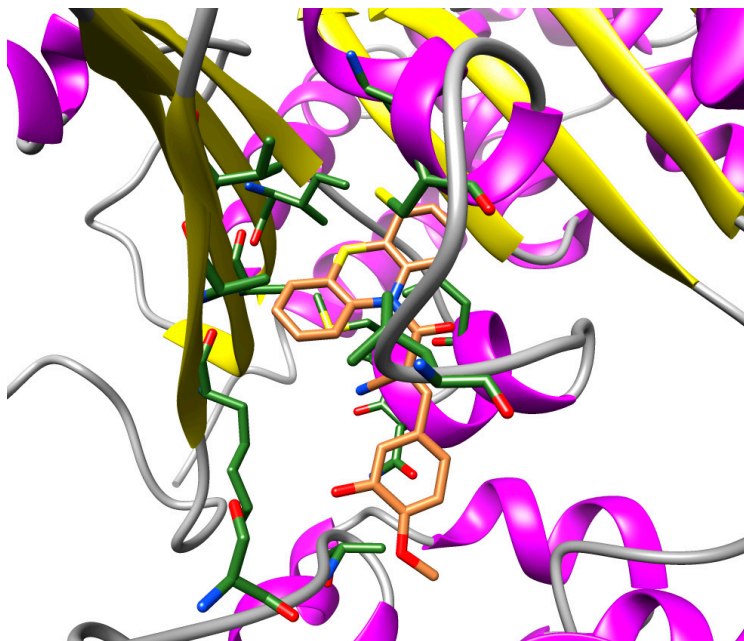


**Docking tubulin (colchicine binding site)**

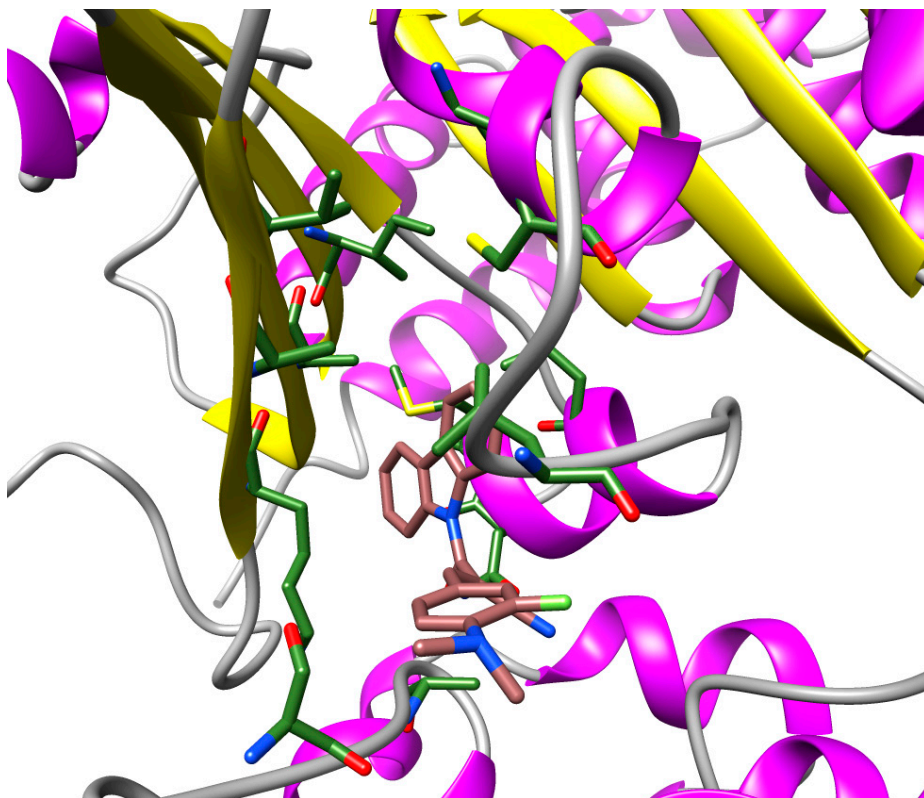
### Compound 11 (40% of the solutions)



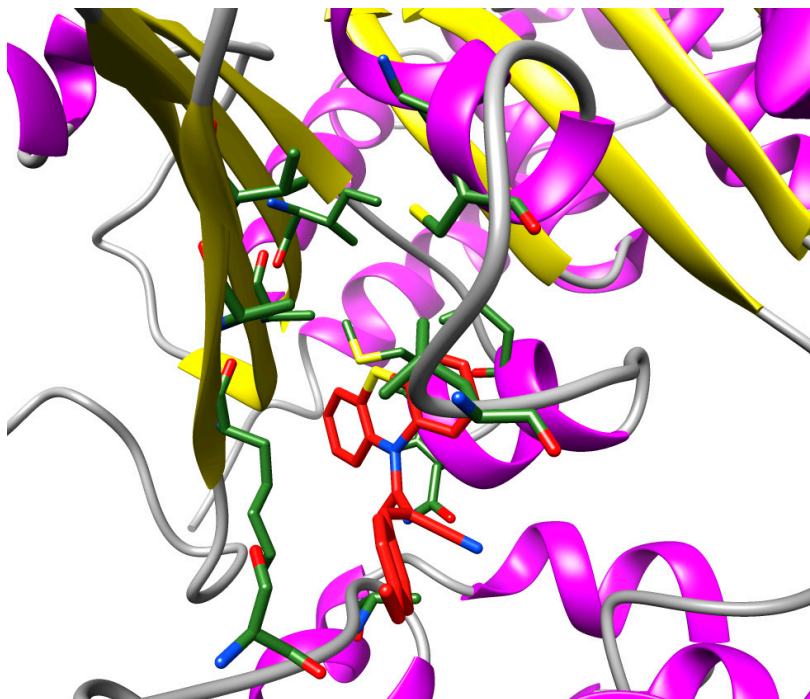
**Compound 11** (60% of the solutions)



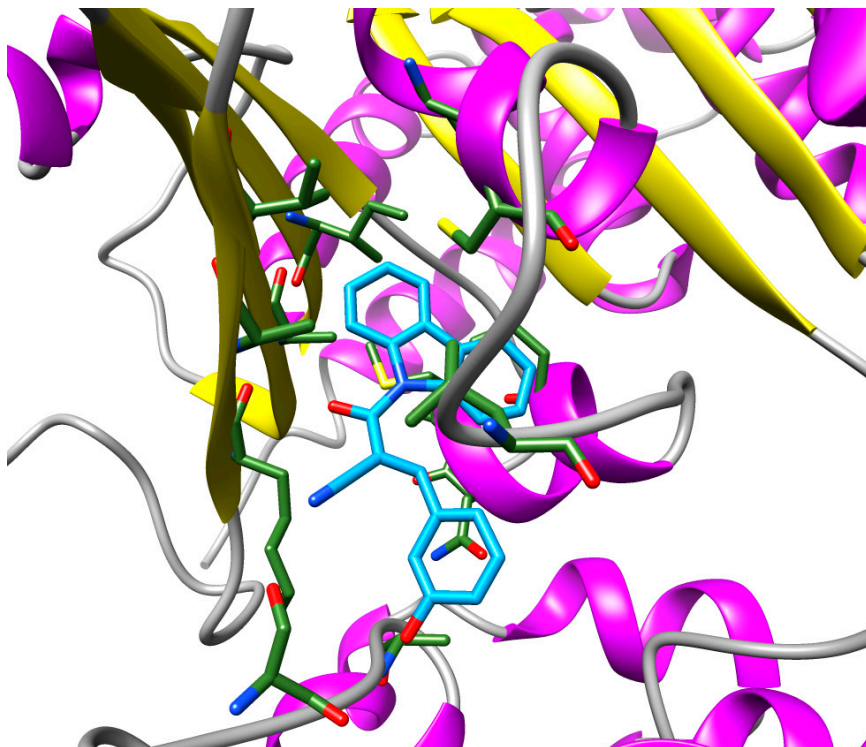
**Compound 3a**



**Compound 3b**

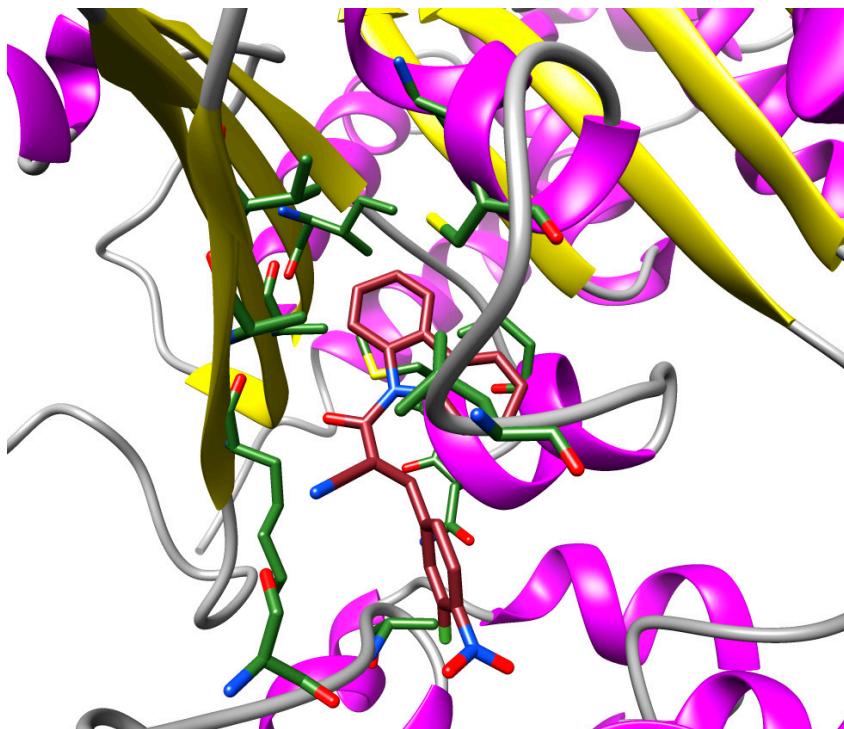


**Compound 3d**

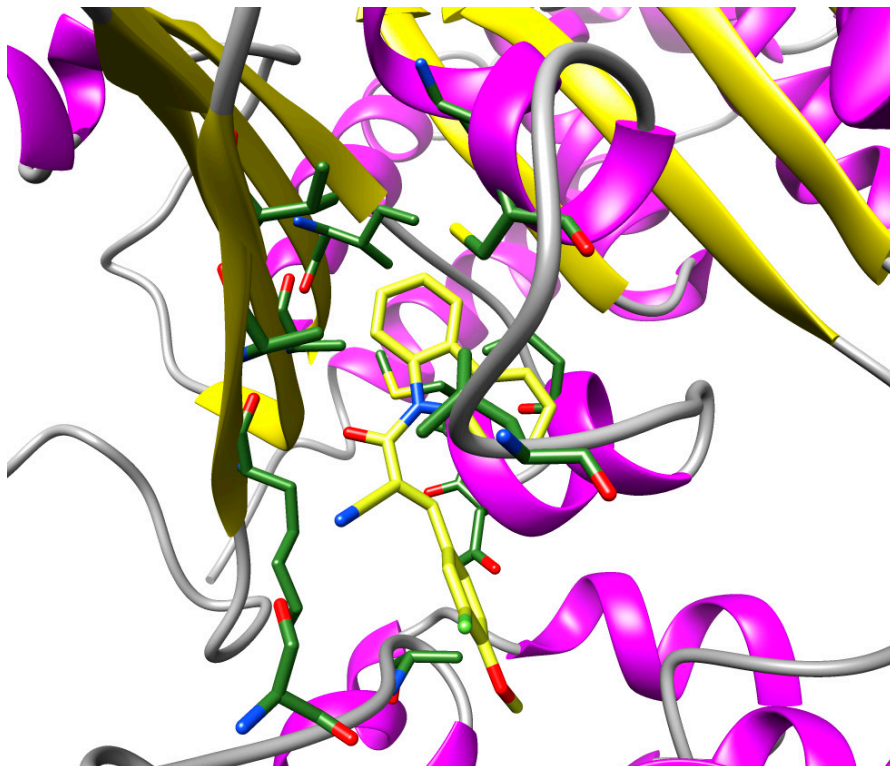




**Compound 3e**

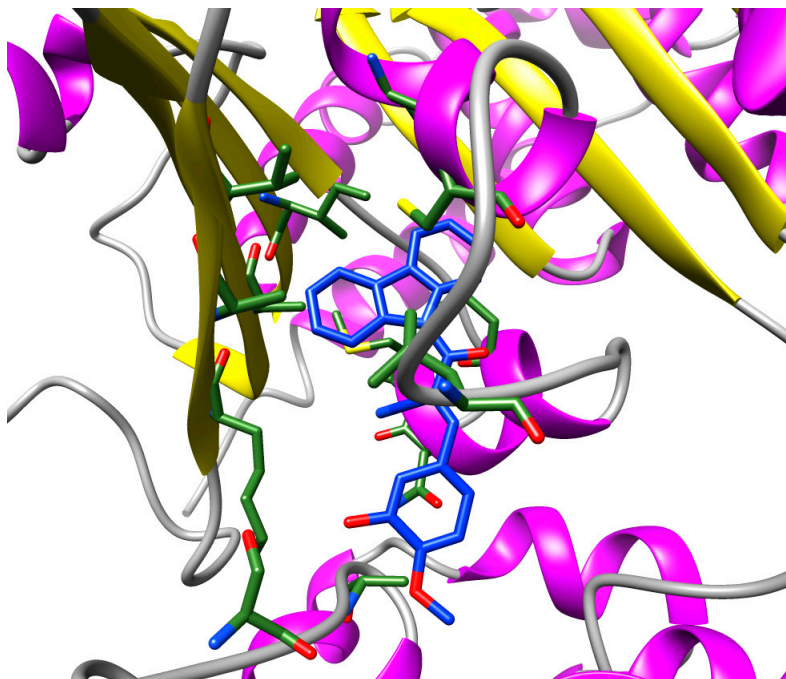


**Compound 3i**

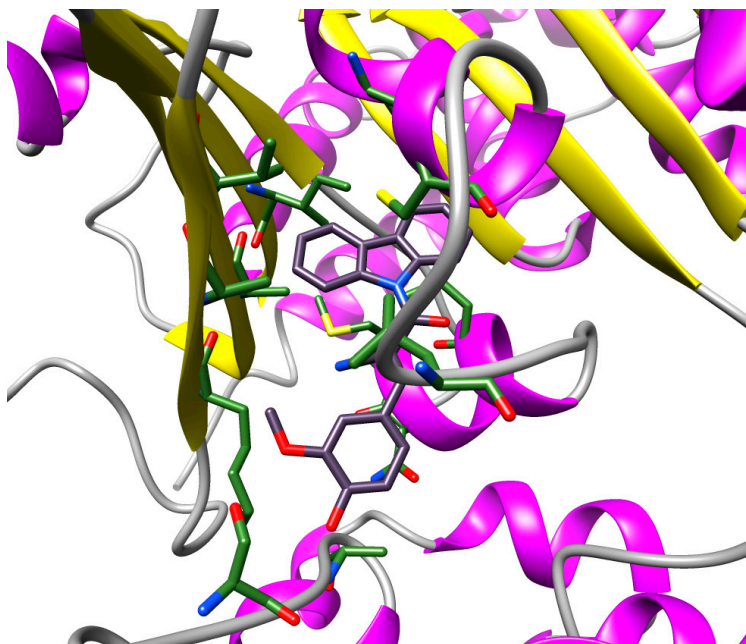




**Compound 3j**



**Compound 3l**



## Phenstatin

