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

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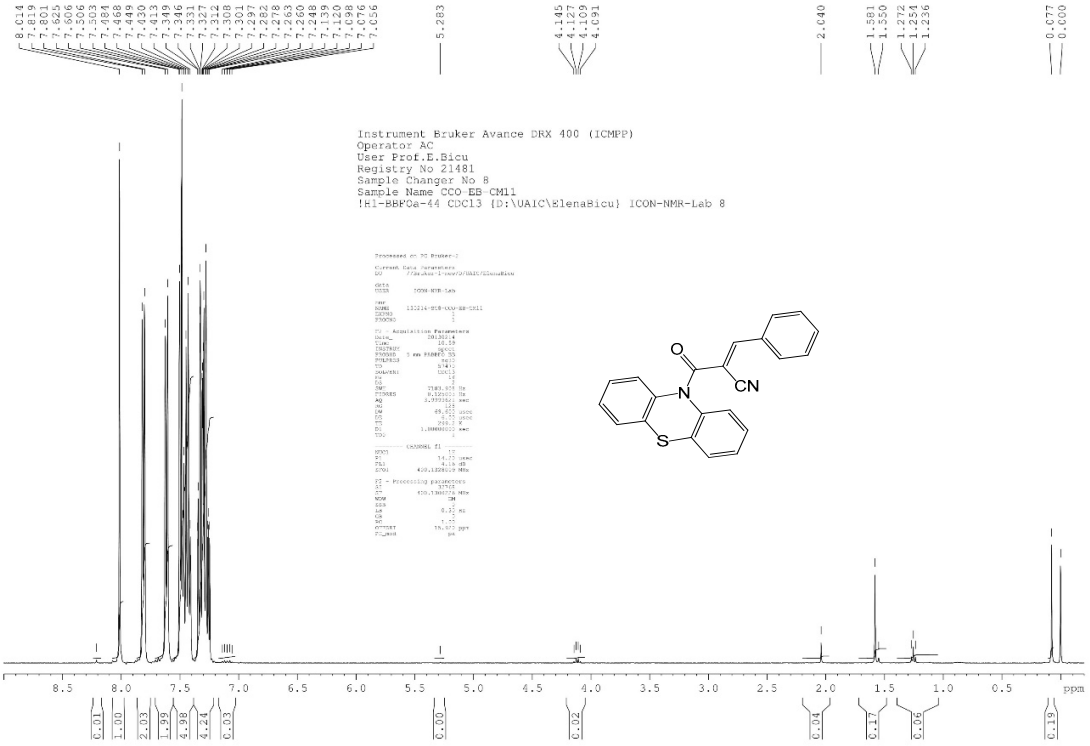
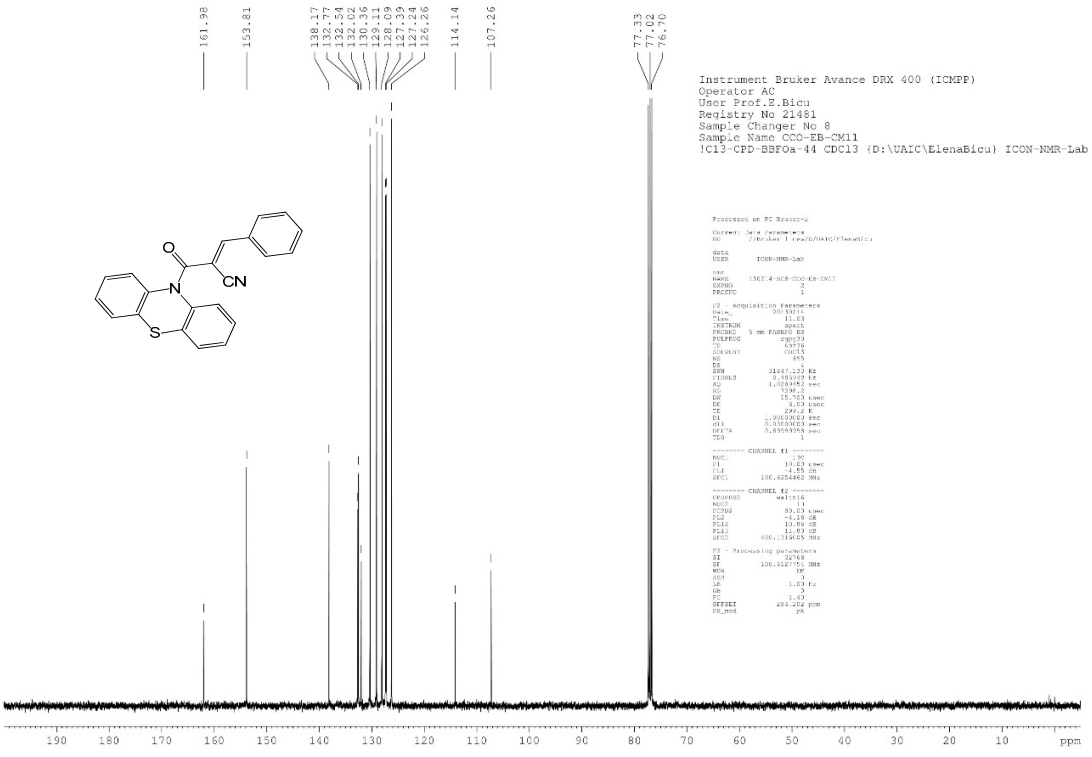
Figure S2. Docking of all dual FTIs/MTIs identified in this study on farnesyltransferase and colchicine binding sites 85

Spectra of compounds

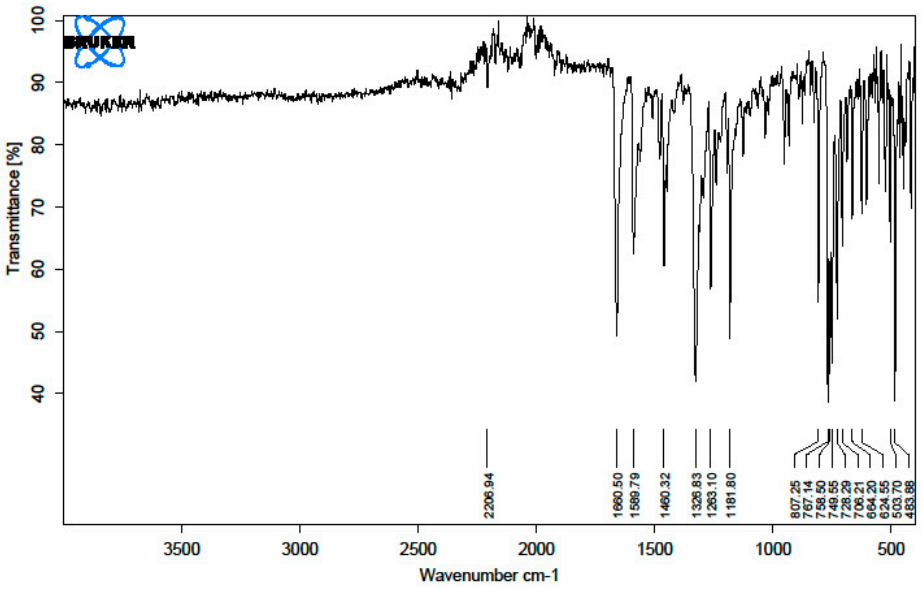
^{1}H NMR (400 MHz, $CDCl_3$)-**1a**



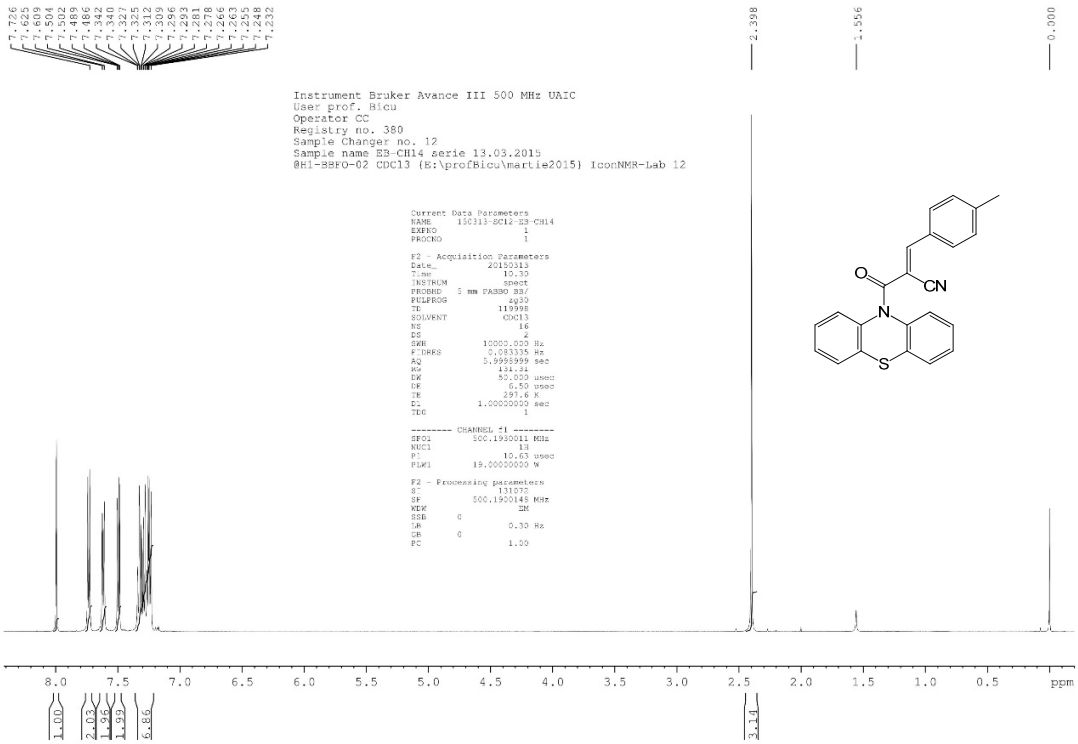
^{13}C NMR (100 MHz, $CDCl_3$)-**1a**



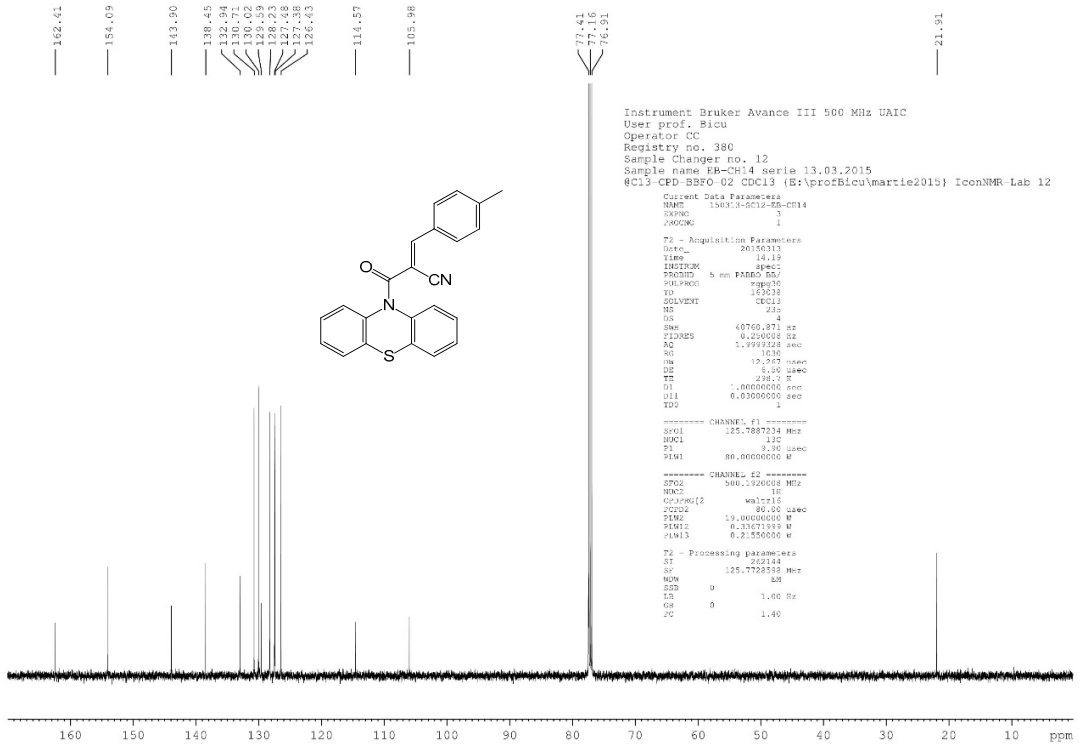
IR-1a



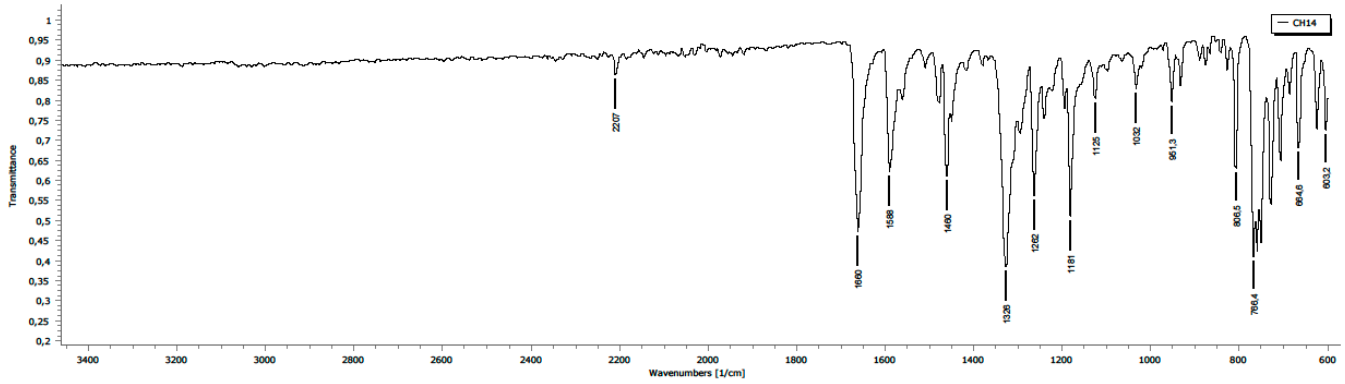
^{1}H NMR (500 MHz, $CDCl_3$)-**1b**



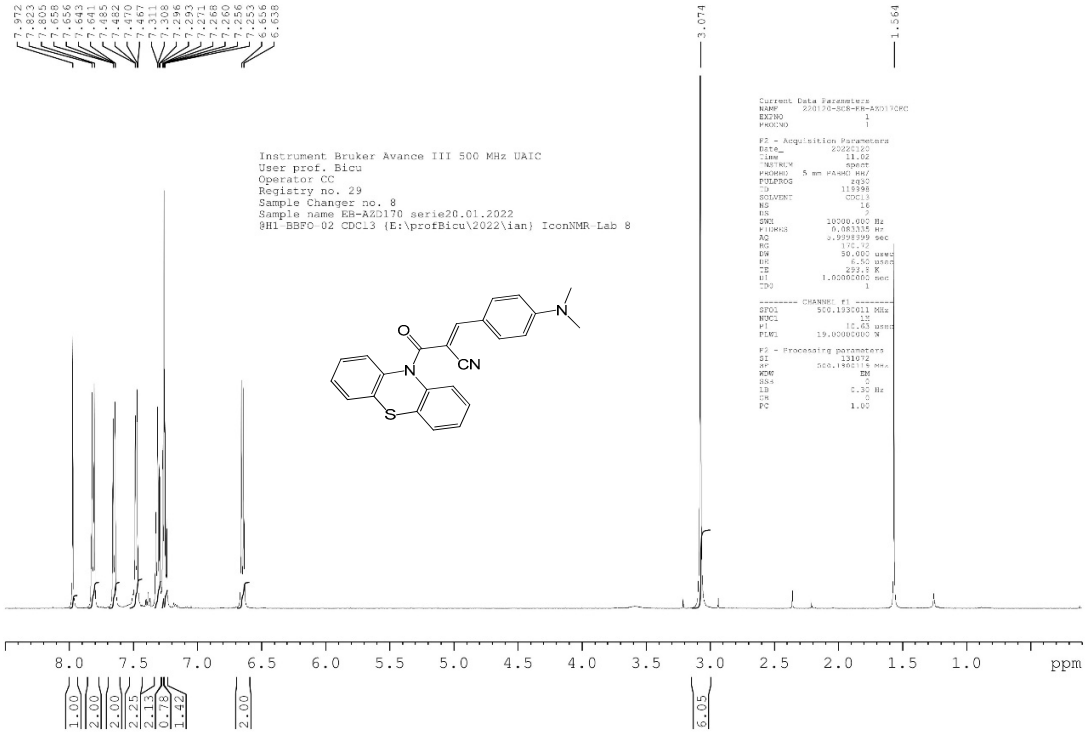
^{13}C NMR (125 MHz, $CDCl_3$)-**1b**



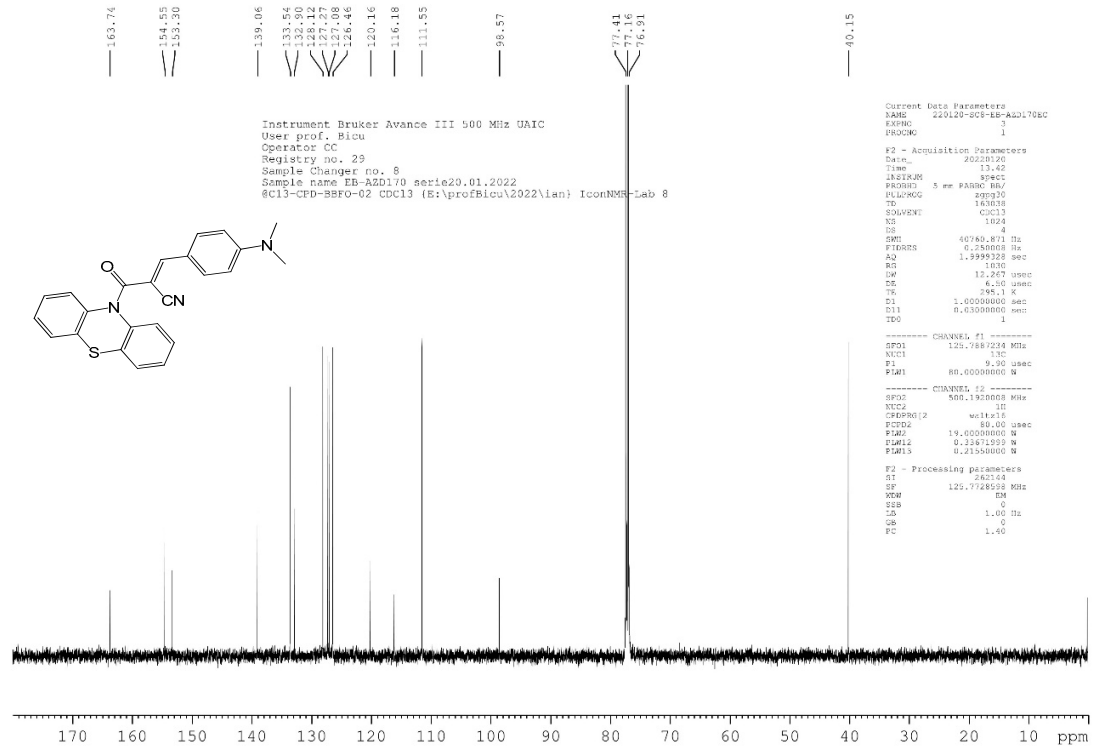
IR-1b



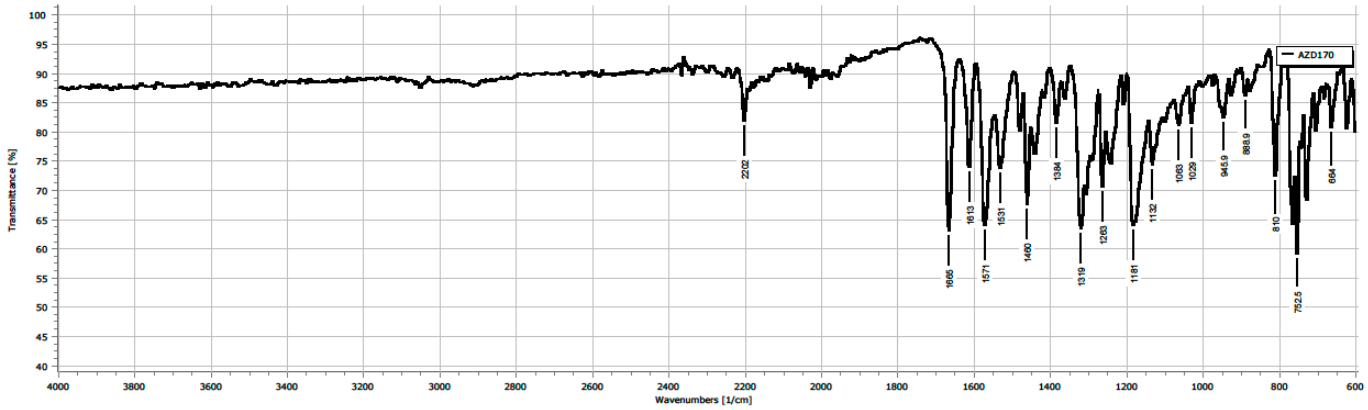
^{1}H NMR (500 MHz, $CDCl_3$)-**1c**



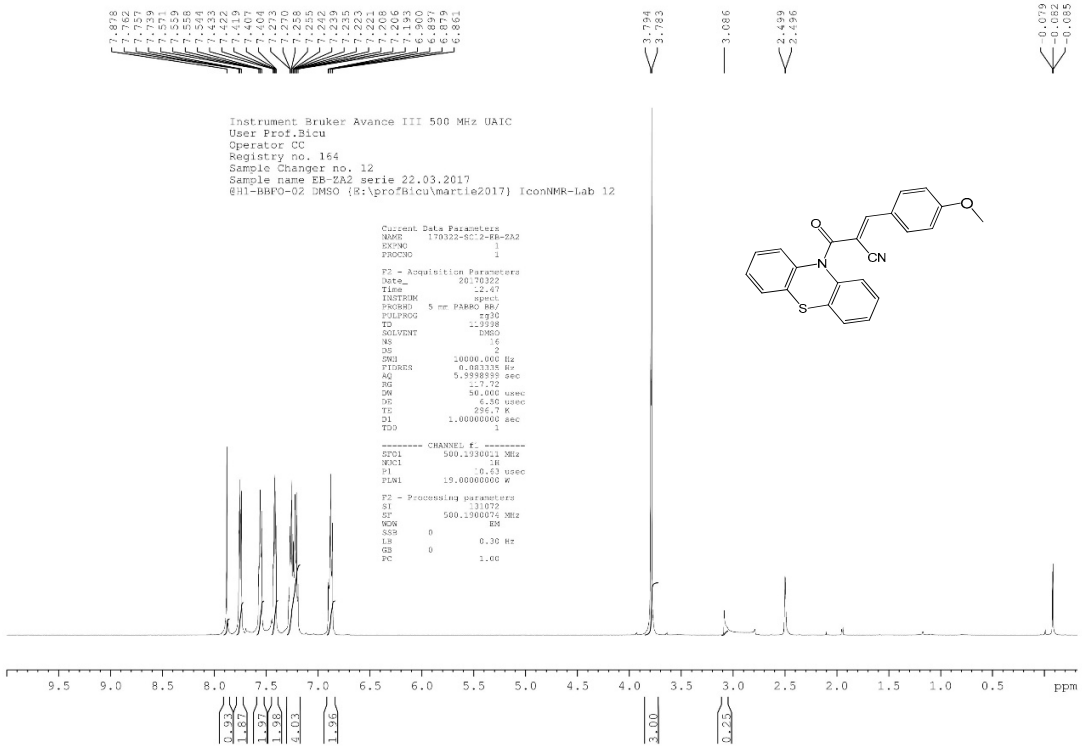
^{13}C NMR (125 MHz, $CDCl_3$)-**1c**



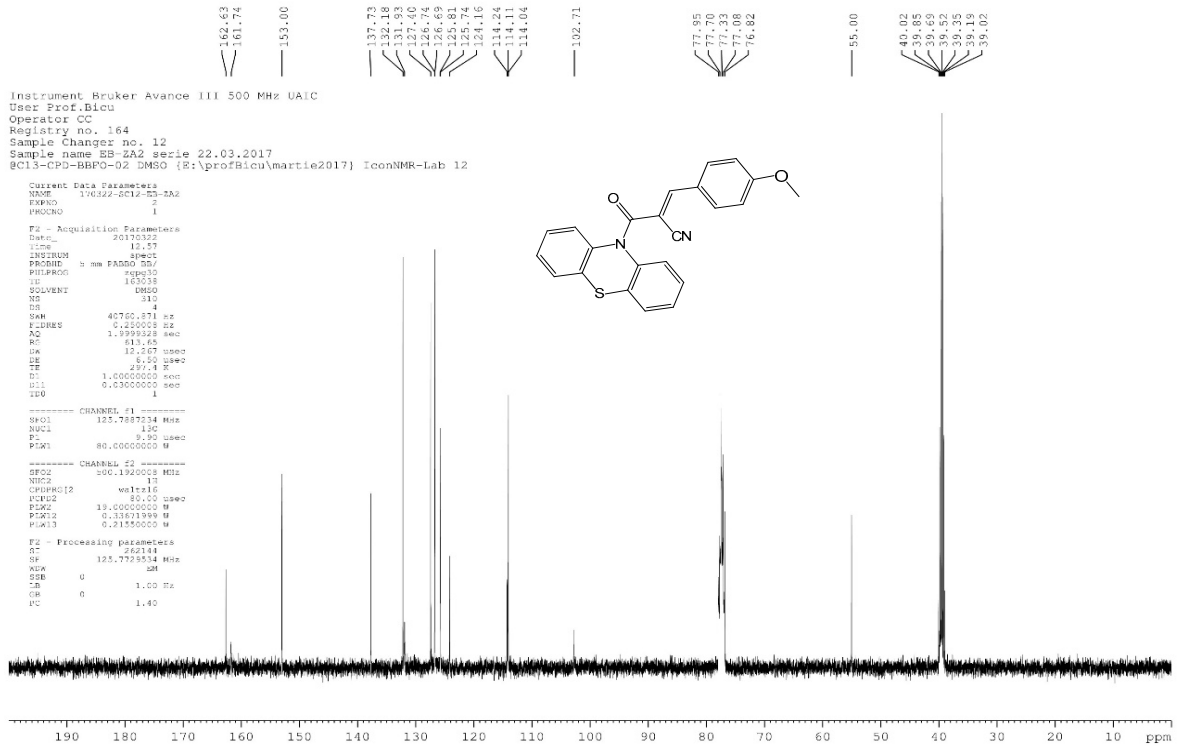
IR-1c



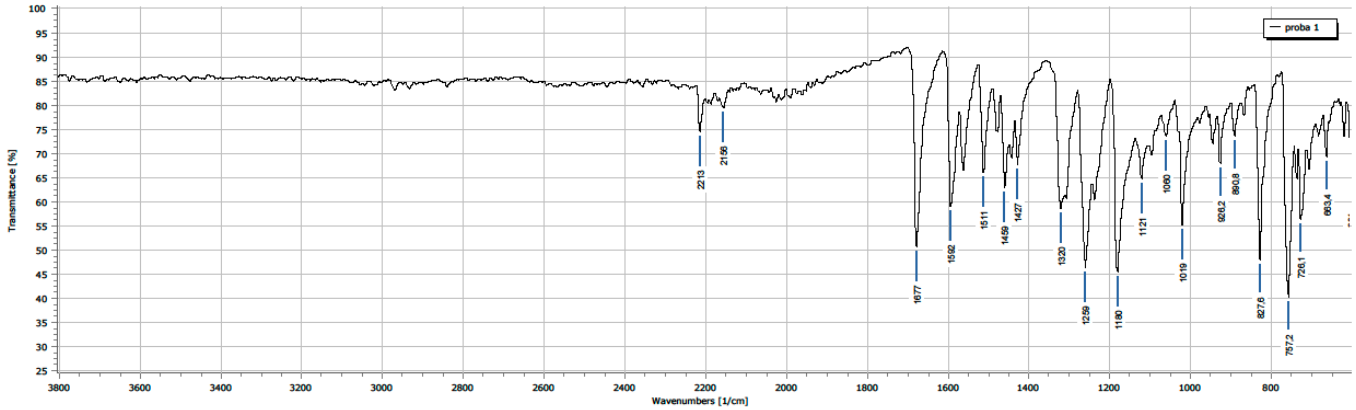
^{1}H NMR (500 MHz, $CDCl_3$)-**1d**



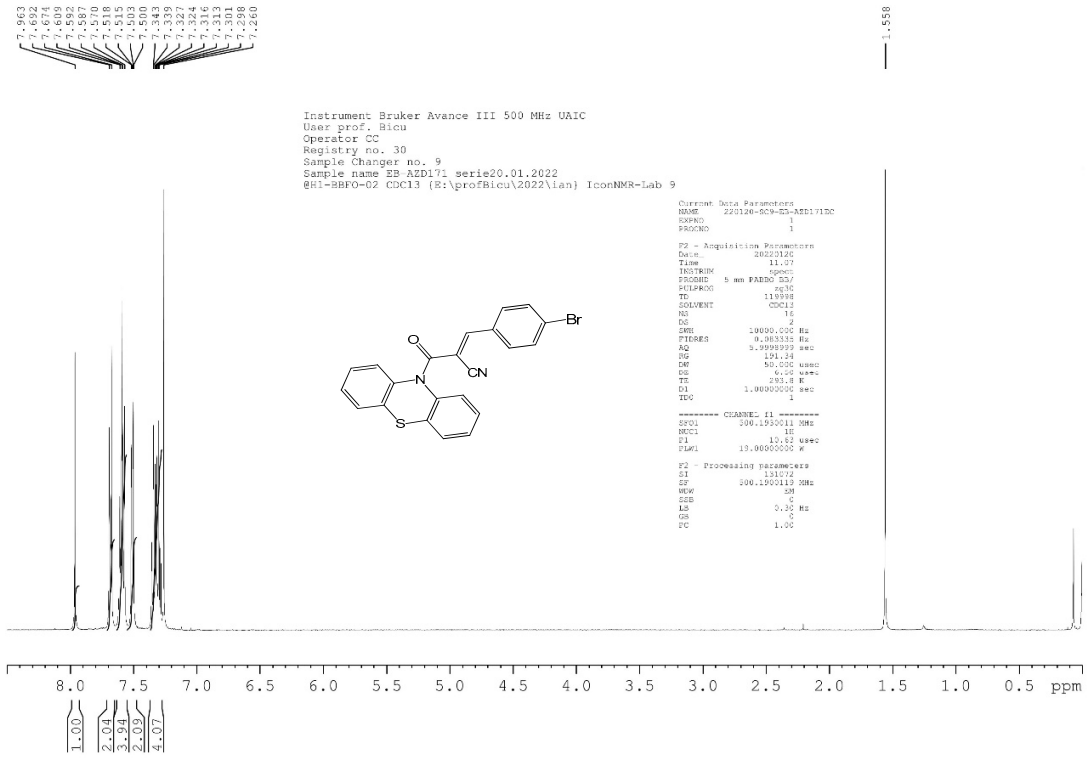
^{13}C NMR (125 MHz, $CDCl_3$)-**1d**



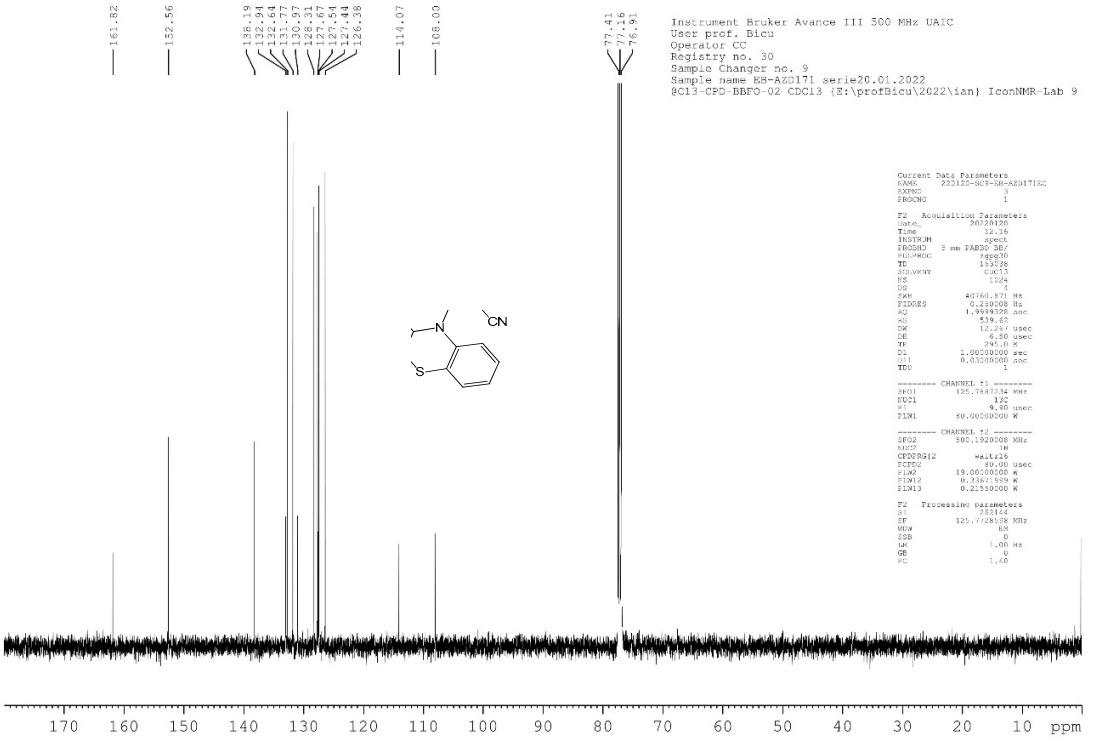
IR-1d



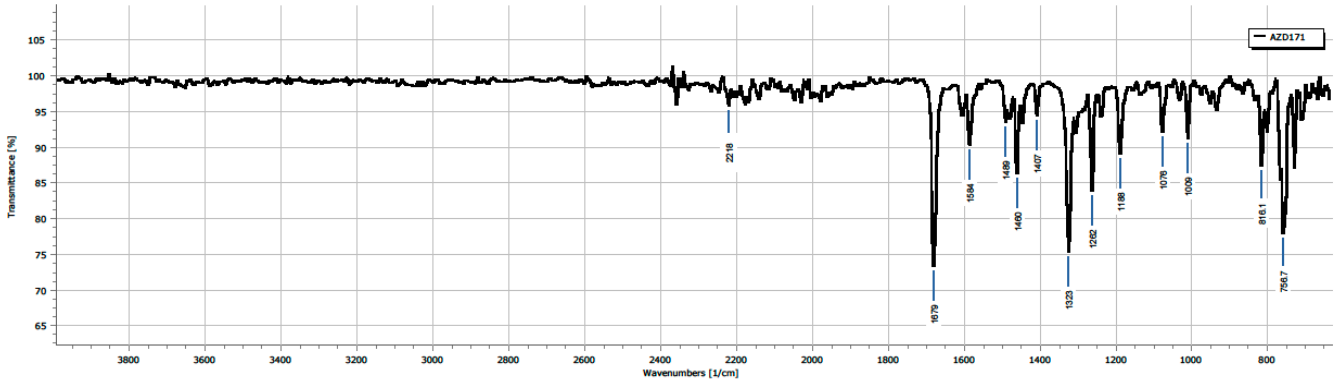
^{1}H NMR (500 MHz, $CDCl_3$)-**1e**



^{13}C NMR (125 MHz, $CDCl_3$)-**1e**



IR-1e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Wavenumbers [1/cm]
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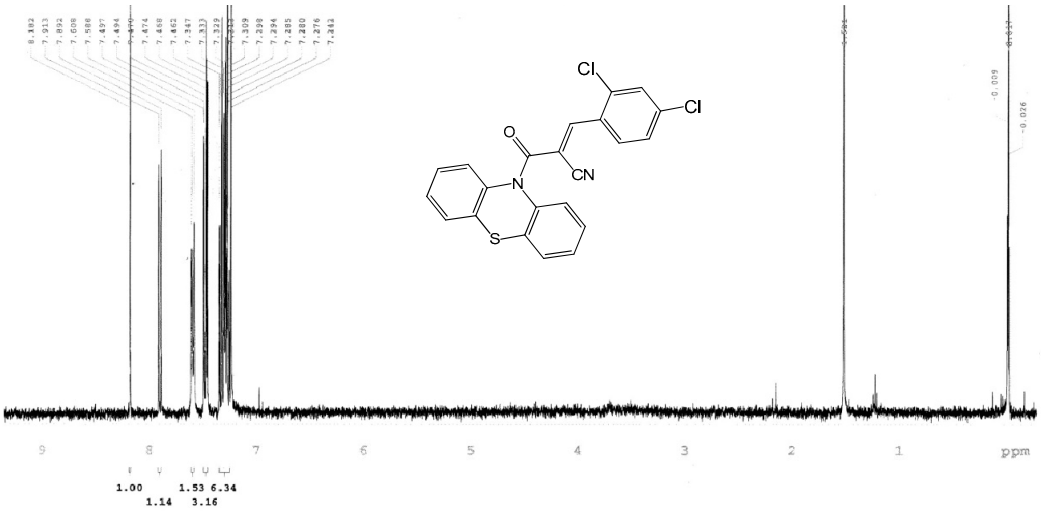
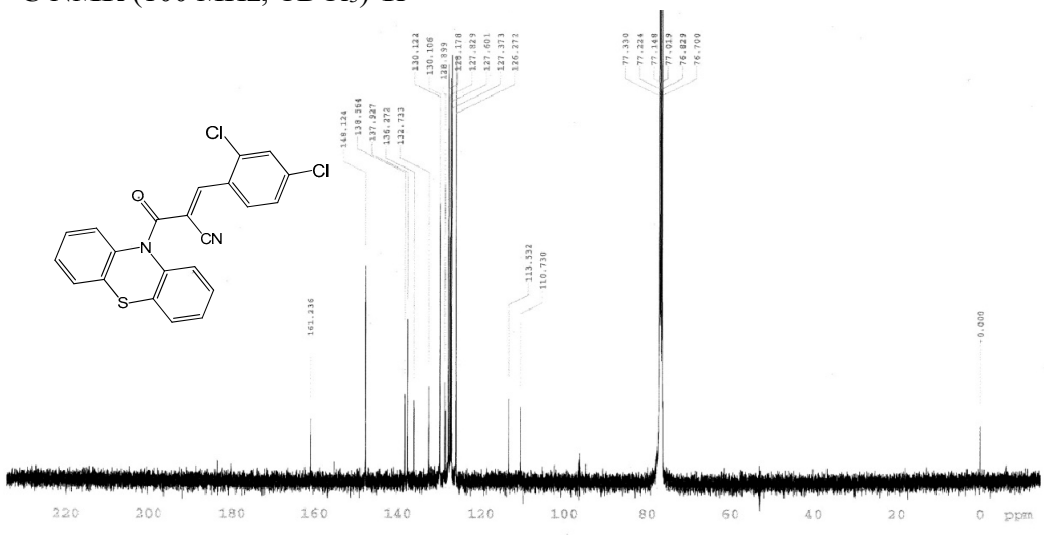
1188
1076
1009
816.1
756.7
679

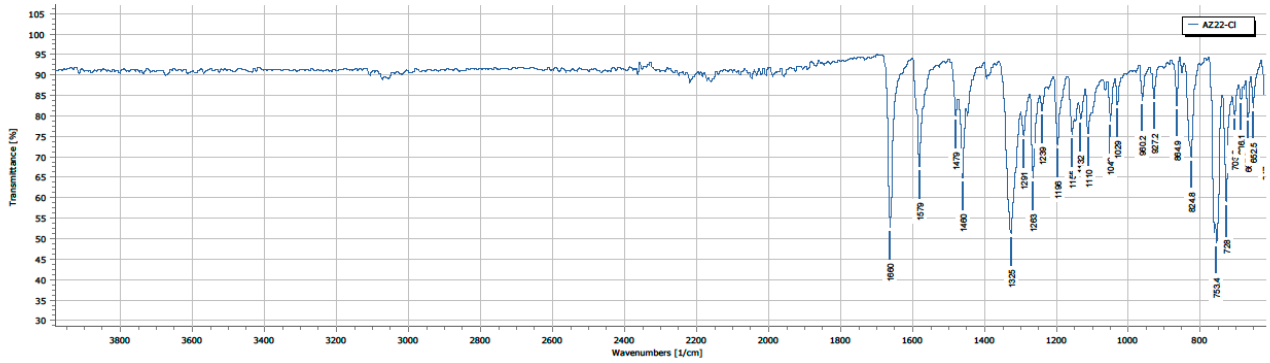
^{1}H NMR (400 MHz, $CDCl_3$)-**1f**



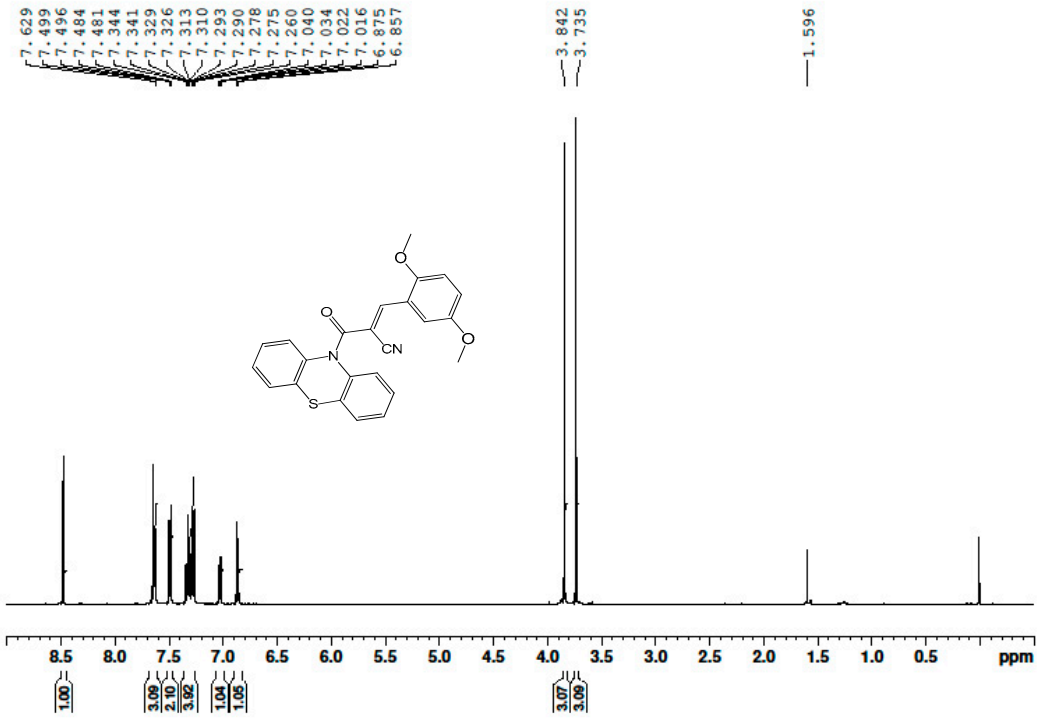
^{13}C NMR (100 MHz, $CDCl_3$)-**1f**



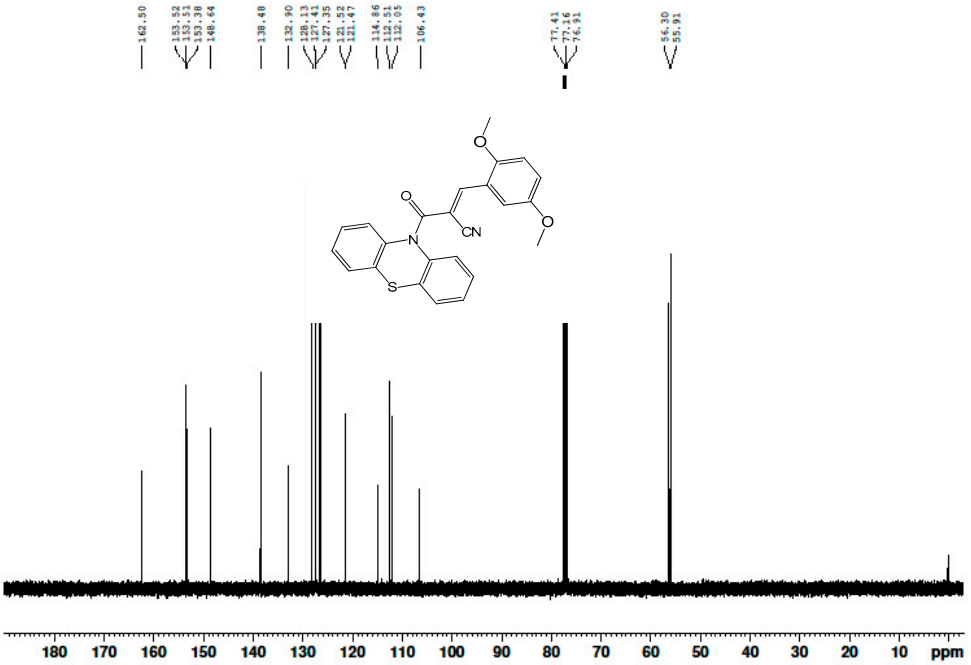
IR-1f



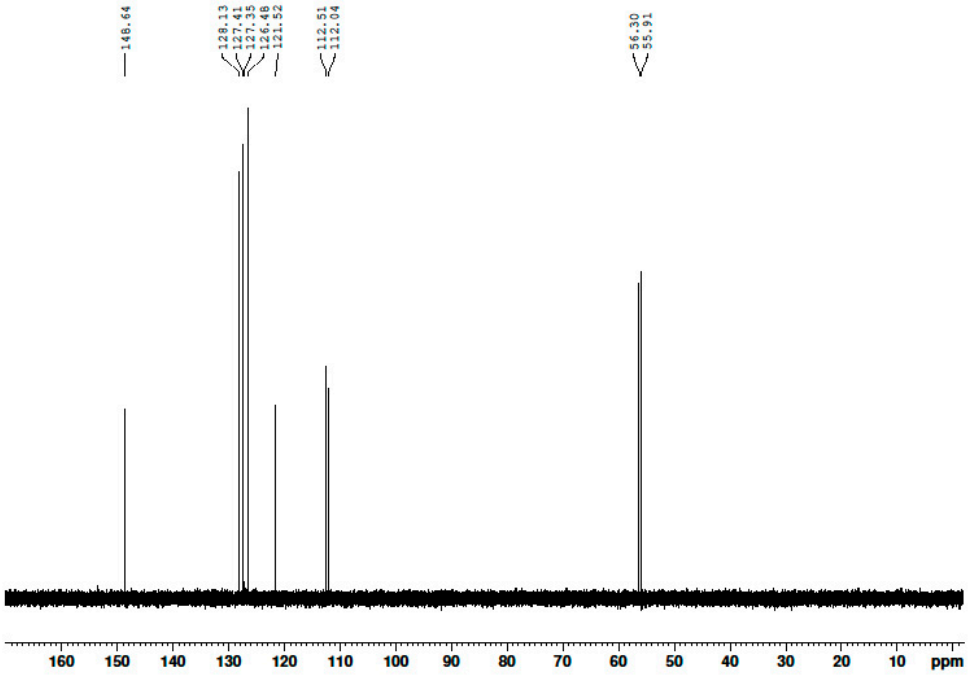
^{1}H NMR (500 MHz, $CDCl_3$)-**1g**



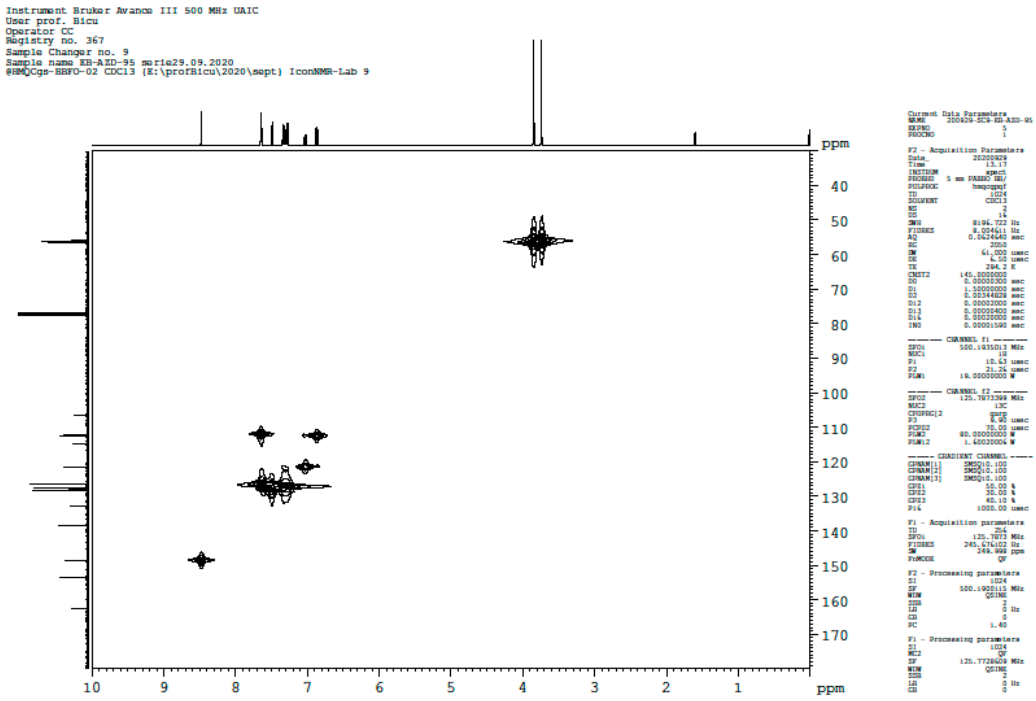
^{13}C NMR (125 MHz, $CDCl_3$)-**1g**



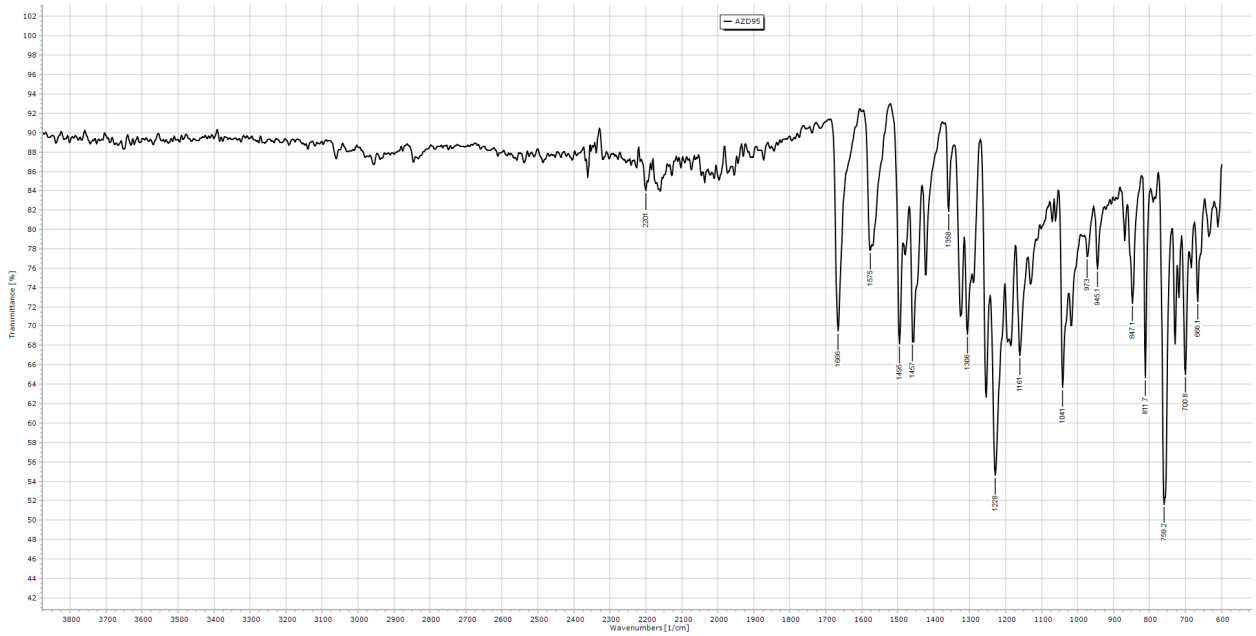
^{13}C-DEPT NMR (125 MHz, $CDCl_3$)-**1g**



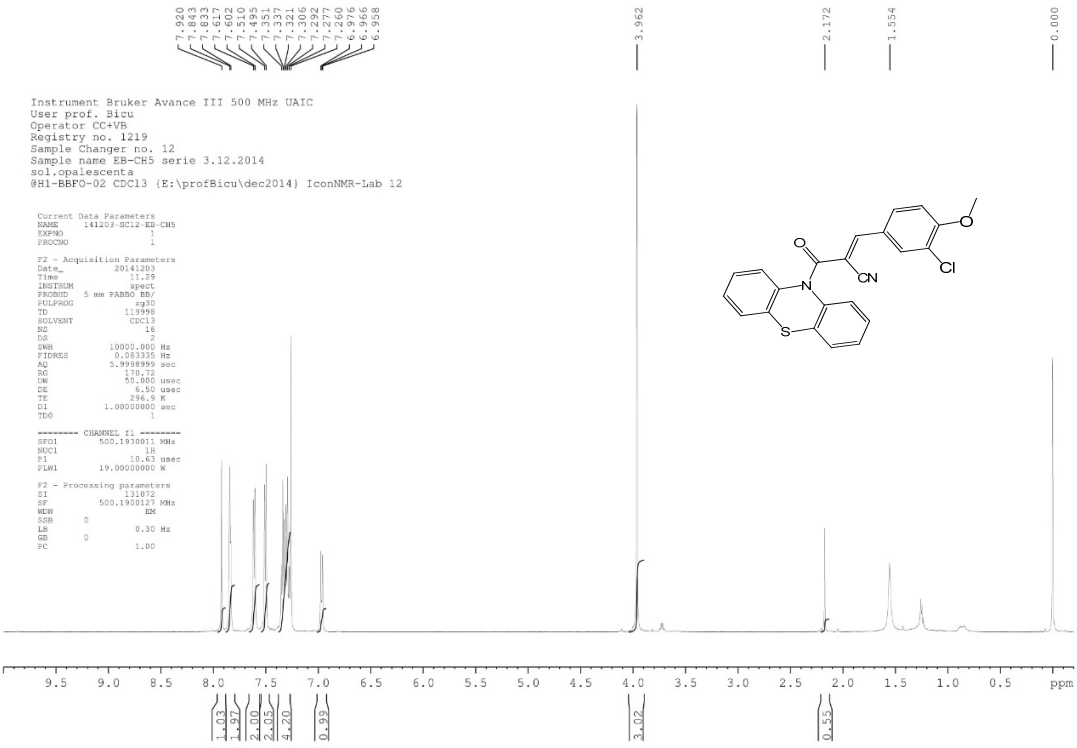
HMQC NMR (500 MHz, $CDCl_3$)-**1g**



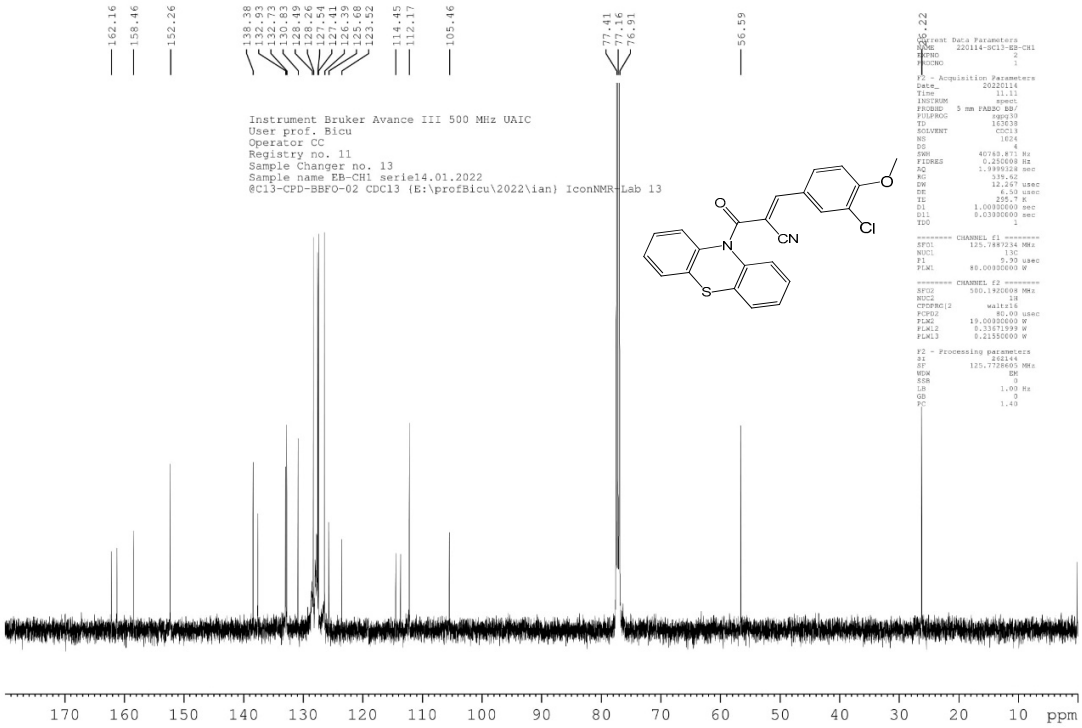
IR-1g



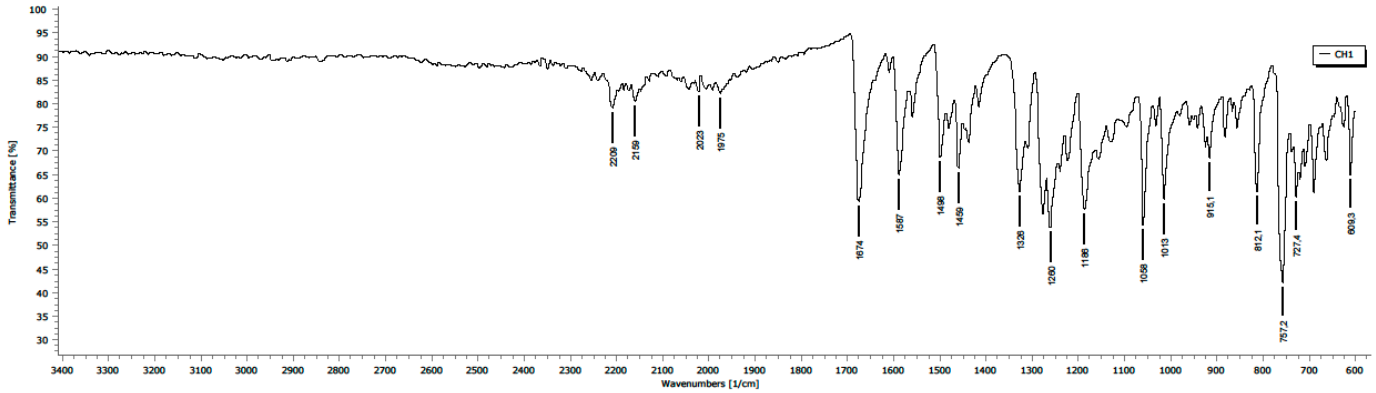
^{1}H NMR (500 MHz, $CDCl_3$)- **1h**



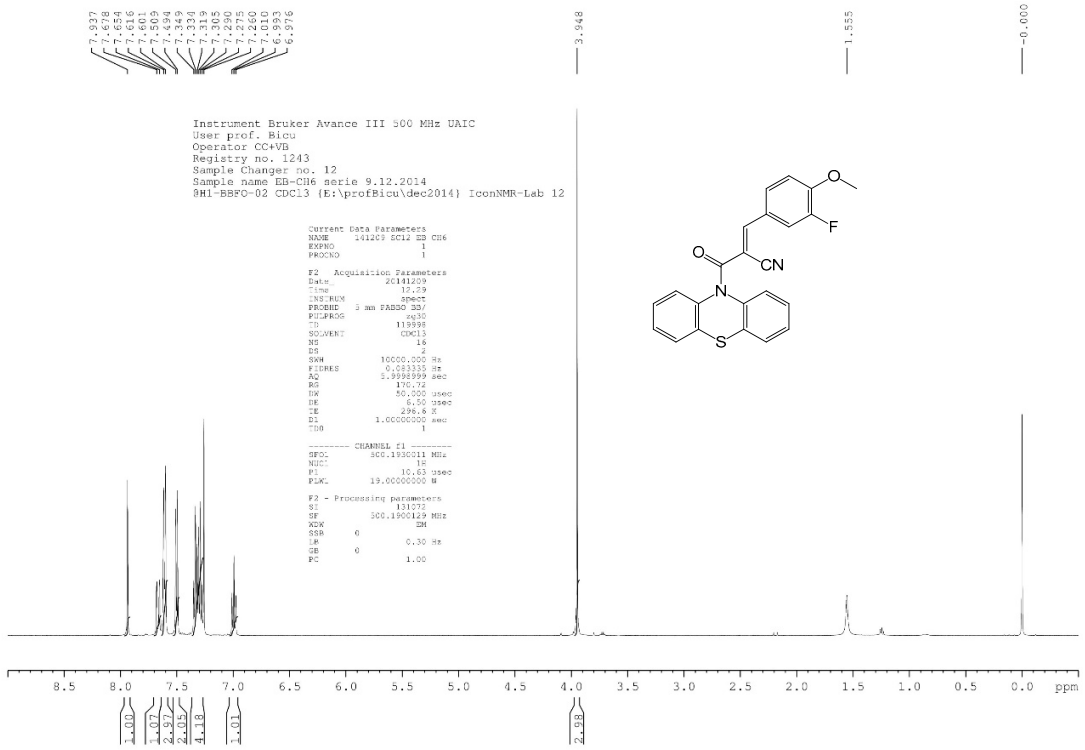
^{13}C NMR (125 MHz, $CDCl_3$)-**1h**



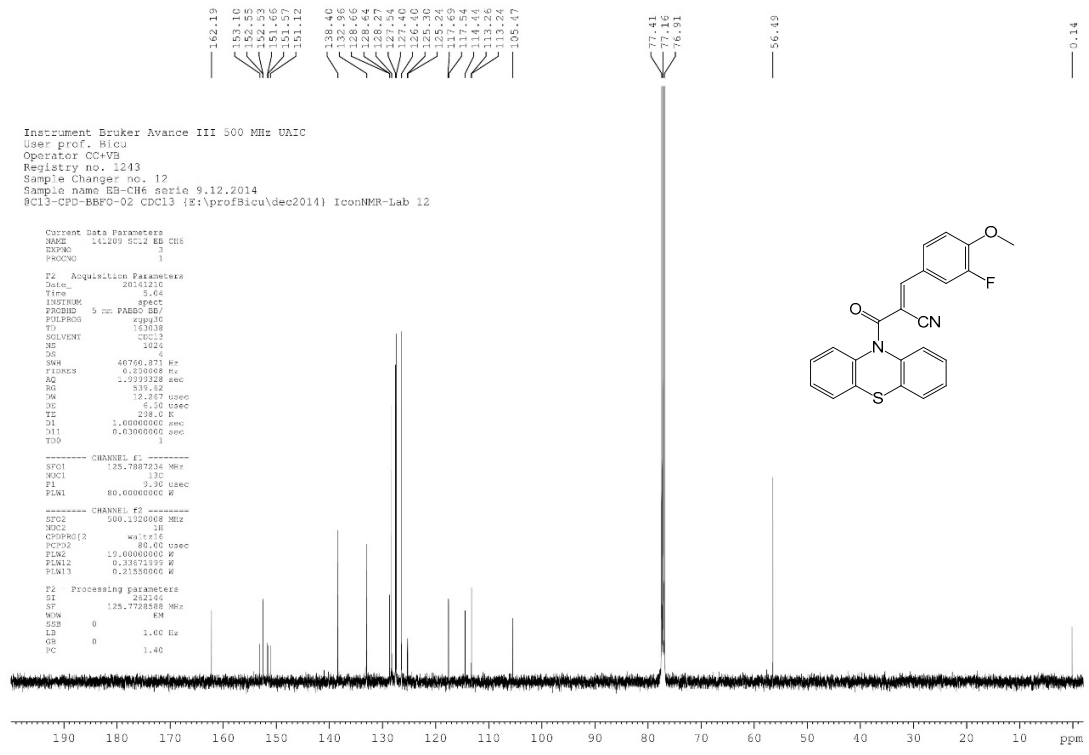
IR-1h



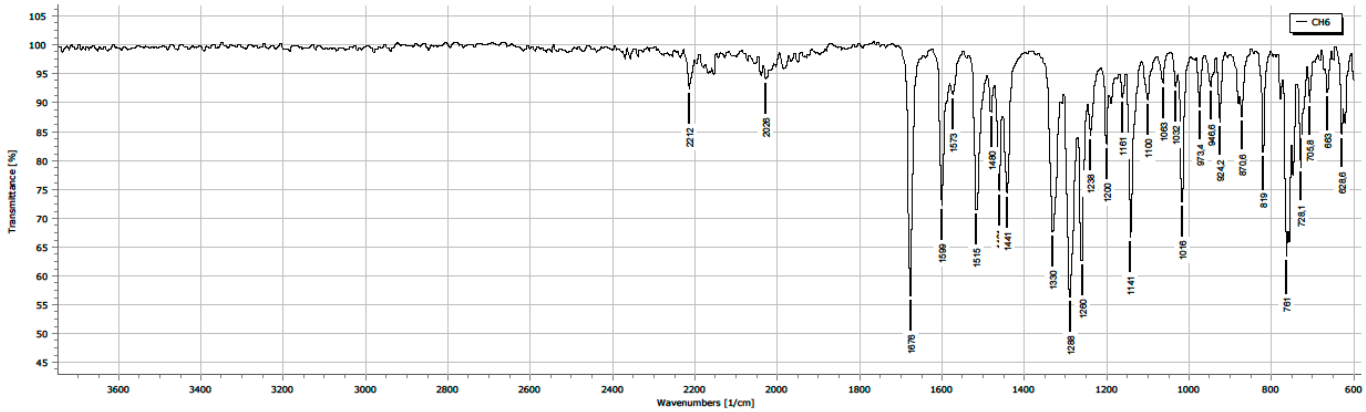
^{1}H NMR (500 MHz, $CDCl_3$)- **1i**



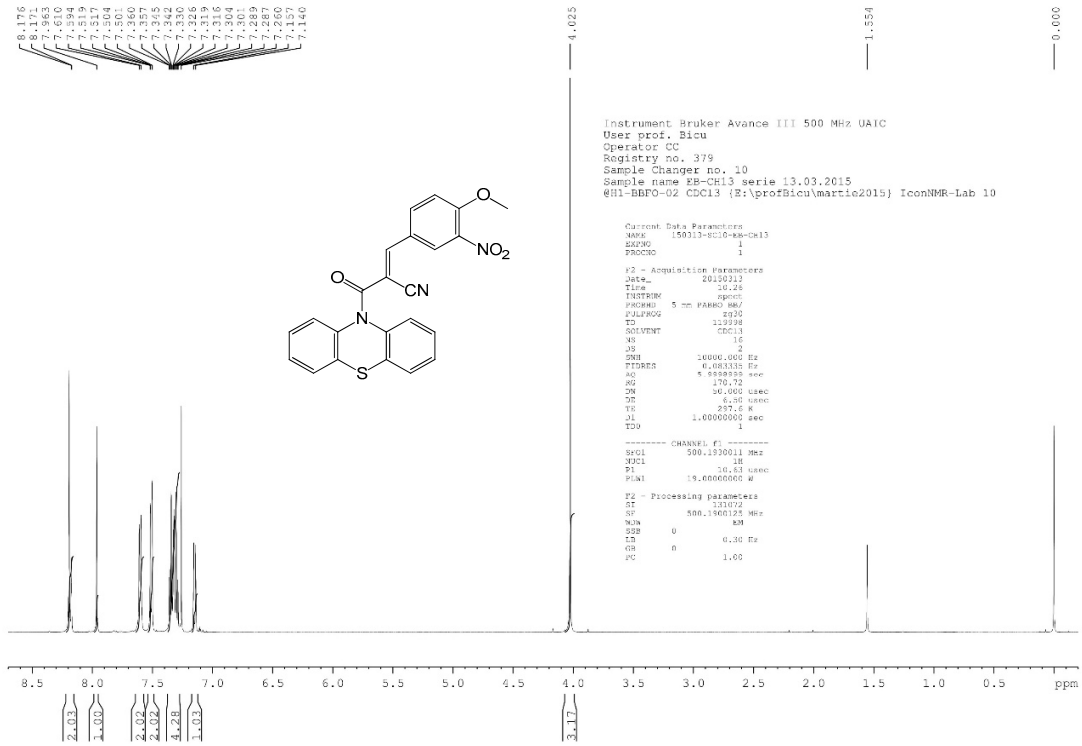
^{13}C NMR (125 MHz, $CDCl_3$)-**1i**



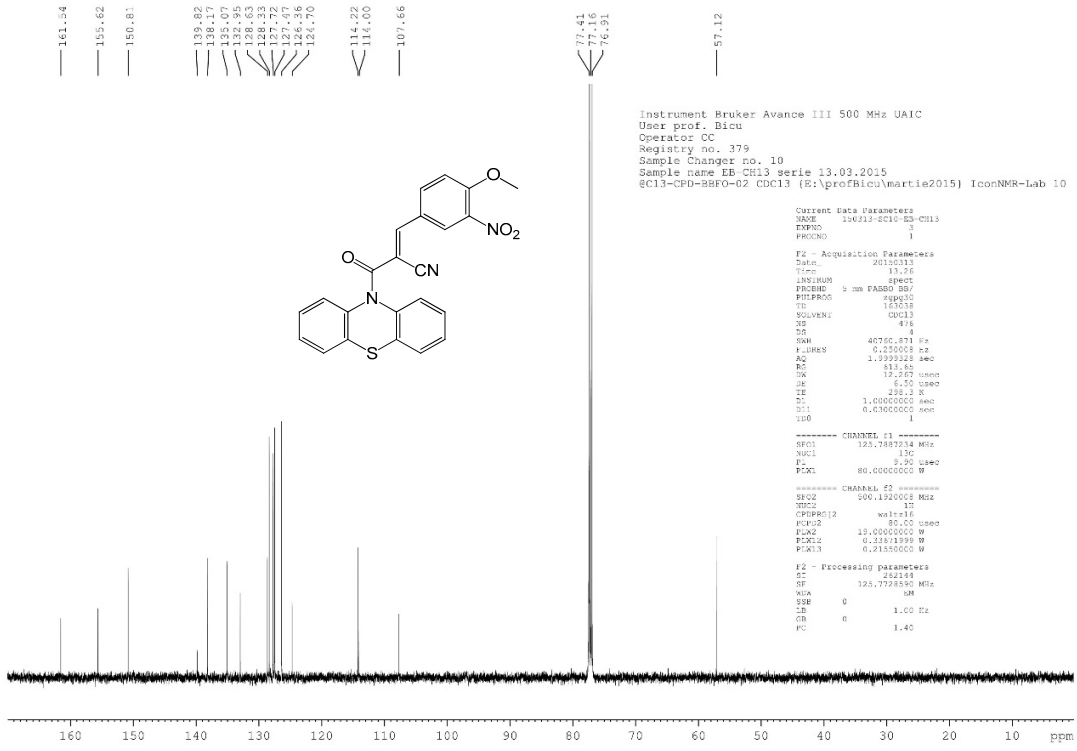
IR-1i



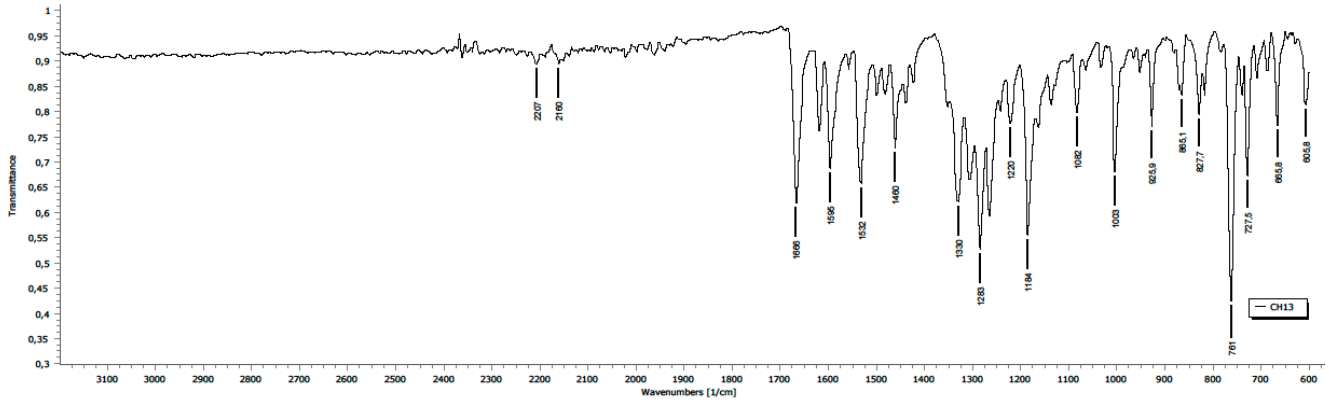
^{1}H NMR (500 MHz, $CDCl_3$)- **1j**



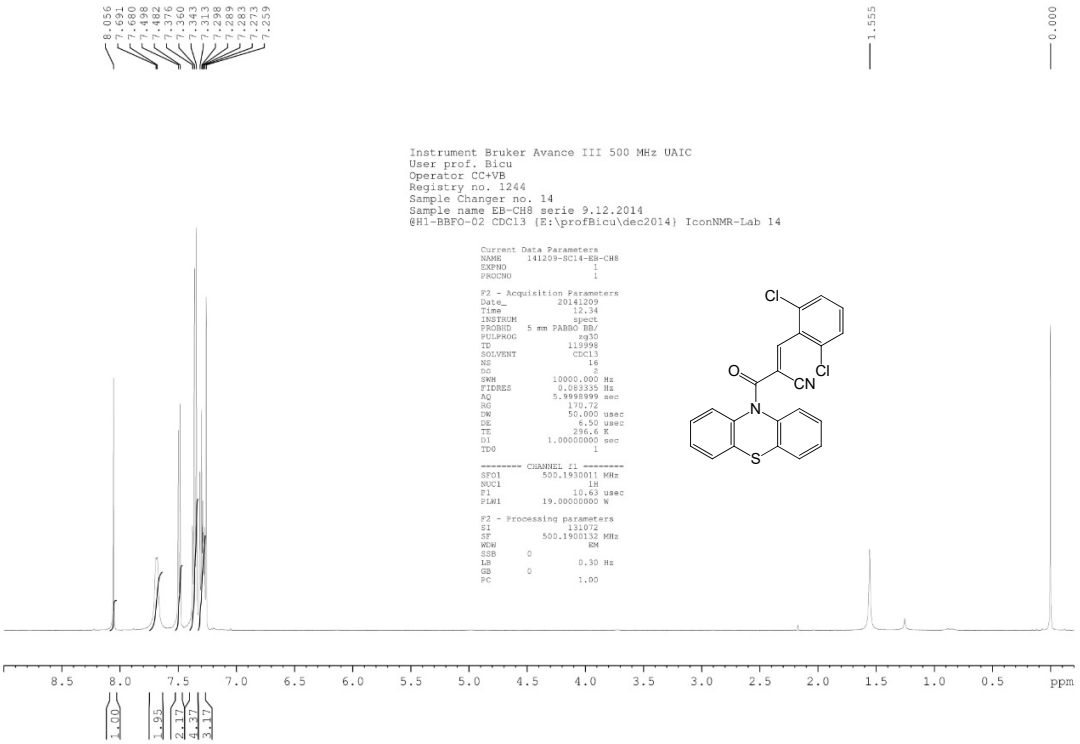
^{13}C NMR (125 MHz, $CDCl_3$)-**1j**



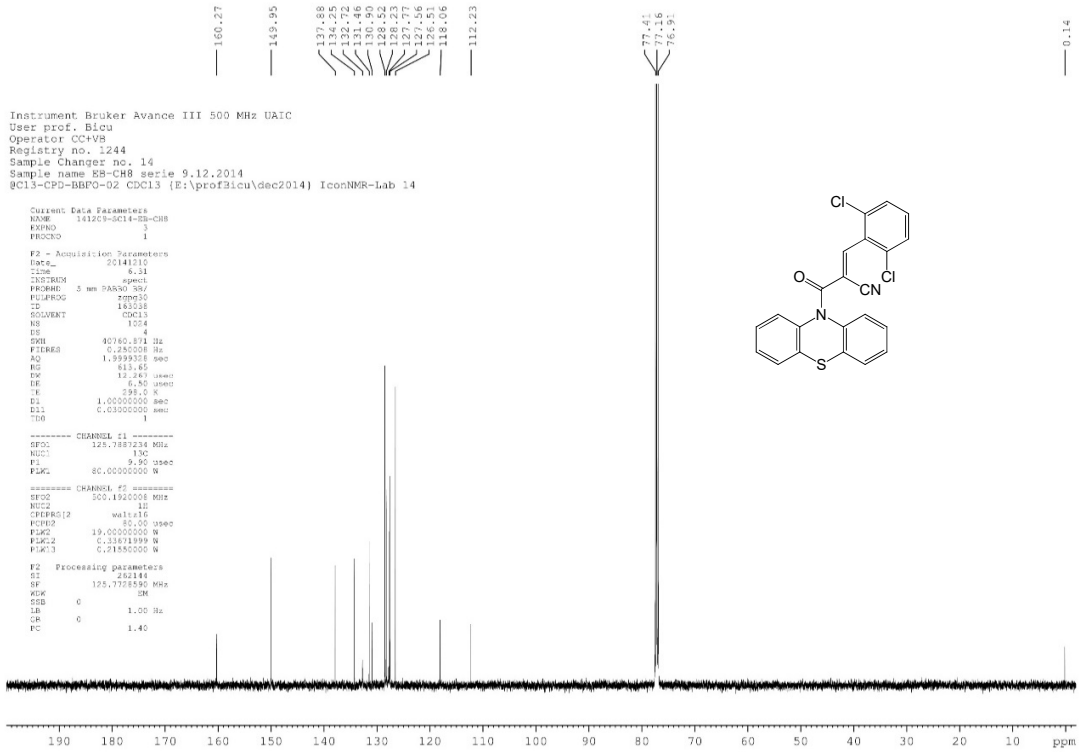
IR-1j



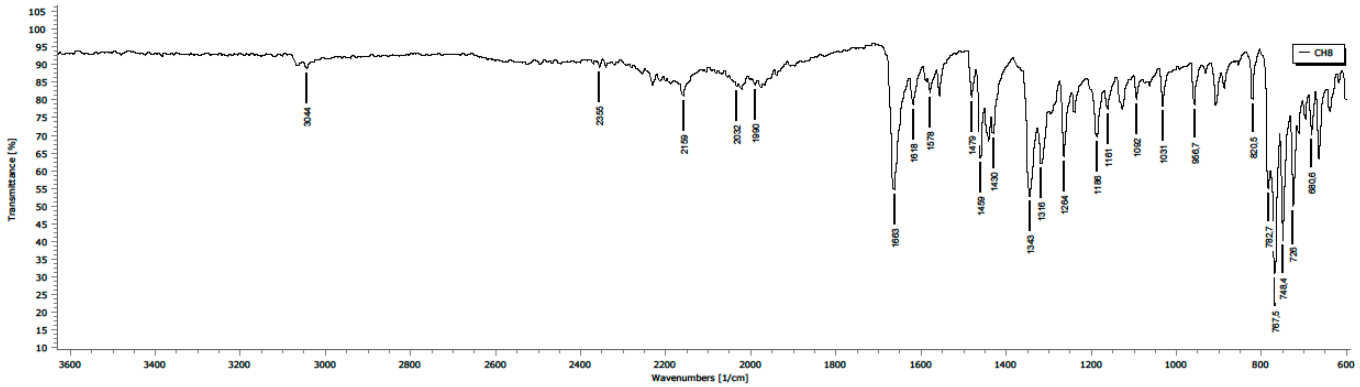
^{1}H NMR (500 MHz, $CDCl_3$)- **1k**



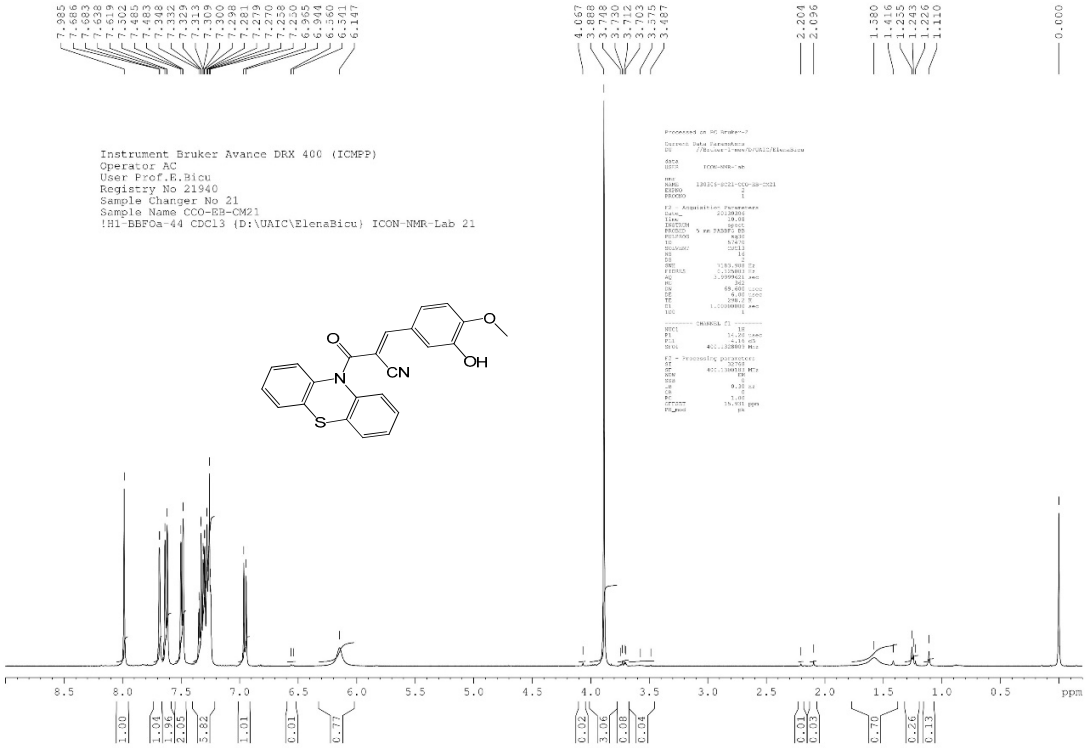
^{13}C NMR (125 MHz, $CDCl_3$)-**1k**



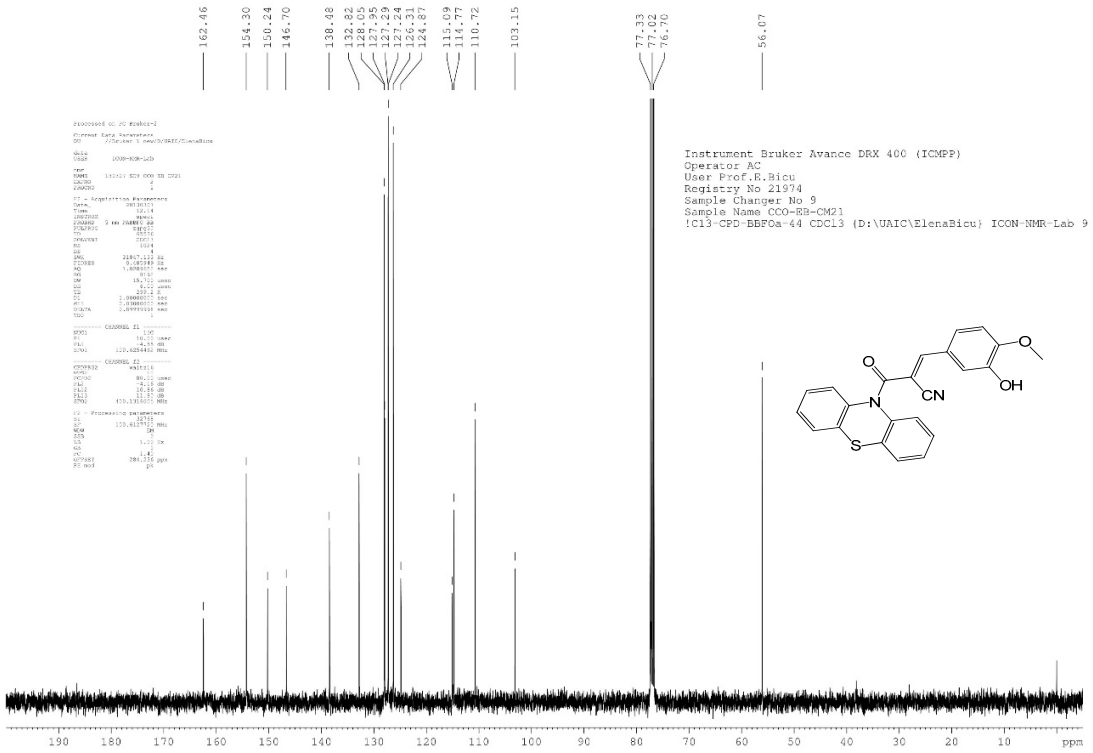
IR-1k



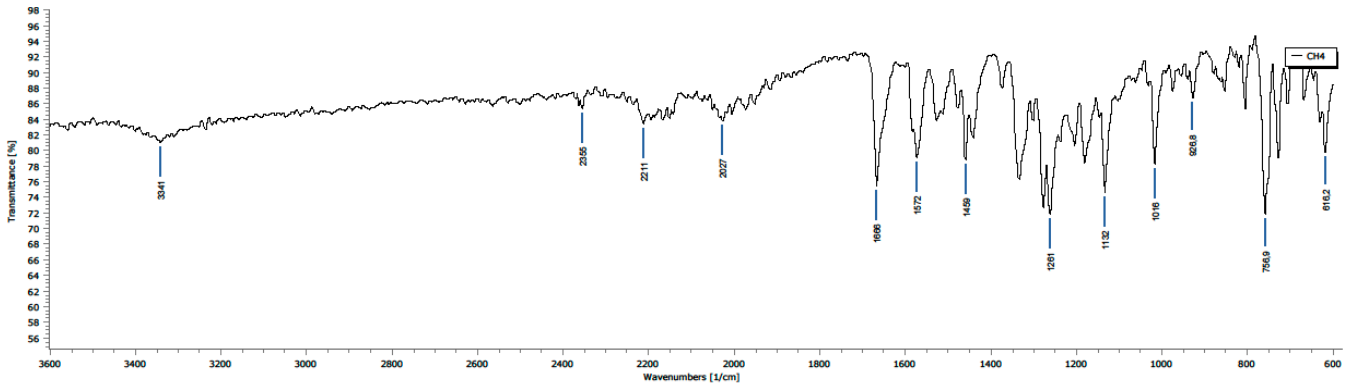
^{1}H NMR (400 MHz, $CDCl_3$)- **1l**



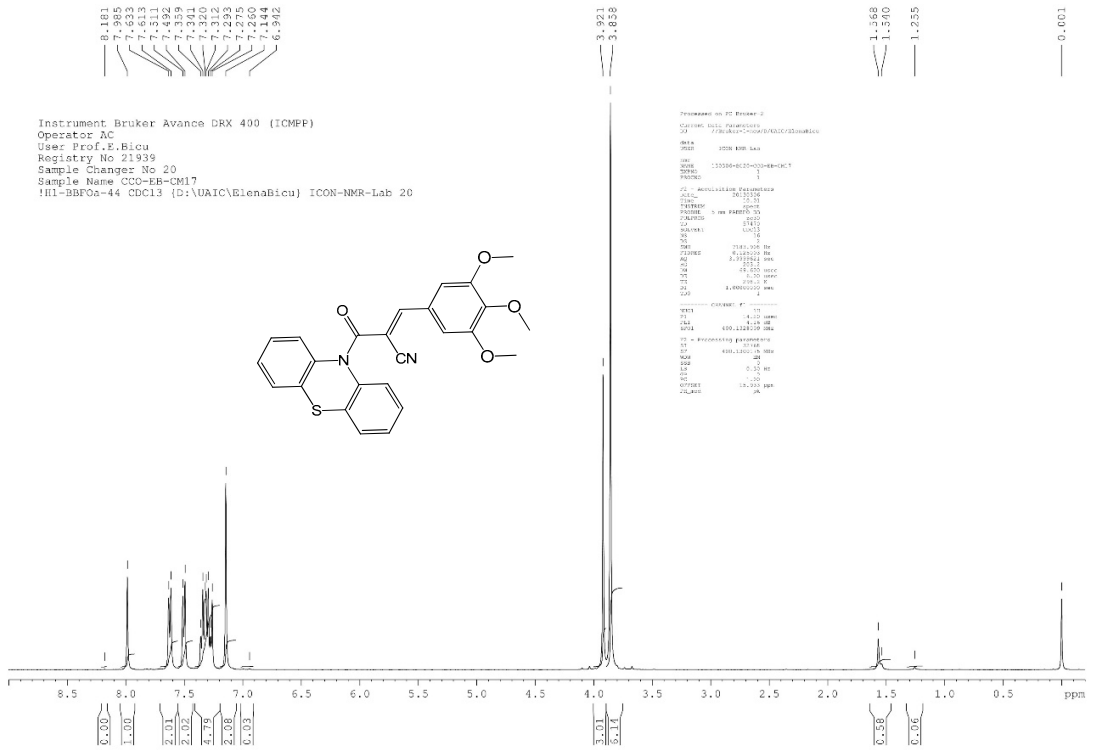
^{13}C NMR (100 MHz, $CDCl_3$)-**1l**



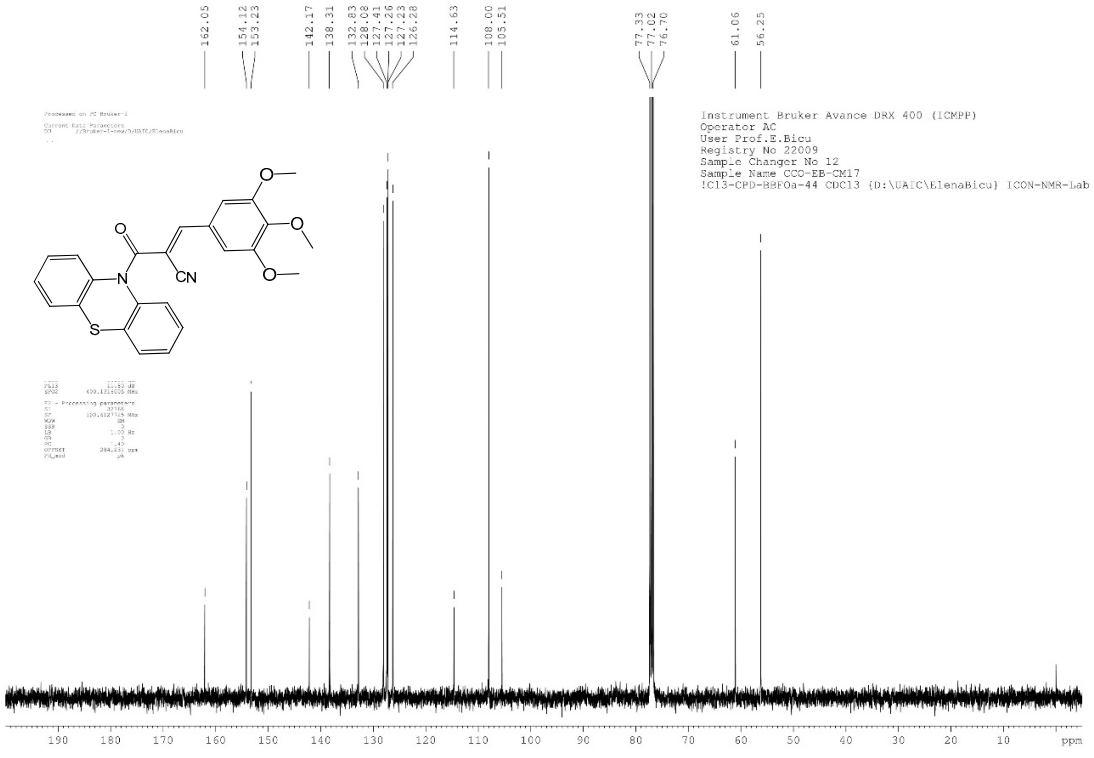
IR-1l



^{1}H NMR (400 MHz, $CDCl_3$)-**1m**



^{13}C NMR (100 MHz, $CDCl_3$)-**1m**



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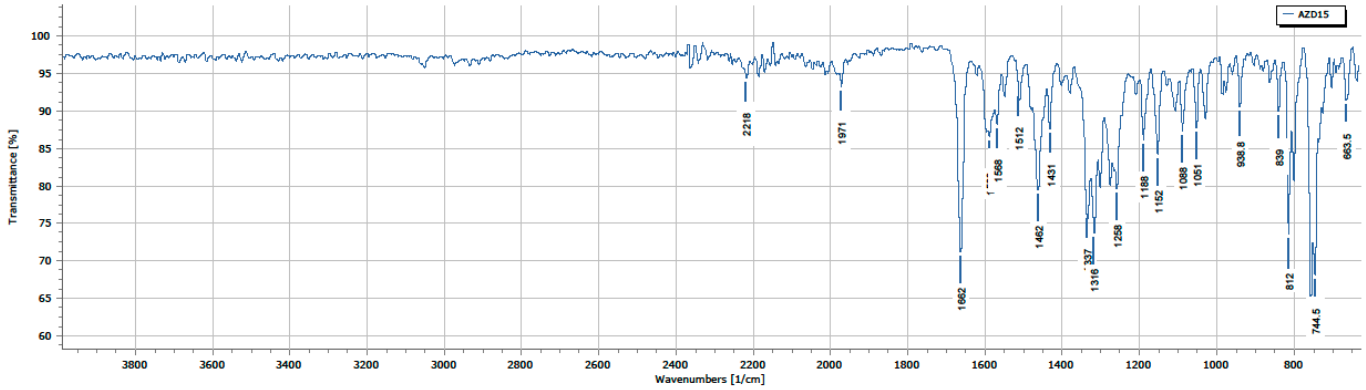
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Wavenumbers [1/cm]
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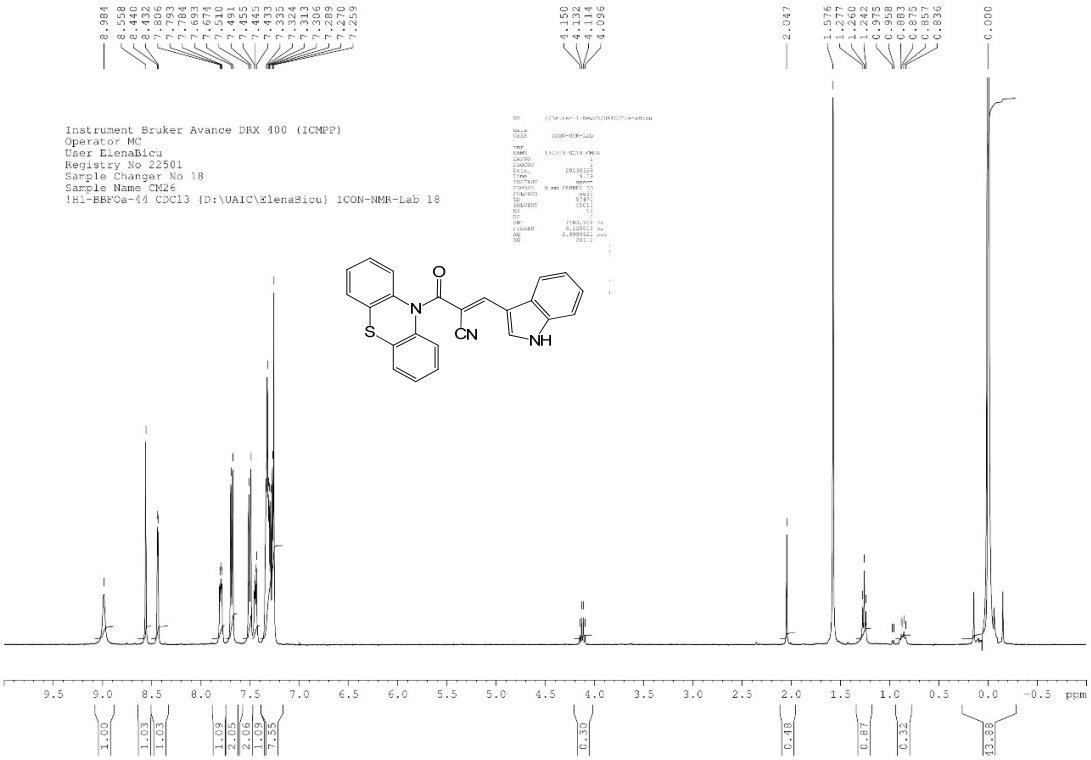
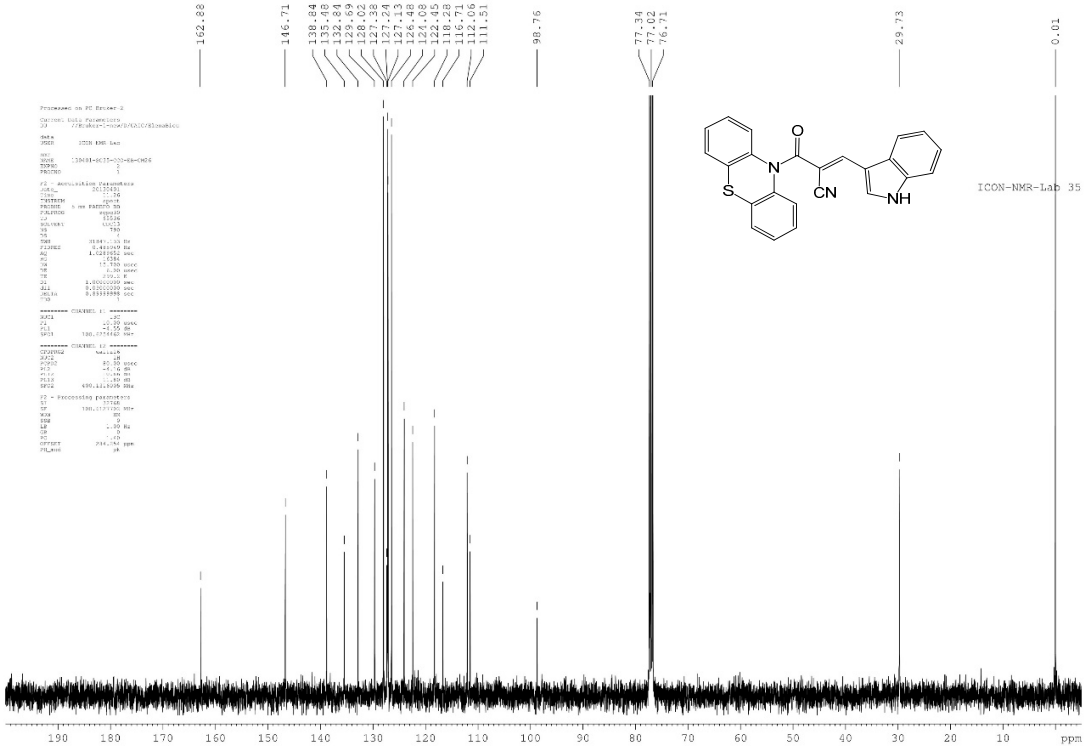
839
812
744.5
663.5

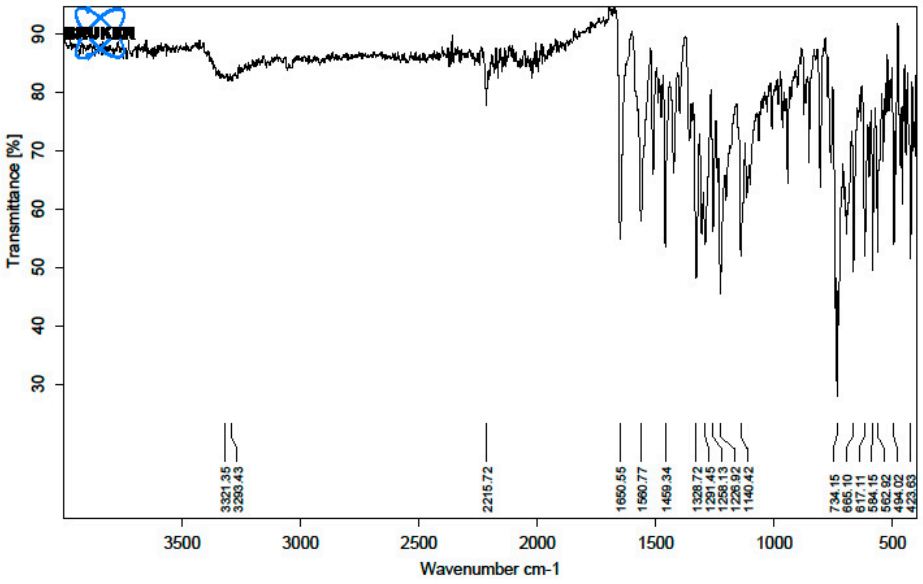
^{1}H NMR (400 MHz, $CDCl_3$)- **1n**



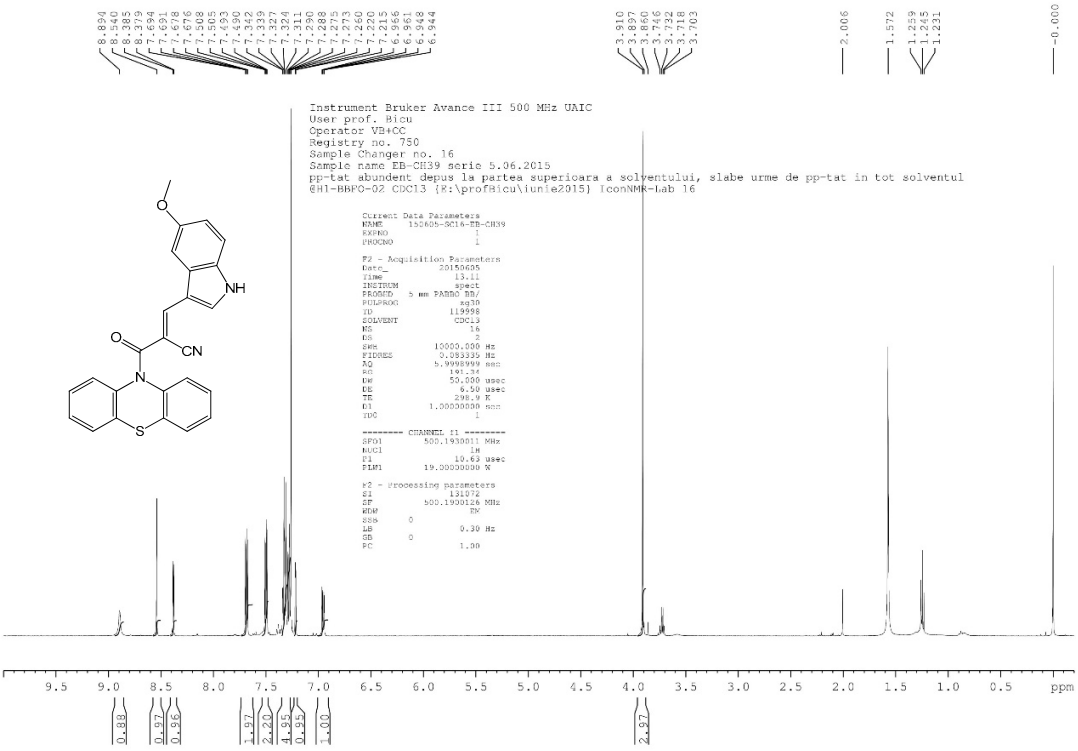
^{13}C NMR (100 MHz, $CDCl_3$)-**1n**



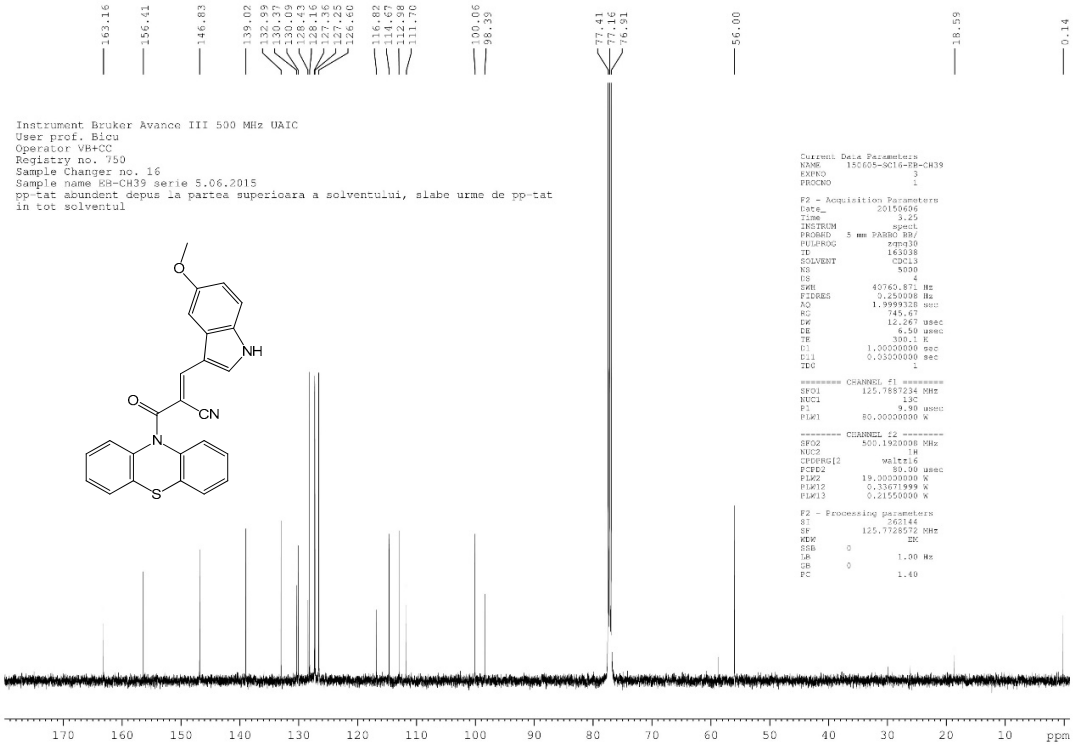
IR-1n



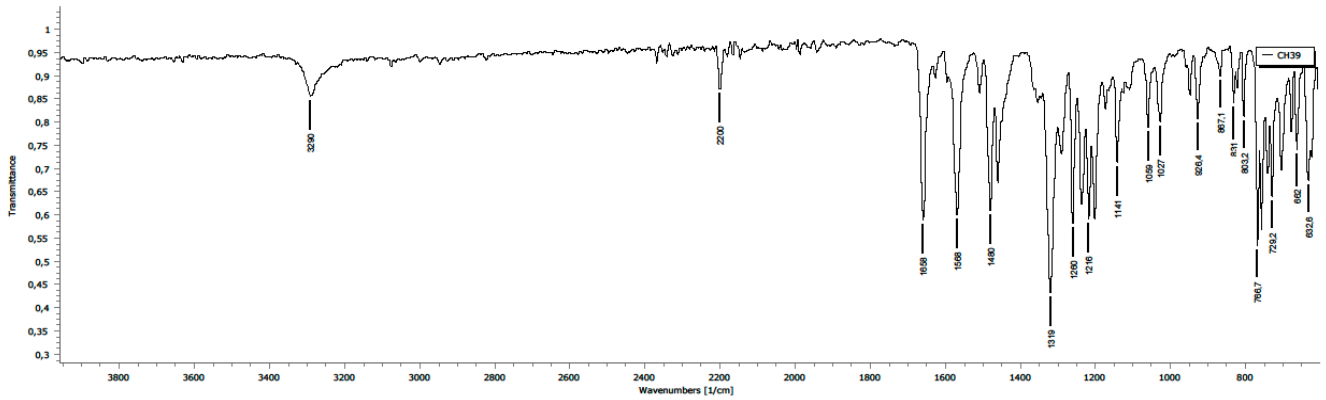
^{1}H NMR (500 MHz, $CDCl_3$)- **1o**



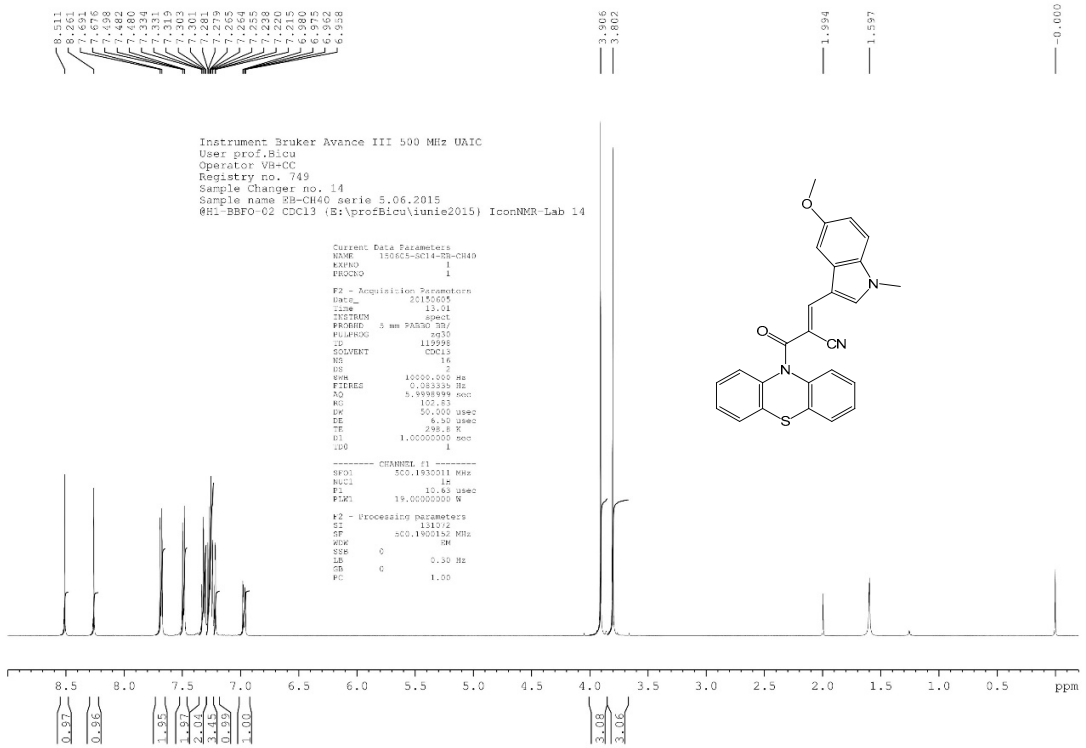
^{13}C NMR (125 MHz, $CDCl_3$)-**1o**



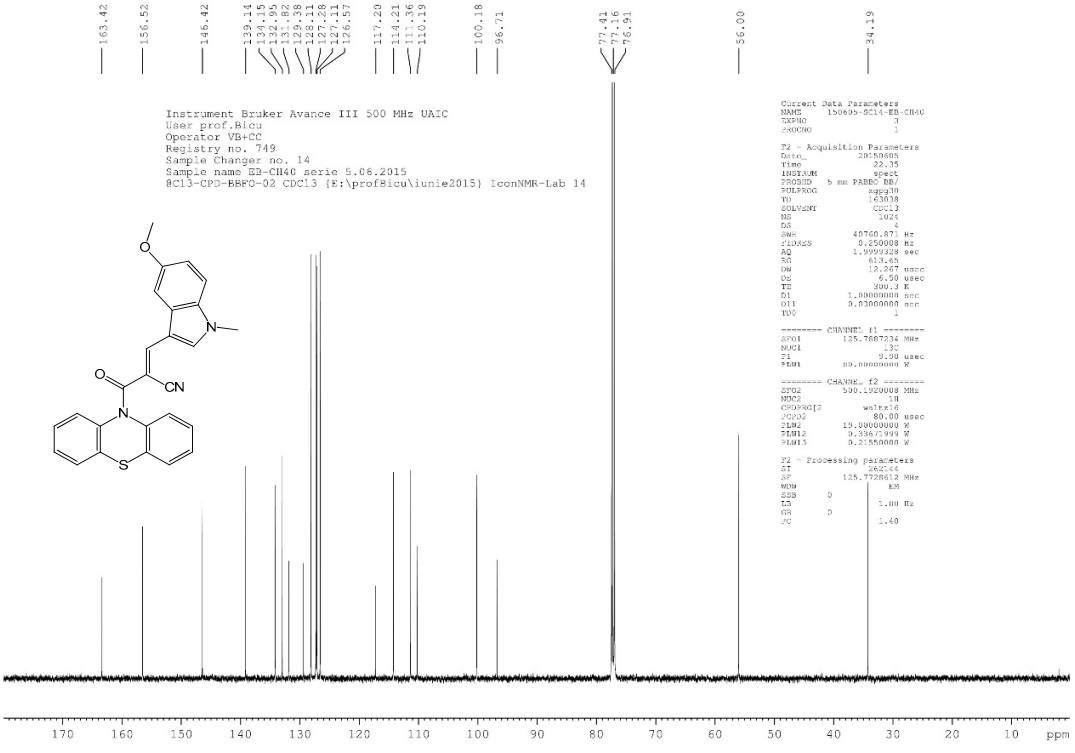
IR-1o



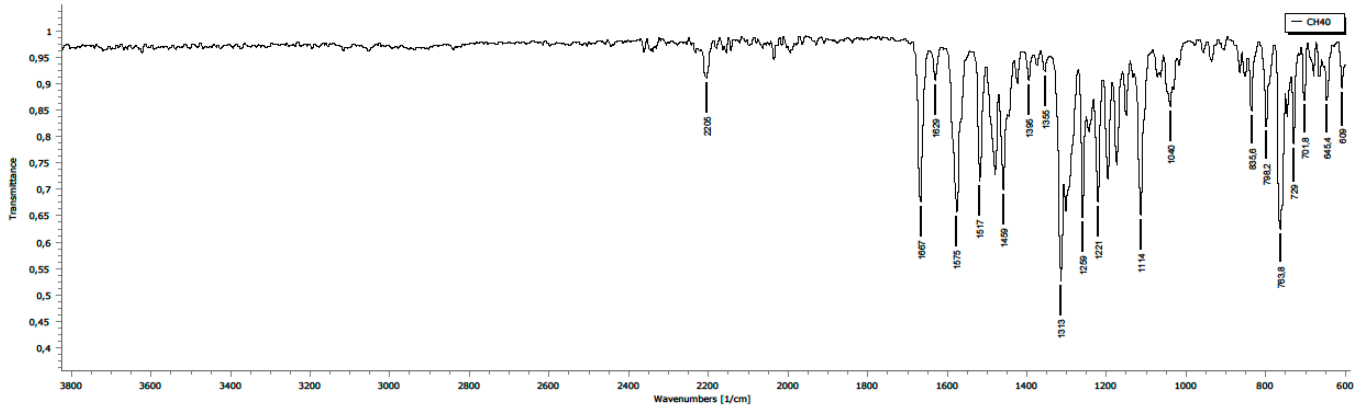
^{1}H NMR (500 MHz, $CDCl_3$)- **1p**



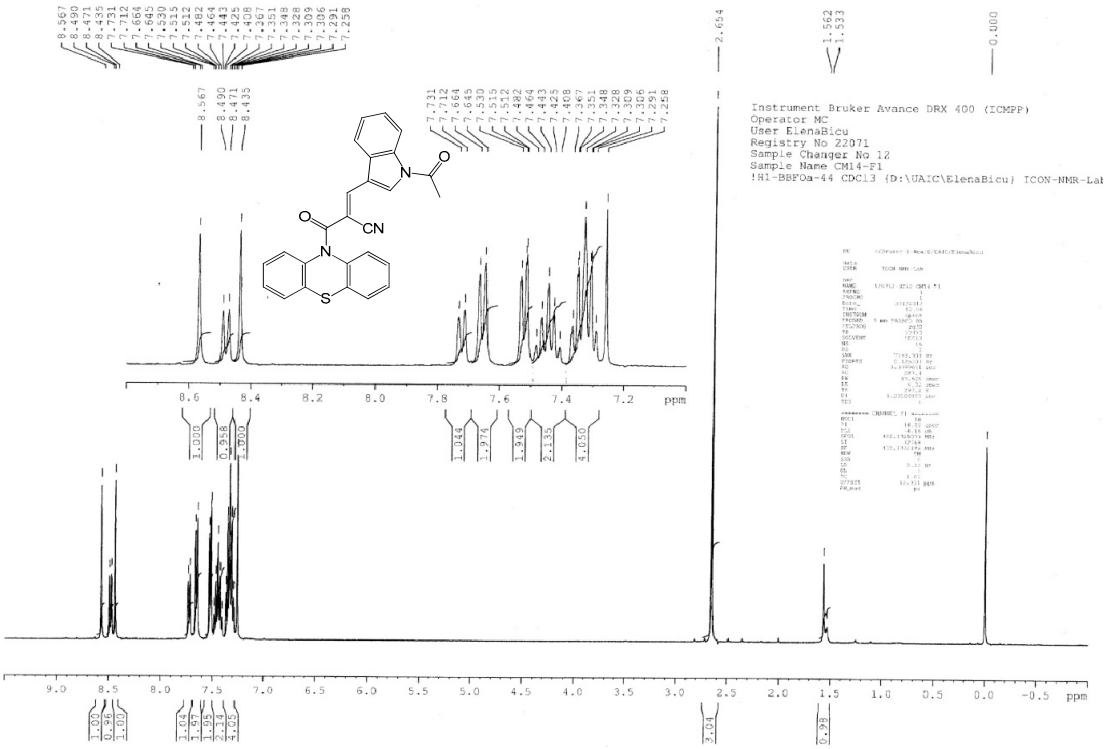
^{13}C NMR (125 MHz, $CDCl_3$)-**1p**



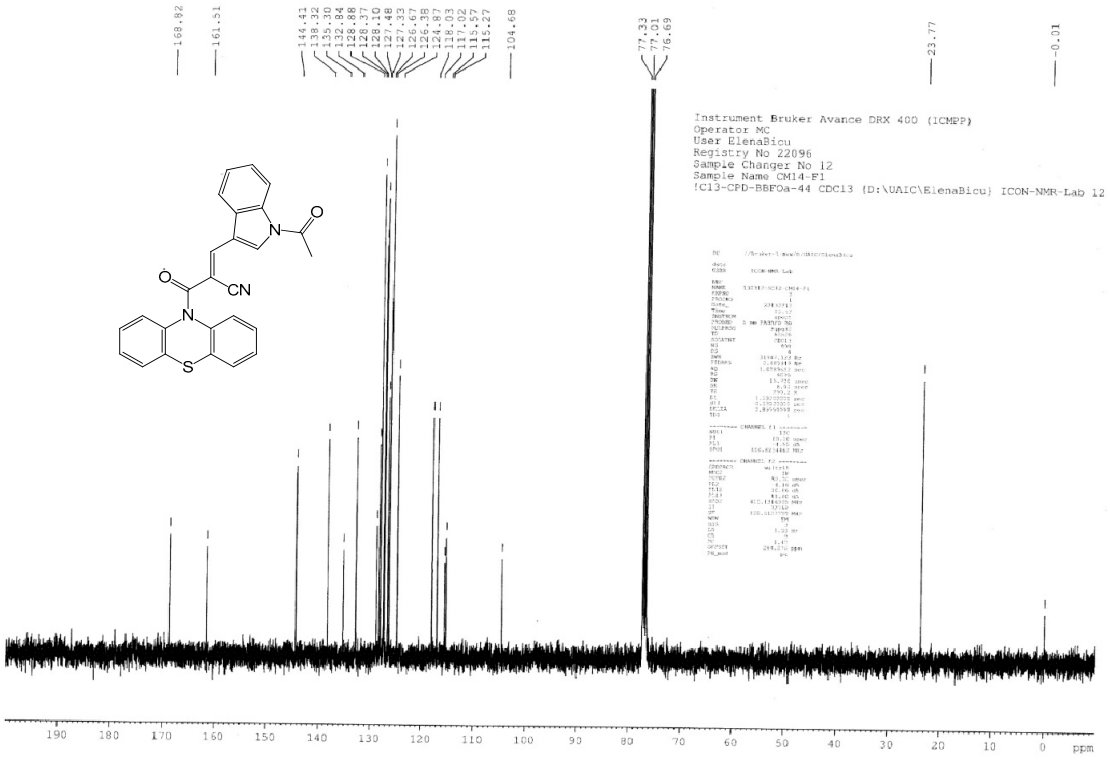
IR-1p



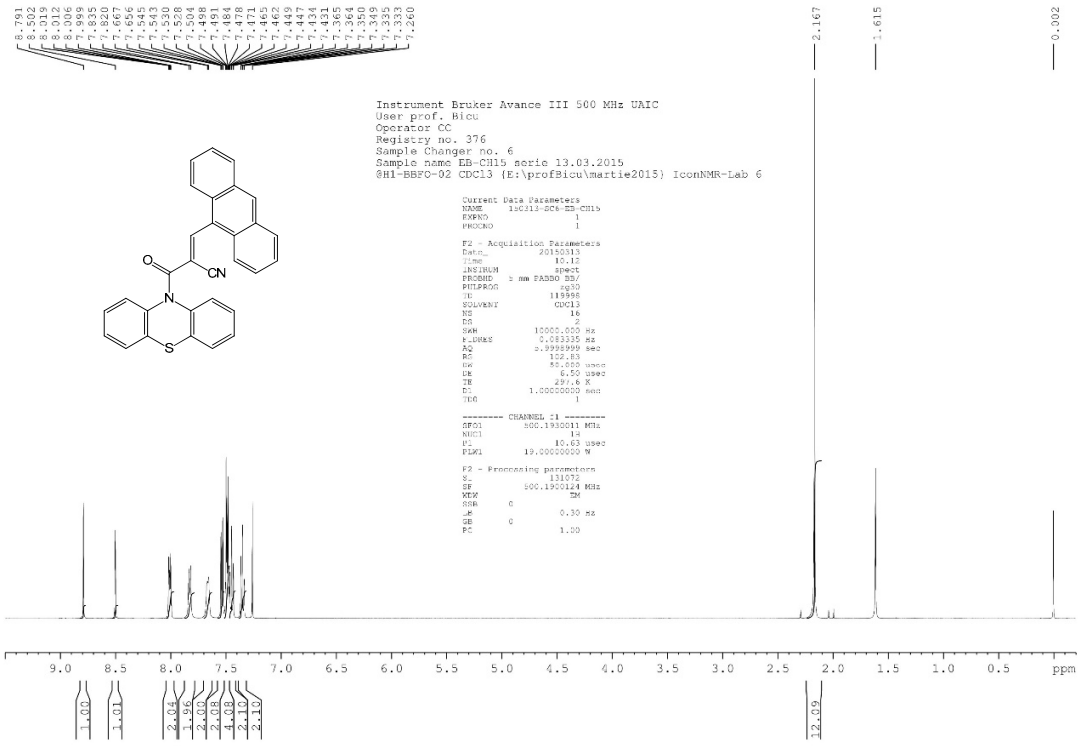
^{1}H NMR (400 MHz, $CDCl_3$)- **1q**



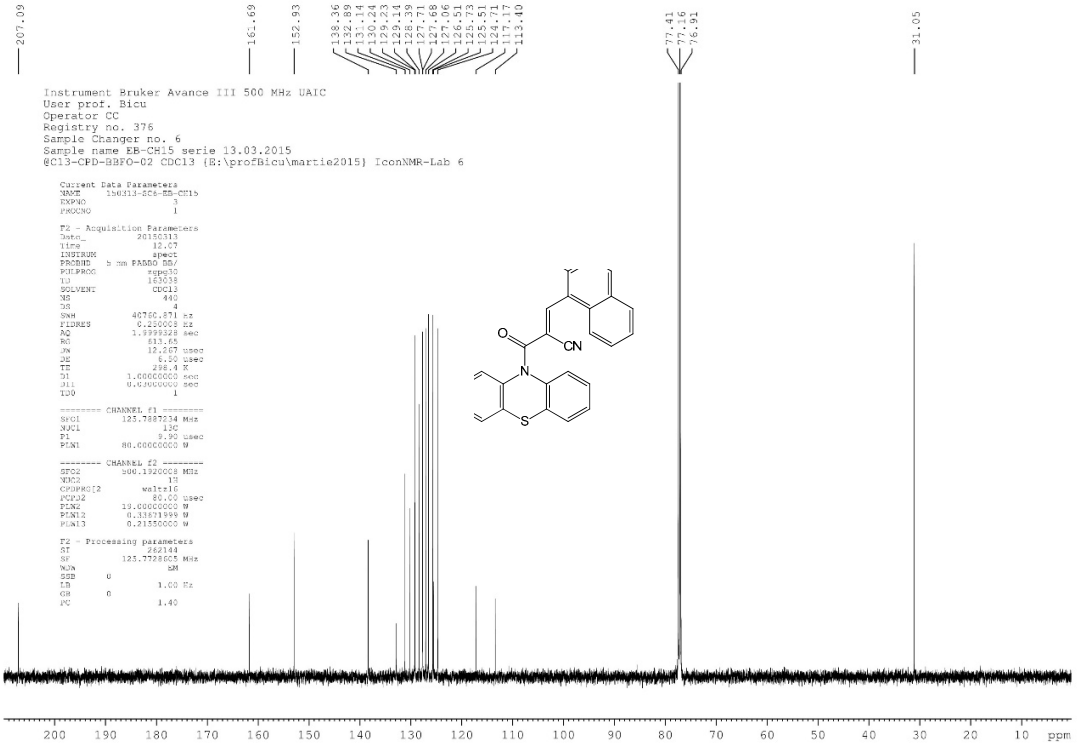
^{13}C NMR (100 MHz, $CDCl_3$)-**1q**



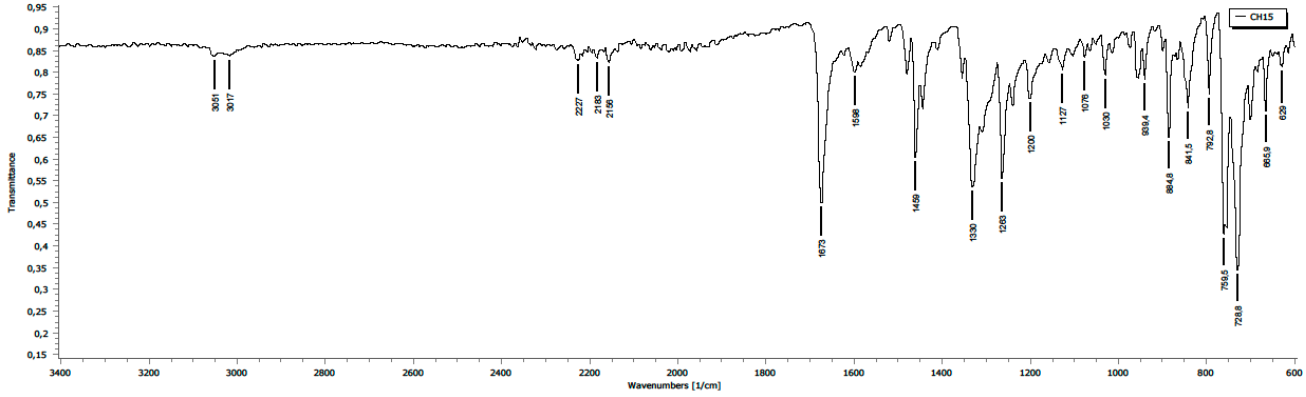
^{1}H NMR (500 MHz, $CDCl_3$)- **1r**



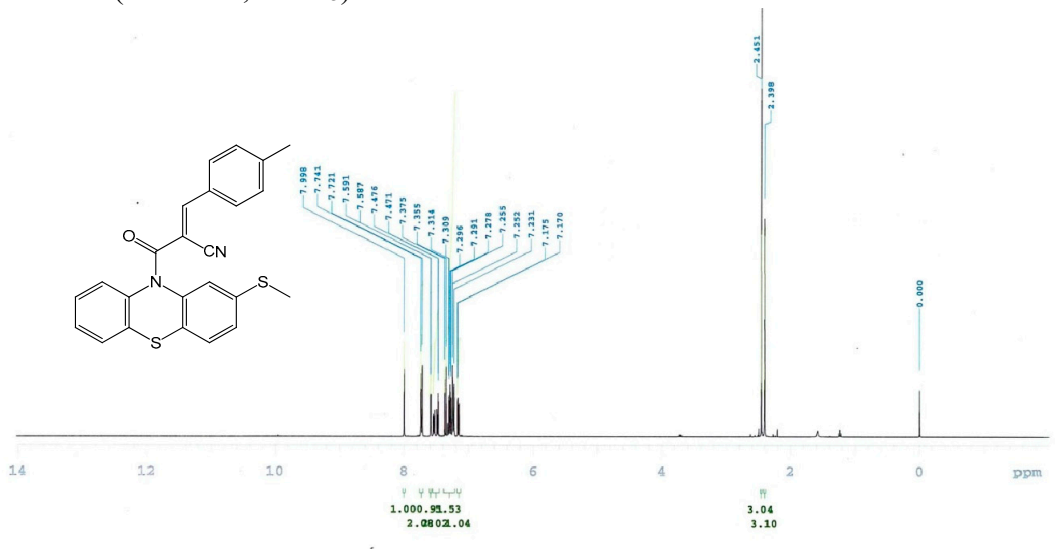
^{13}C NMR (125 MHz, $CDCl_3$)-**1r**



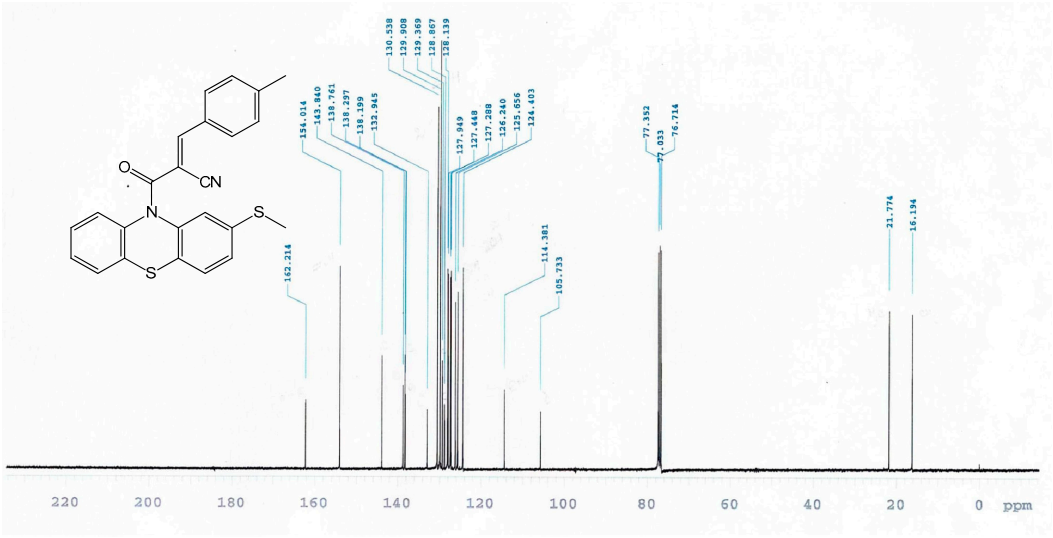
IR-1r



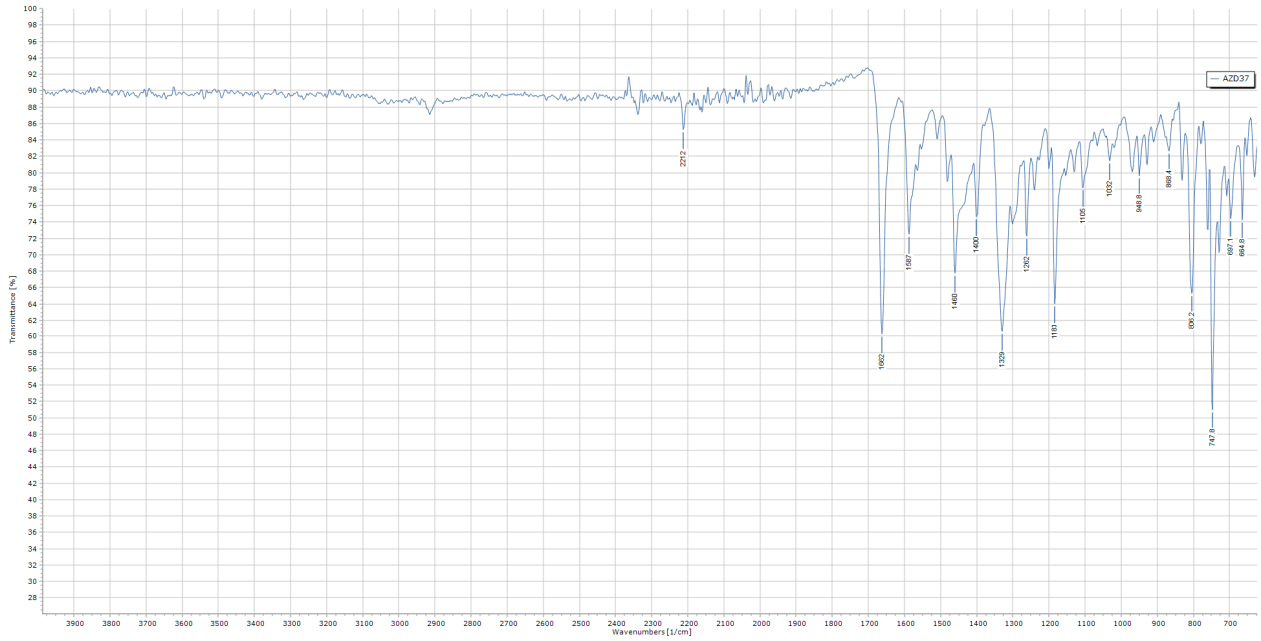
^{1}H NMR (400 MHz, $CDCl_3$)-**2a**



^{13}C NMR (100 MHz, $CDCl_3$)-**2a**



IR-2a


AZD37
Transmittance [%]
Wavenumbers [1/cm]
2212
1902
1587
1460
1400
1329
1262
1181
1105
1032
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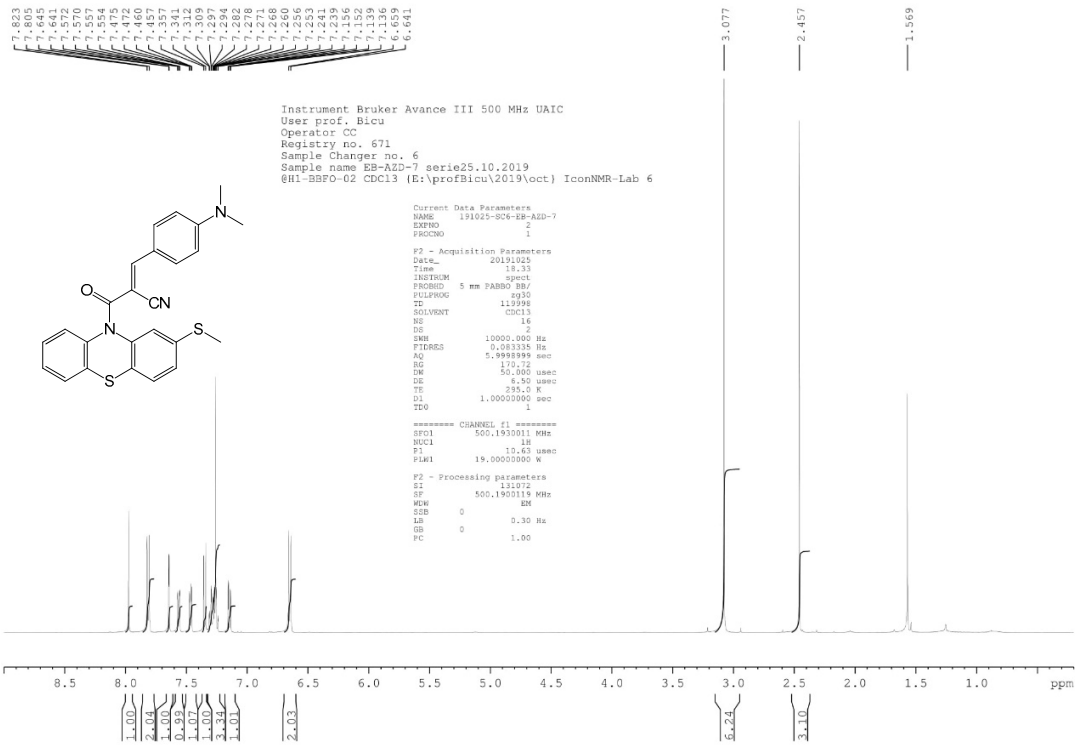
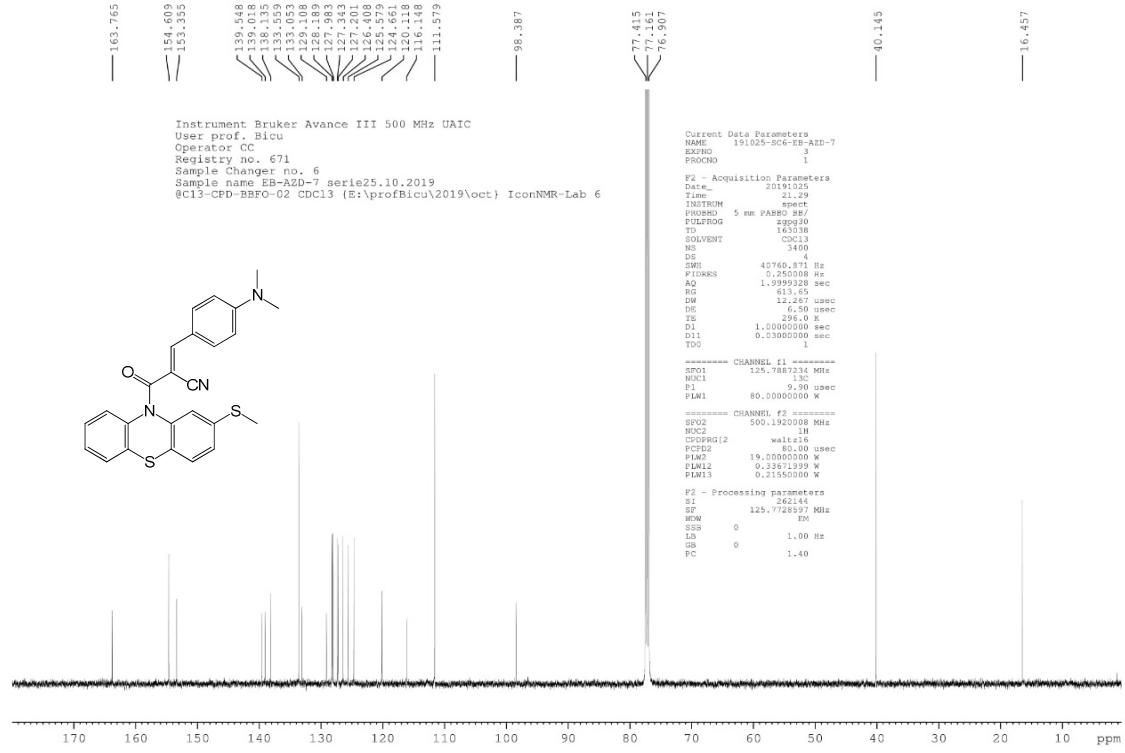
898.4
806.2
747.8
697.1
694.8

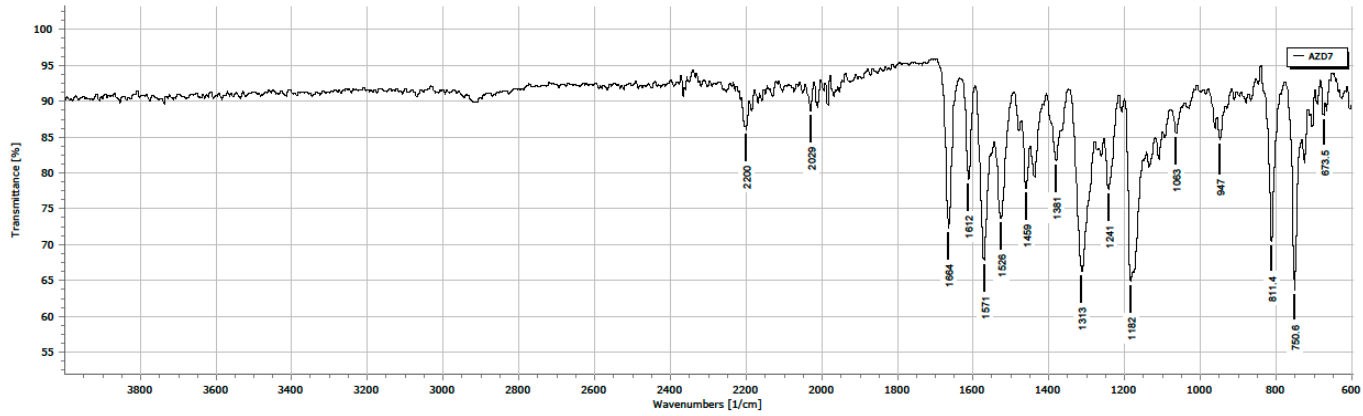
^{1}H NMR (500 MHz, $CDCl_3$)- **2b**



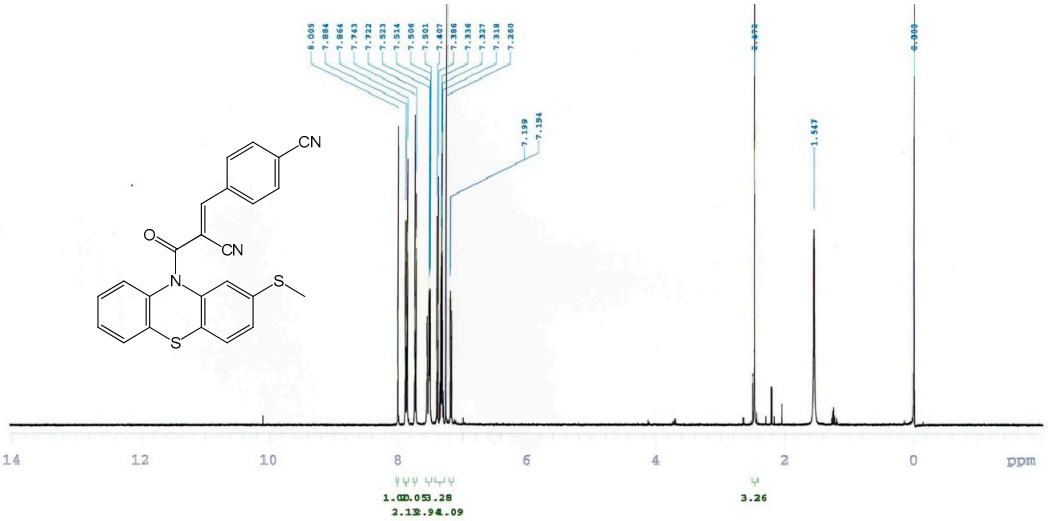
^{13}C NMR (125 MHz, $CDCl_3$)-**2b**



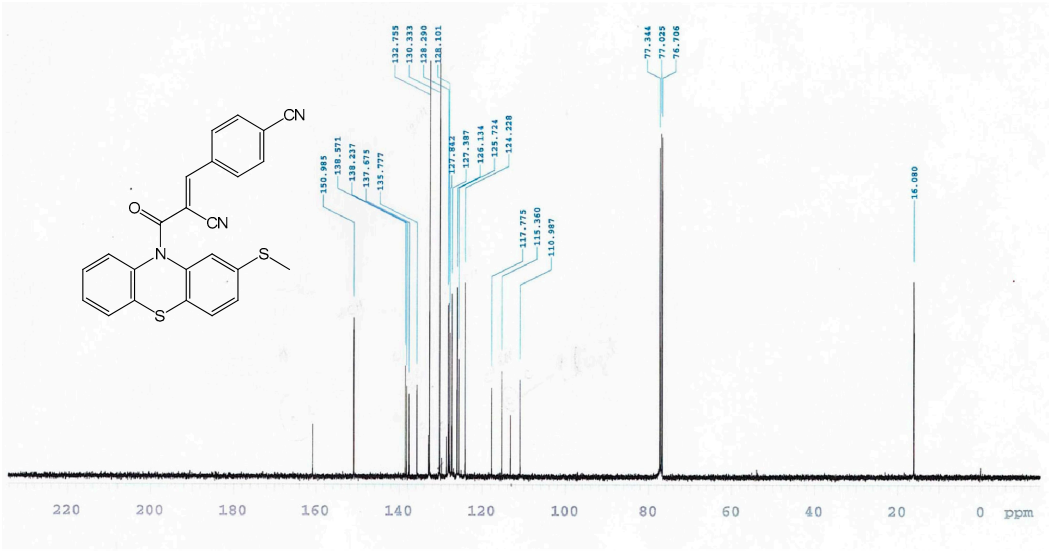
IR-2b



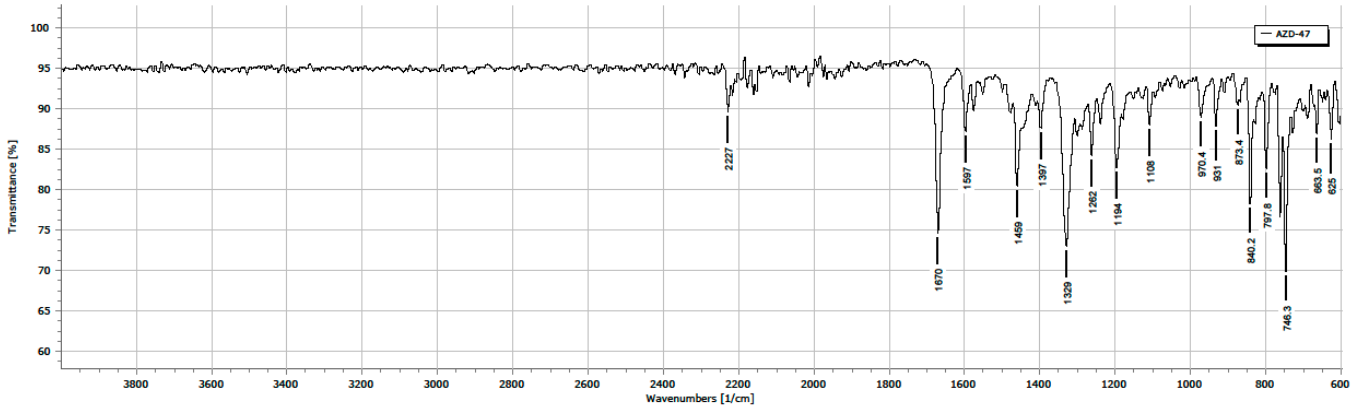
^{1}H NMR (400 MHz, $CDCl_3$)-**2c**



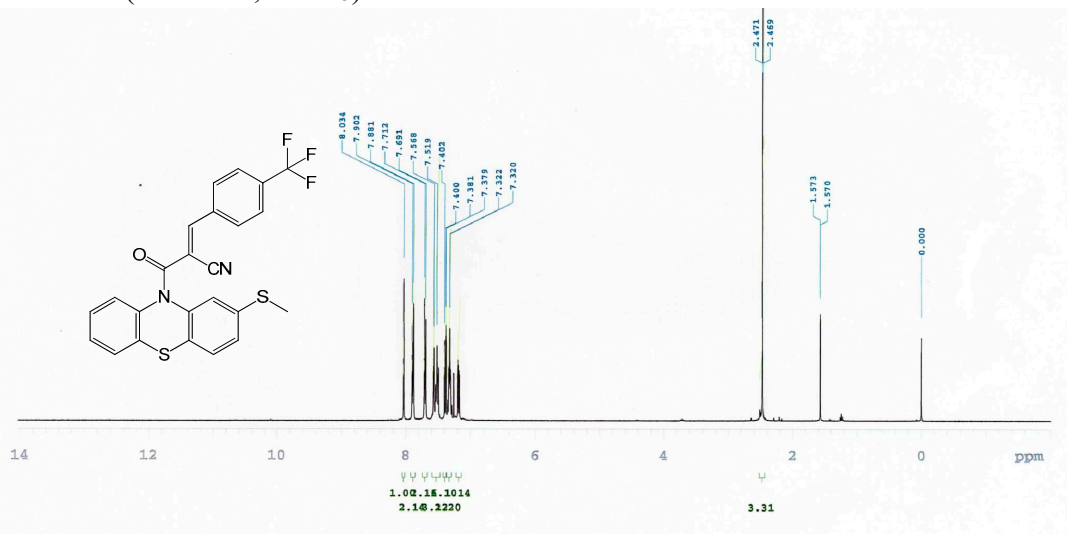
^{13}C NMR (100 MHz, $CDCl_3$)-**2c**



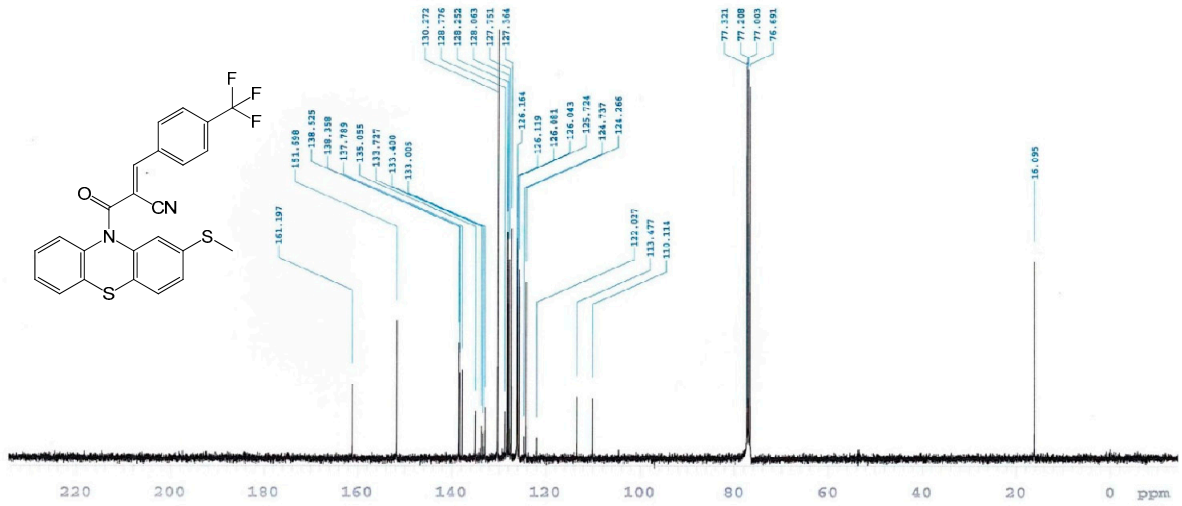
IR-2c



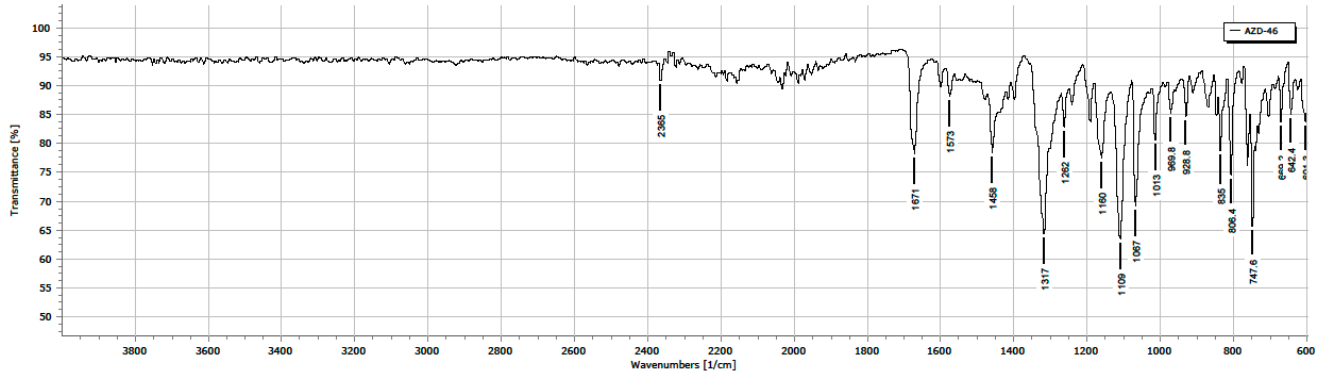
^{1}H NMR (400 MHz, $CDCl_3$)-**2d**



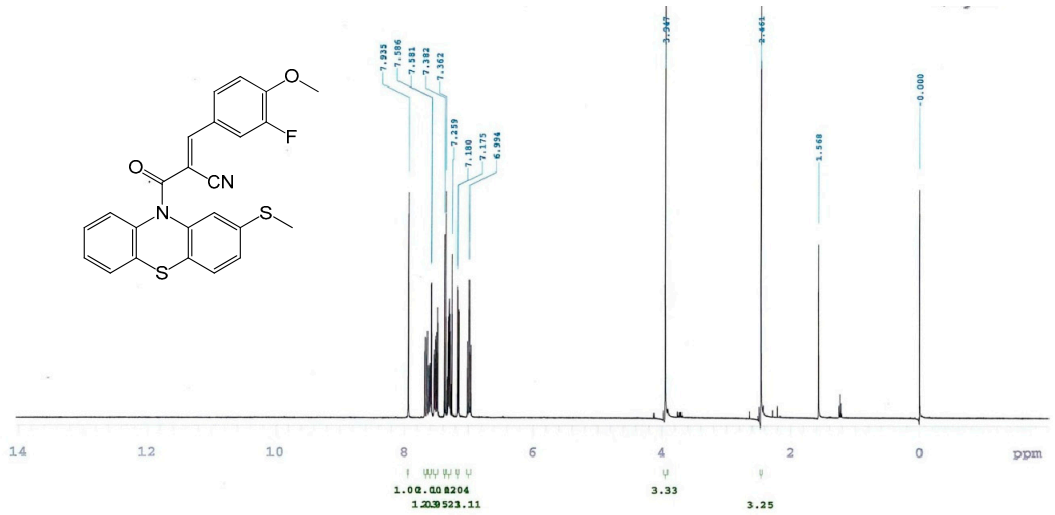
^{13}C NMR (100 MHz, $CDCl_3$)-**2d**



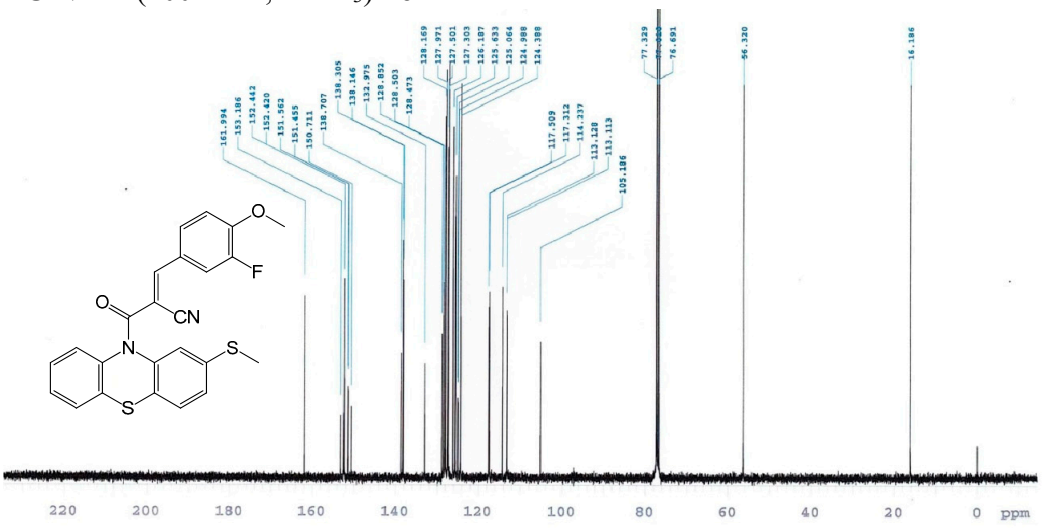
IR-2d



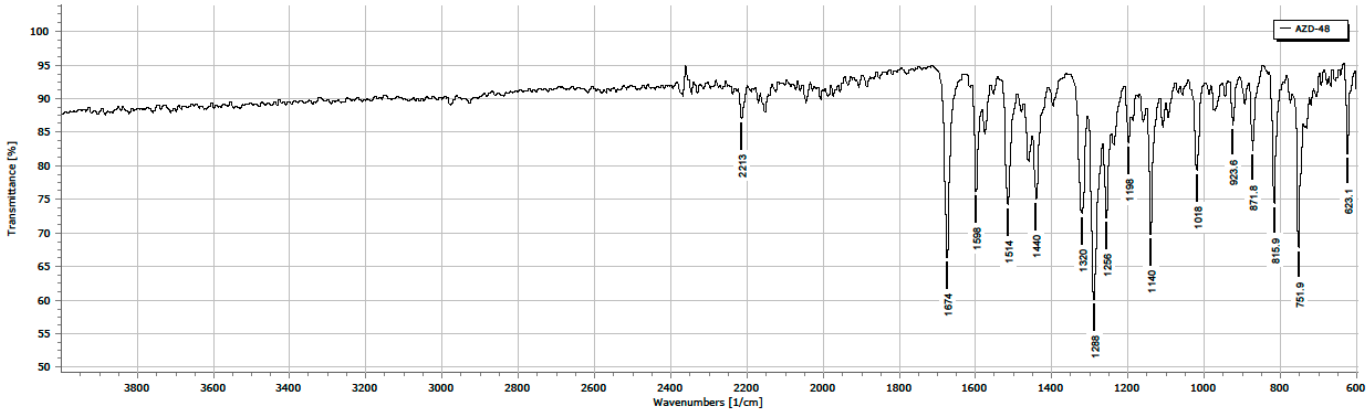
^{1}H NMR (400 MHz, $CDCl_3$)-**2e**



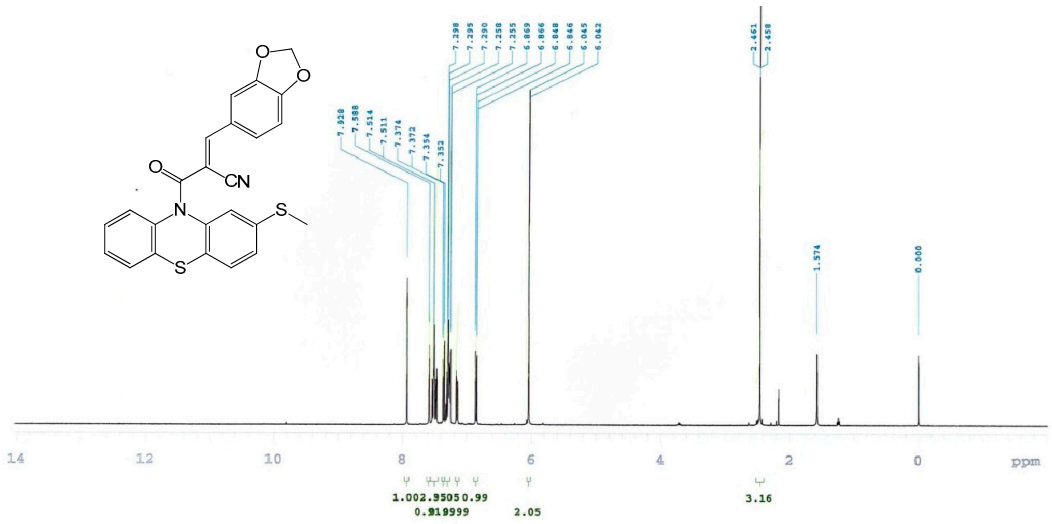
^{13}C NMR (100 MHz, $CDCl_3$)-**2e**



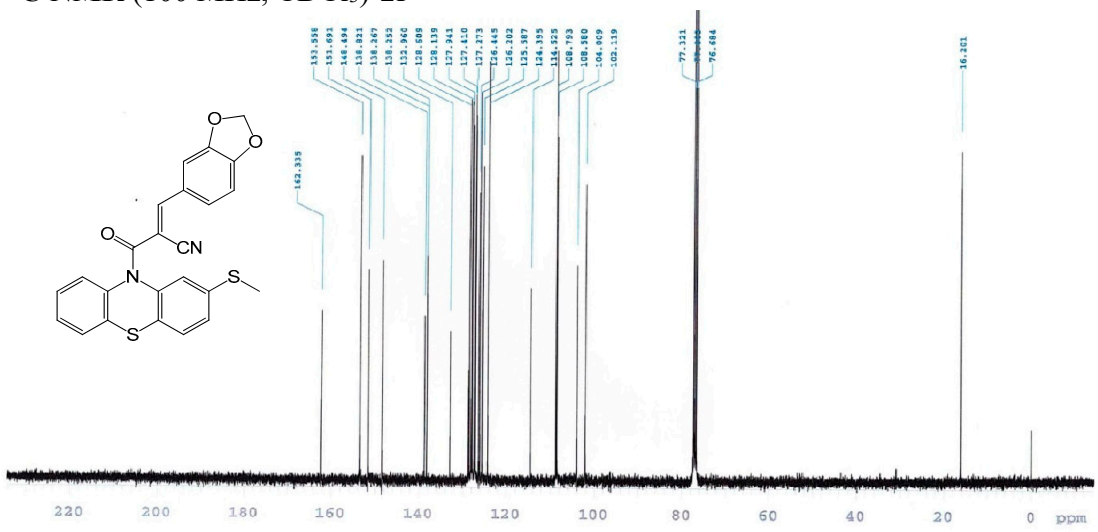
IR-2e


AZD-48
Transmittance [%]
Wavenumbers [1/cm]
2213
1674
1598
1514
1440
1320
1288
1255
1198
1140
1018
923.6
871.8
815.9
751.9
623.1

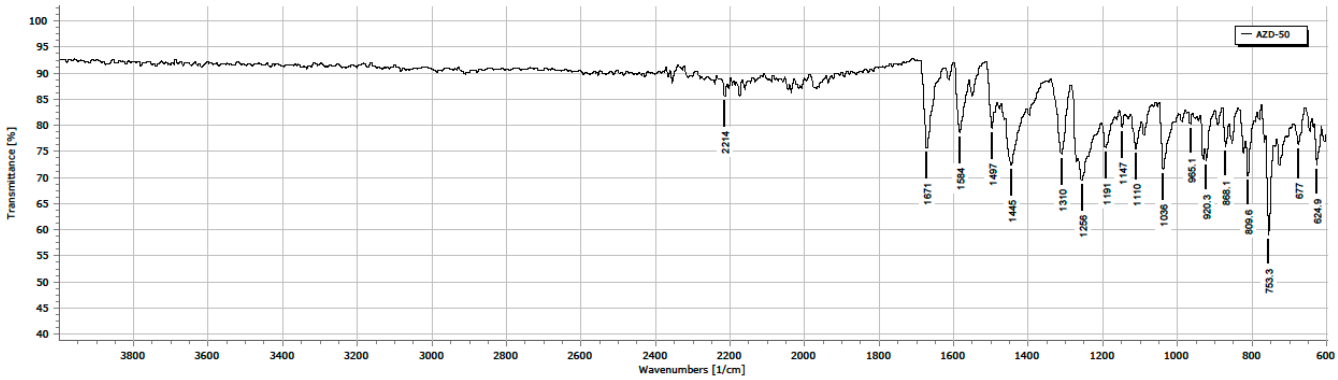
^{1}H NMR (400 MHz, $CDCl_3$)-**2f**



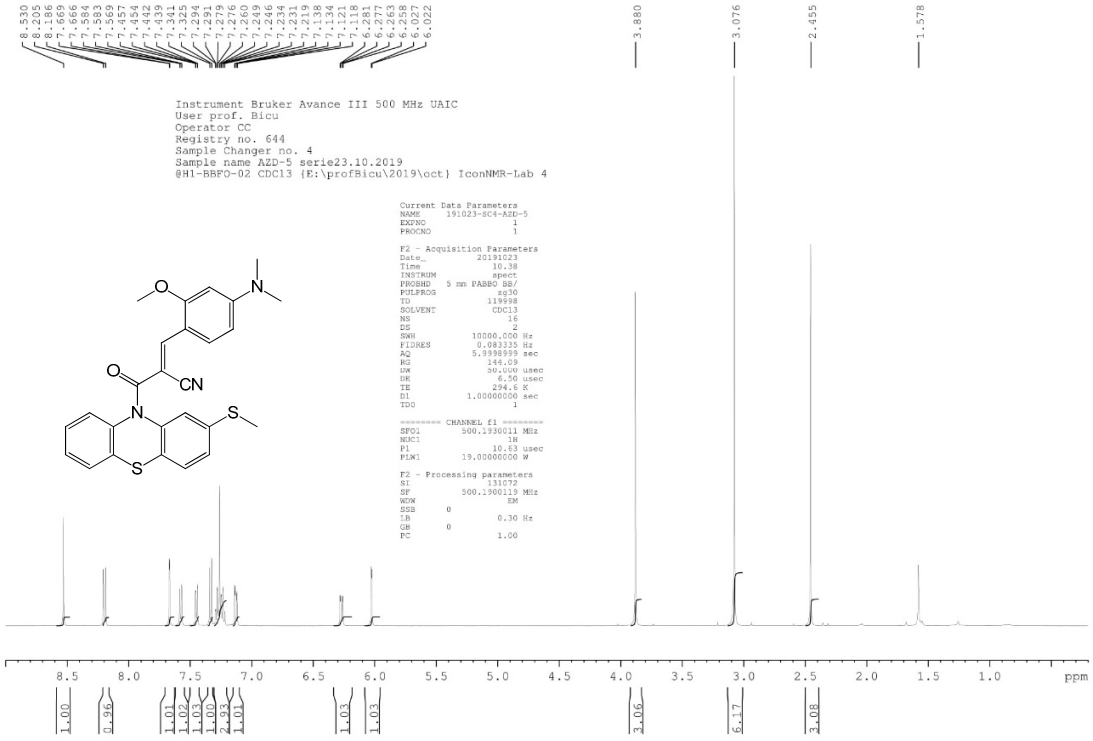
^{13}C NMR (100 MHz, $CDCl_3$)-**2f**



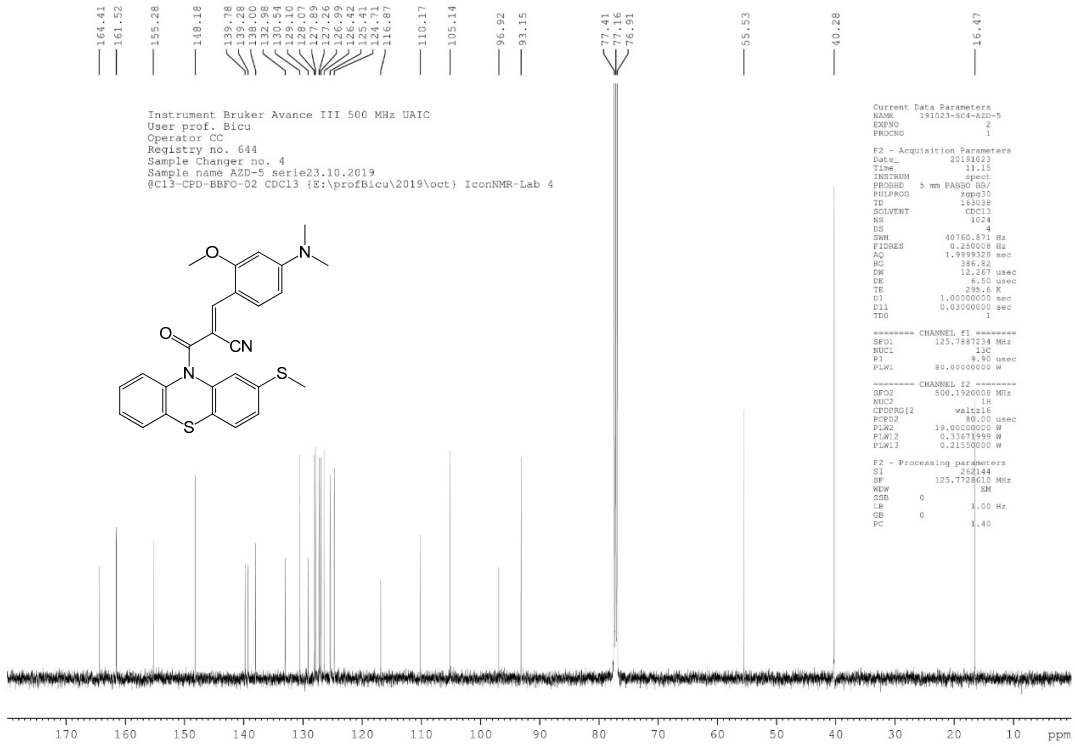
IR-2f



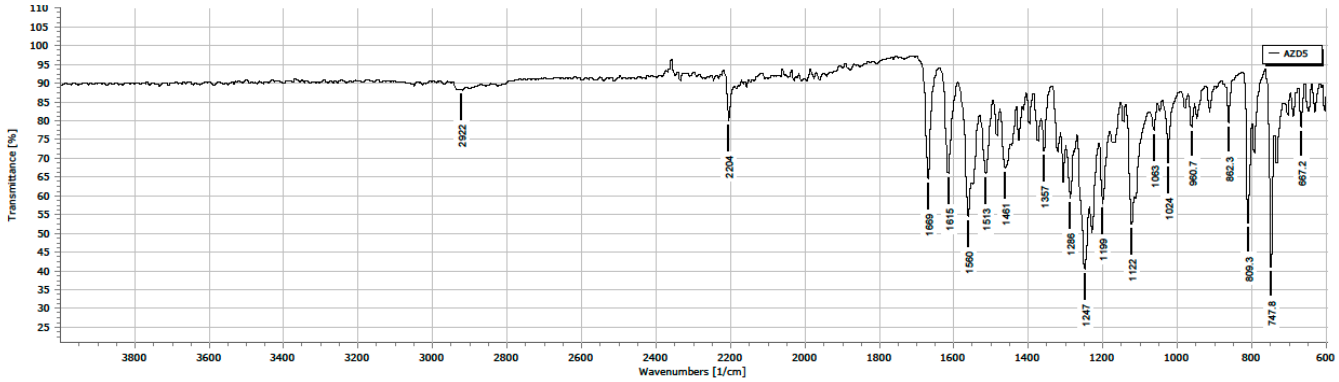
^{1}H NMR (500 MHz, $CDCl_3$)- **2g**



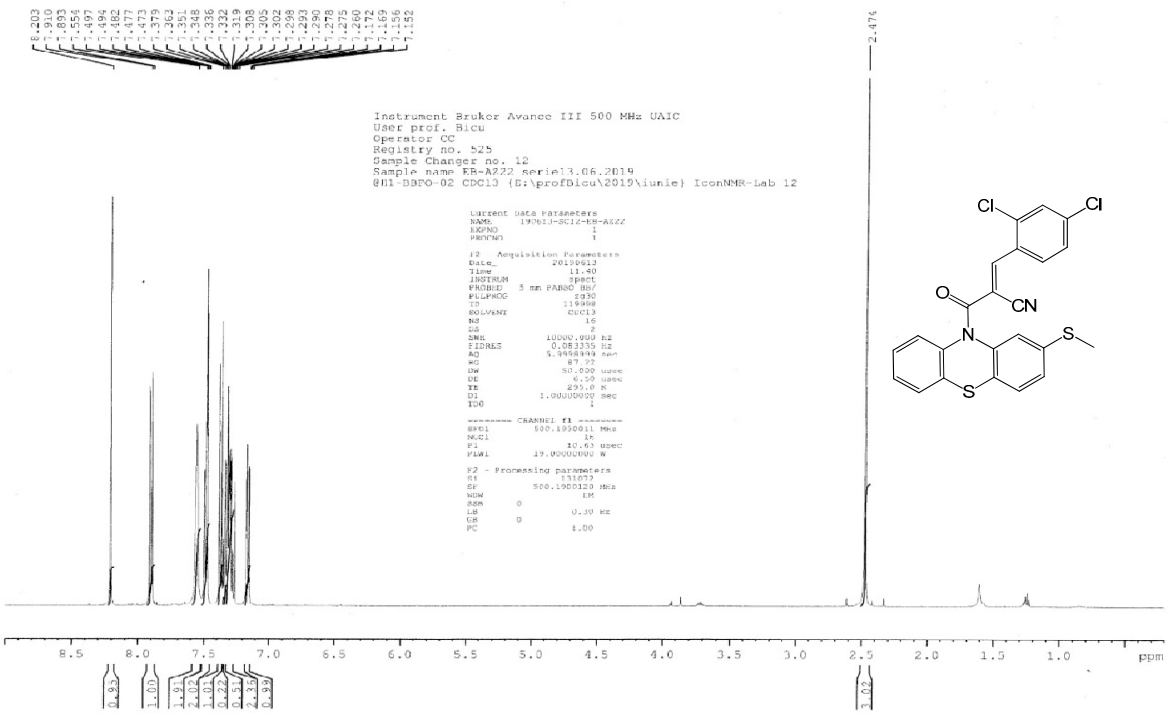
^{13}C NMR (125 MHz, $CDCl_3$)-**2g**



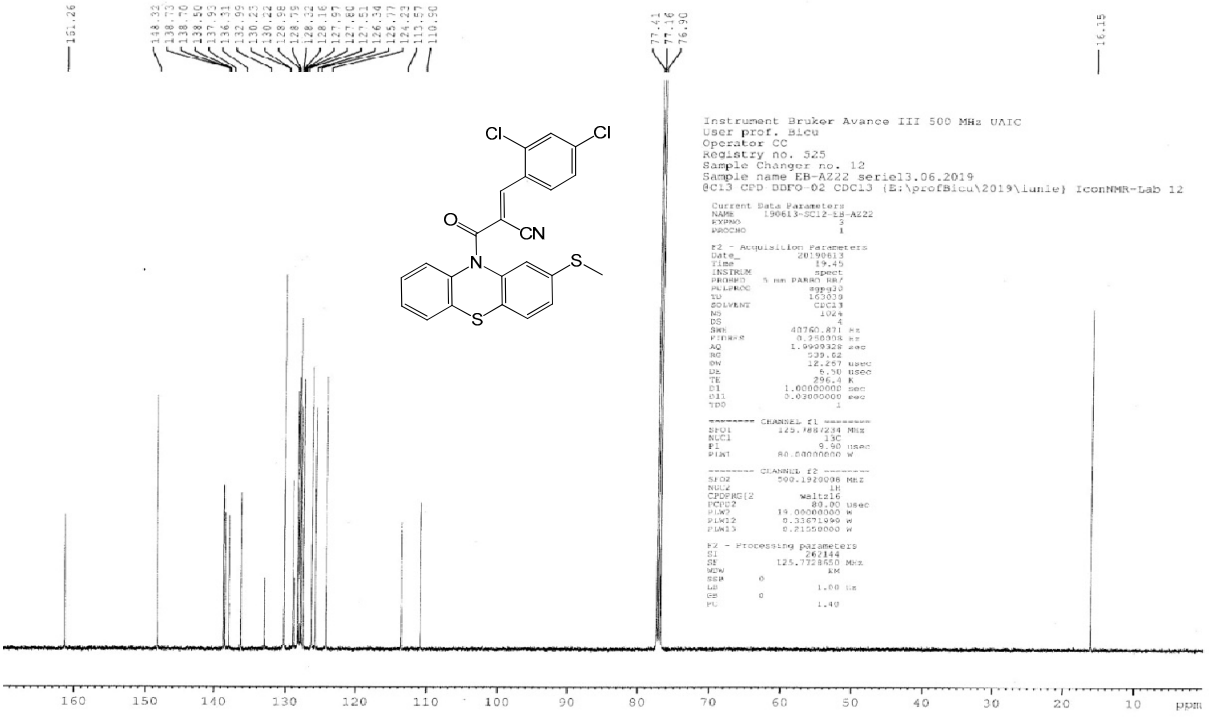
IR-2g



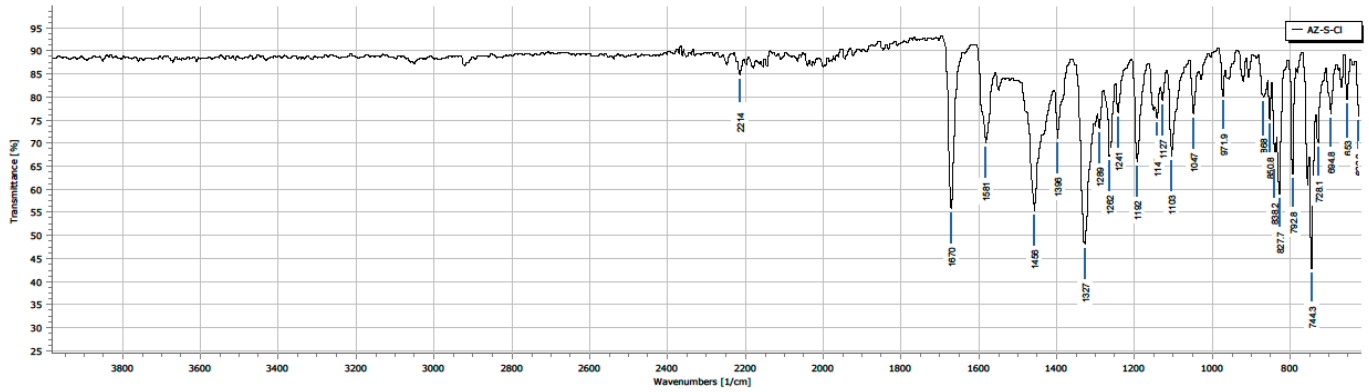
^{1}H NMR (500 MHz, $CDCl_3$)-**2h**



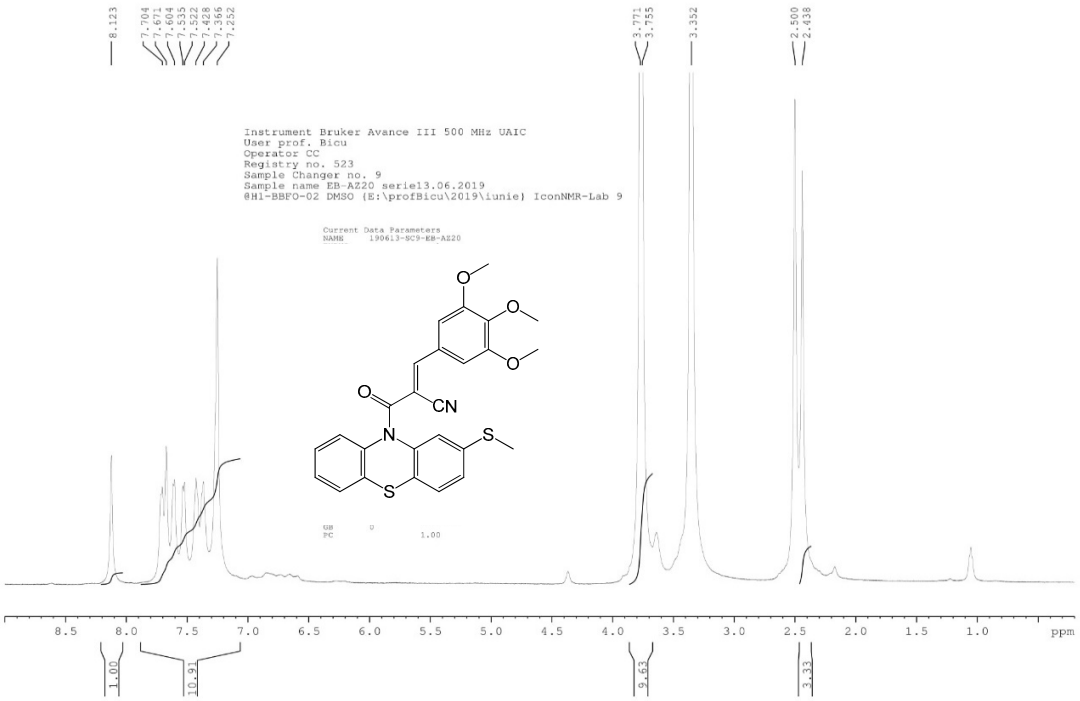
^{13}C NMR (125 MHz, $CDCl_3$)-**2h**



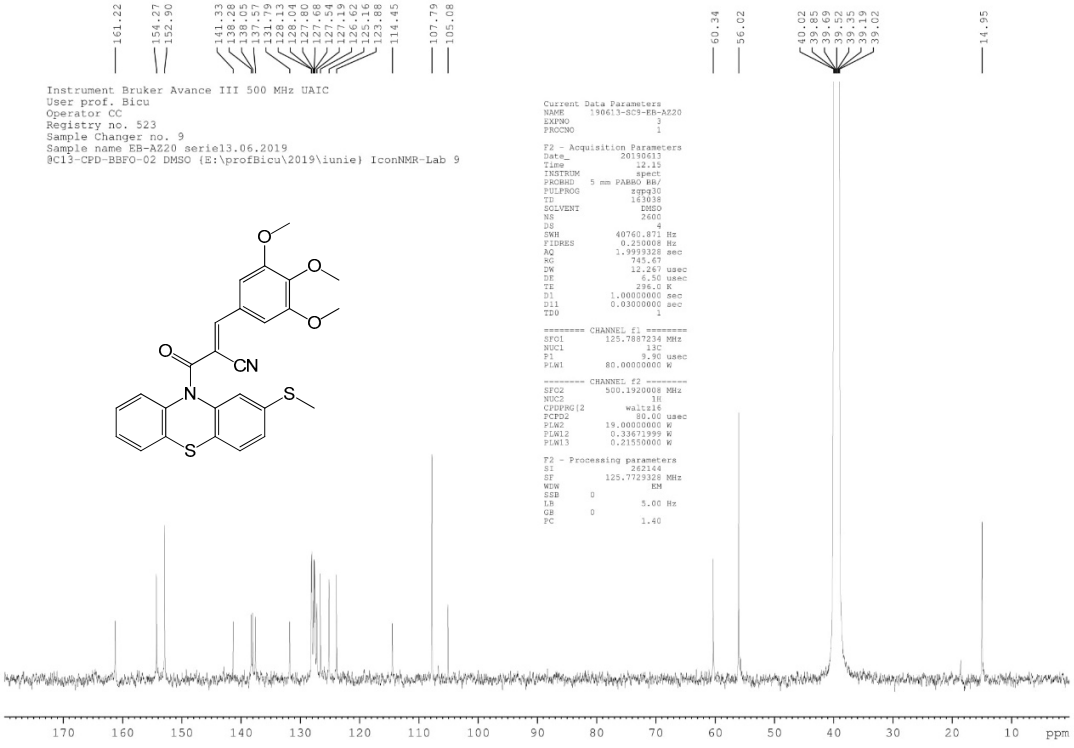
IR-2h



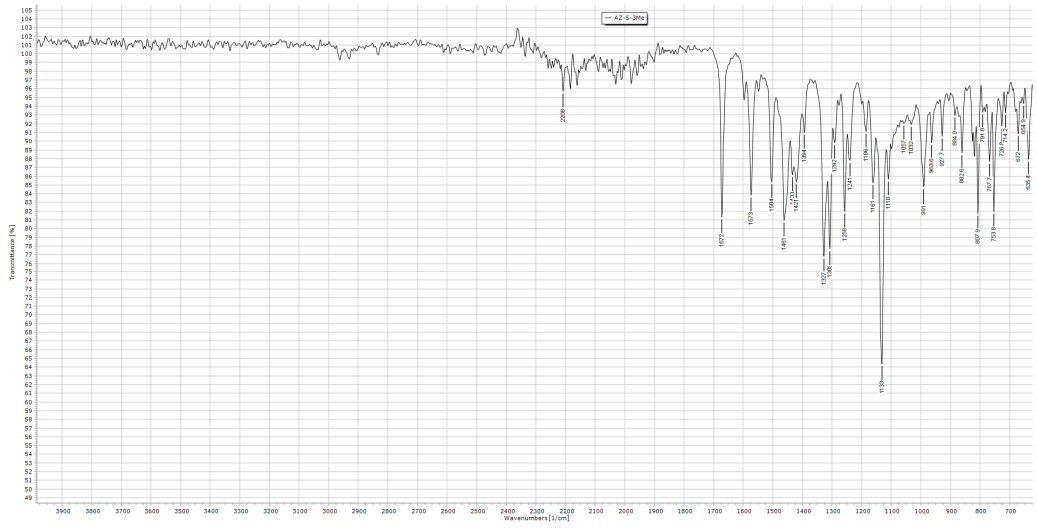
^{1}H NMR (500 MHz, $CDCl_3$)-**2i**



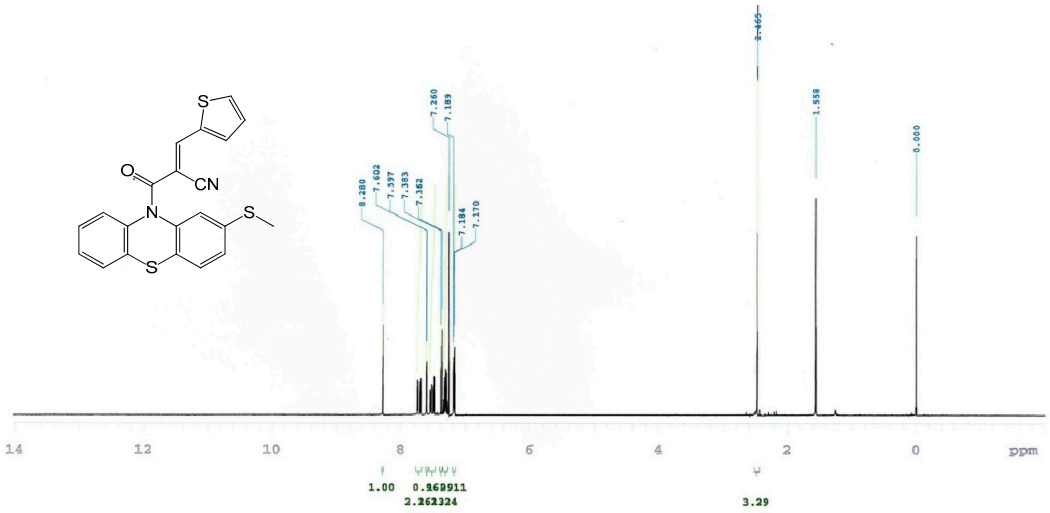
^{13}C NMR (125 MHz, $CDCl_3$)-**2i**



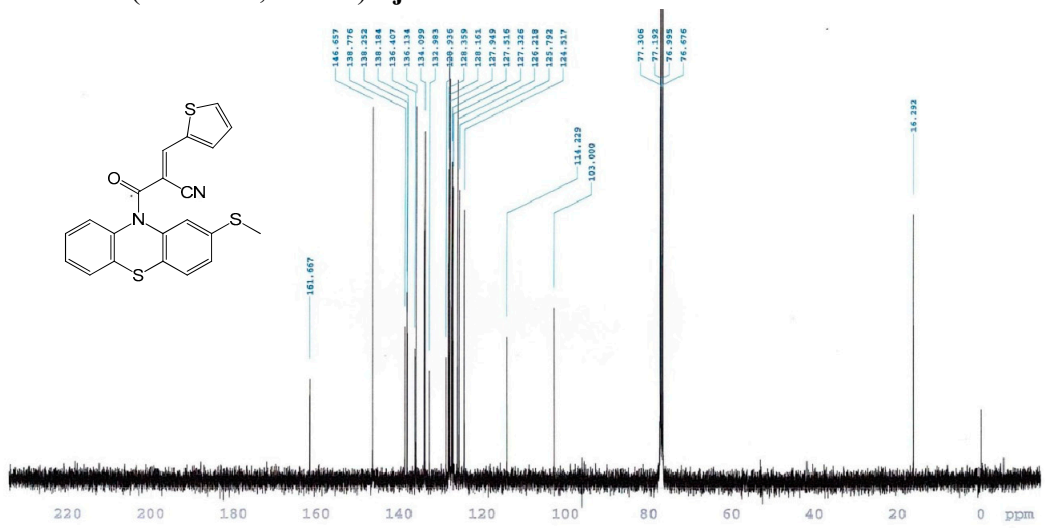
IR-2i



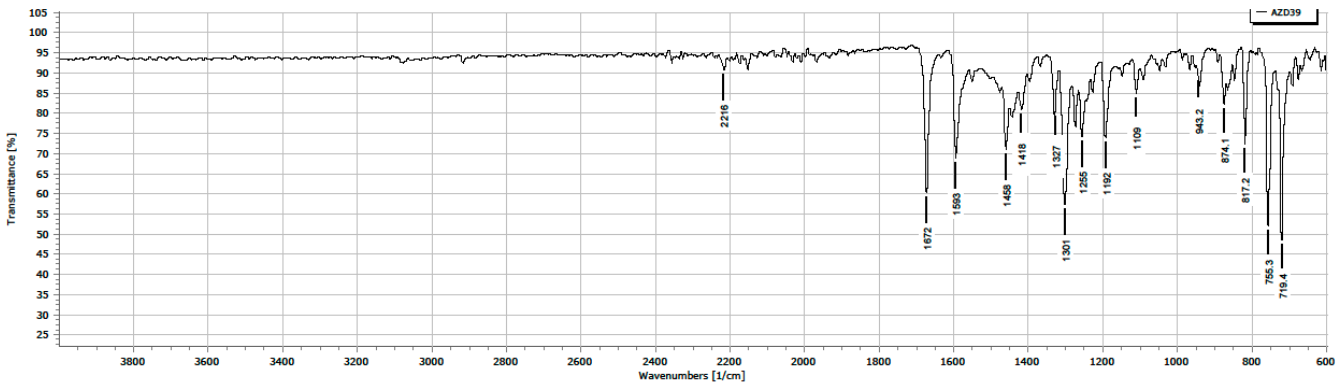
^{1}H NMR (400 MHz, $CDCl_3$)-**2j**



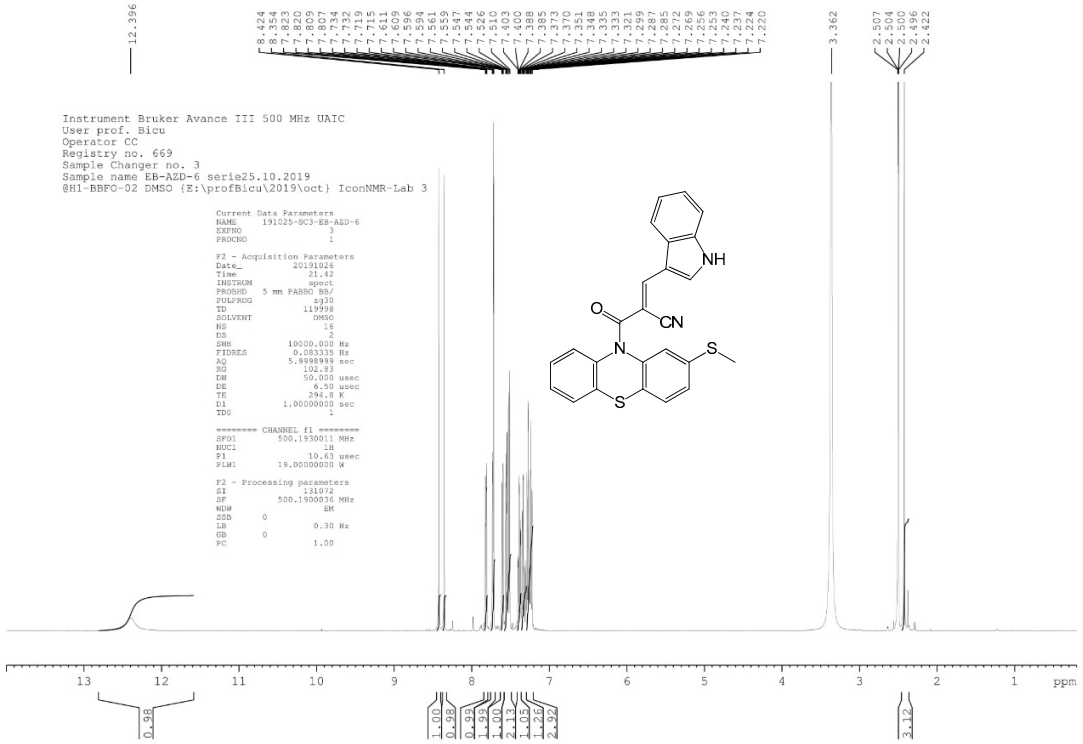
^{13}C NMR (100 MHz, $CDCl_3$)-**2j**



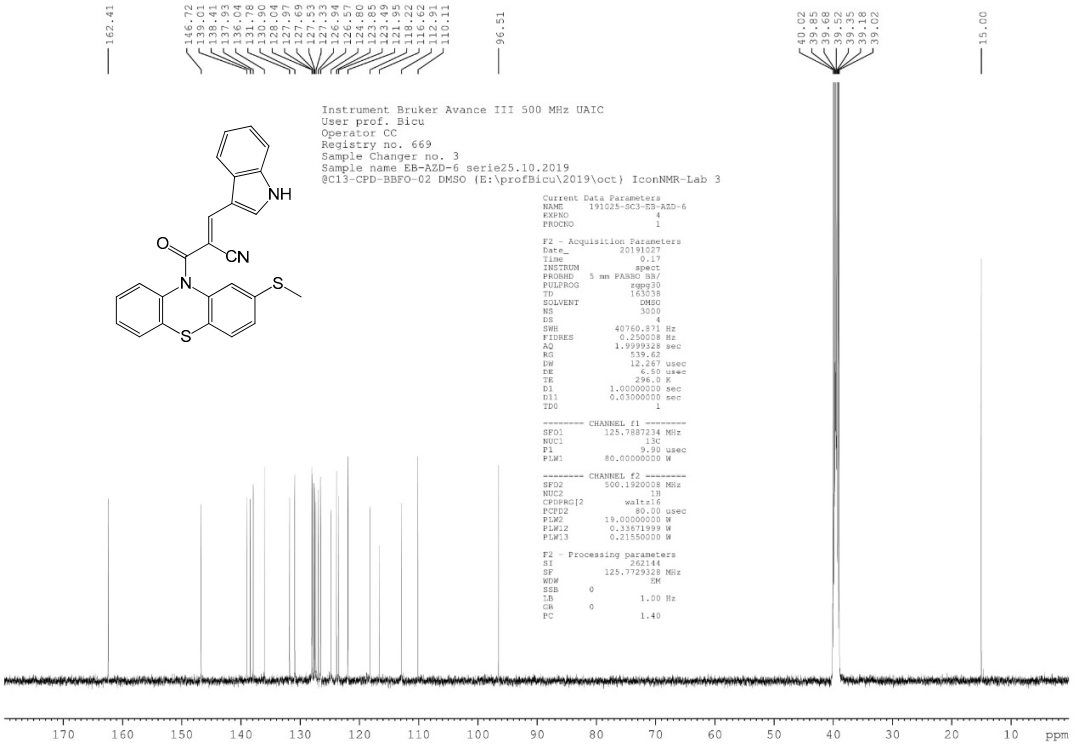
IR-2j



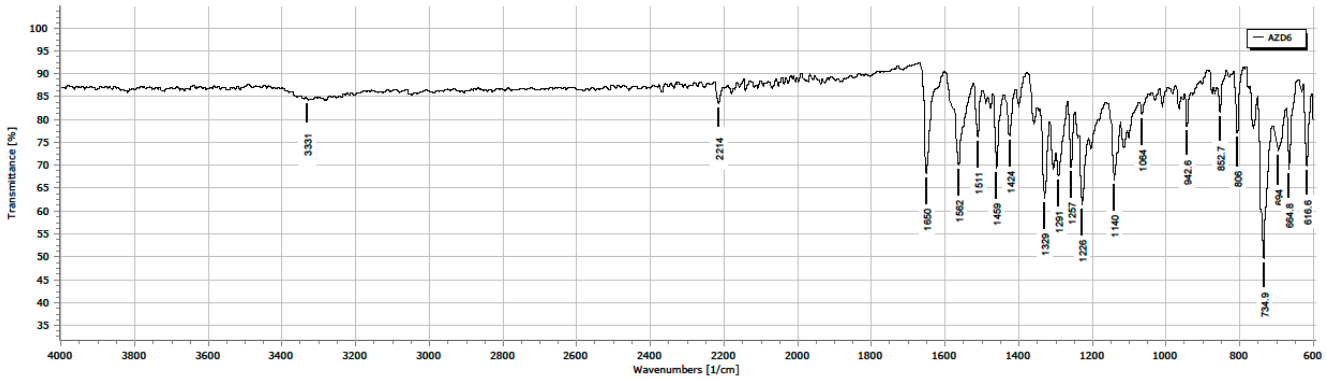
^{1}H NMR (500 MHz, DMSO-d_6)- **2k**



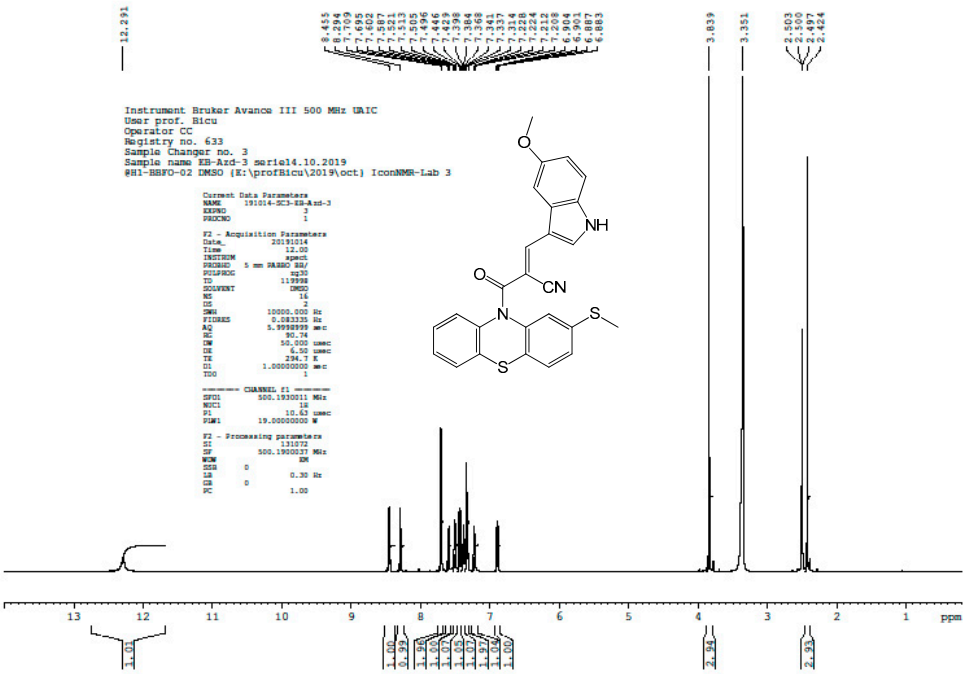
^{13}C NMR (125 MHz, DMSO-d_6)-**2k**



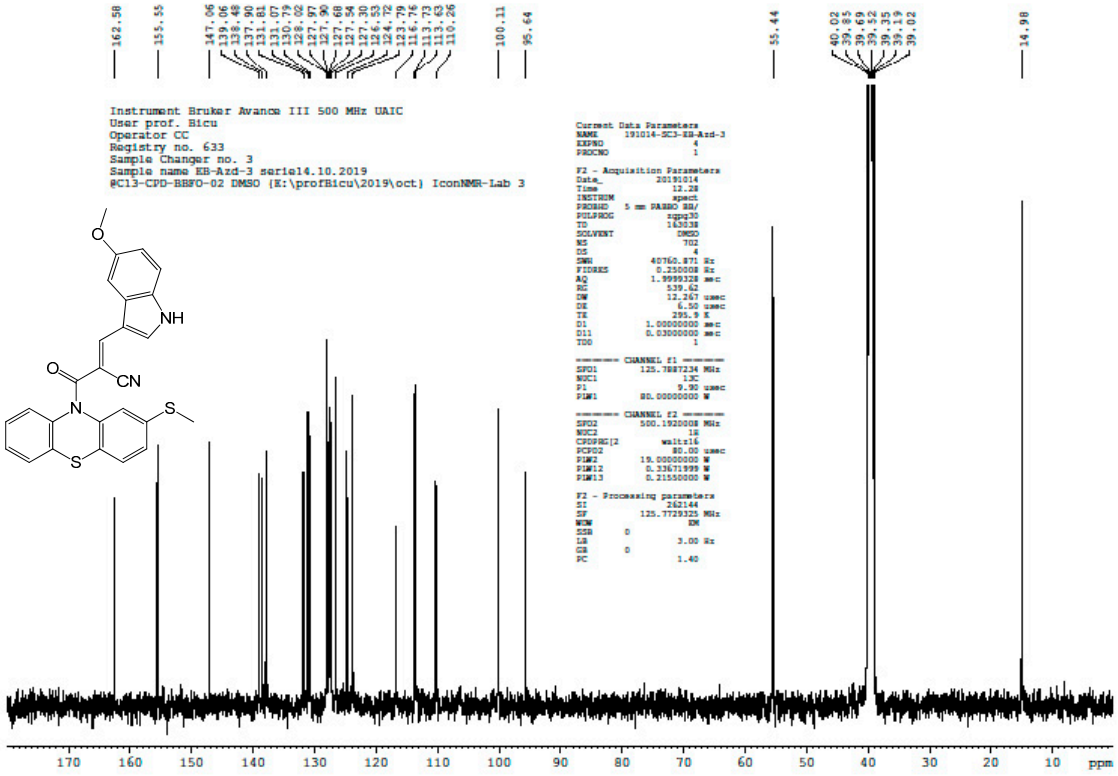
IR-2k



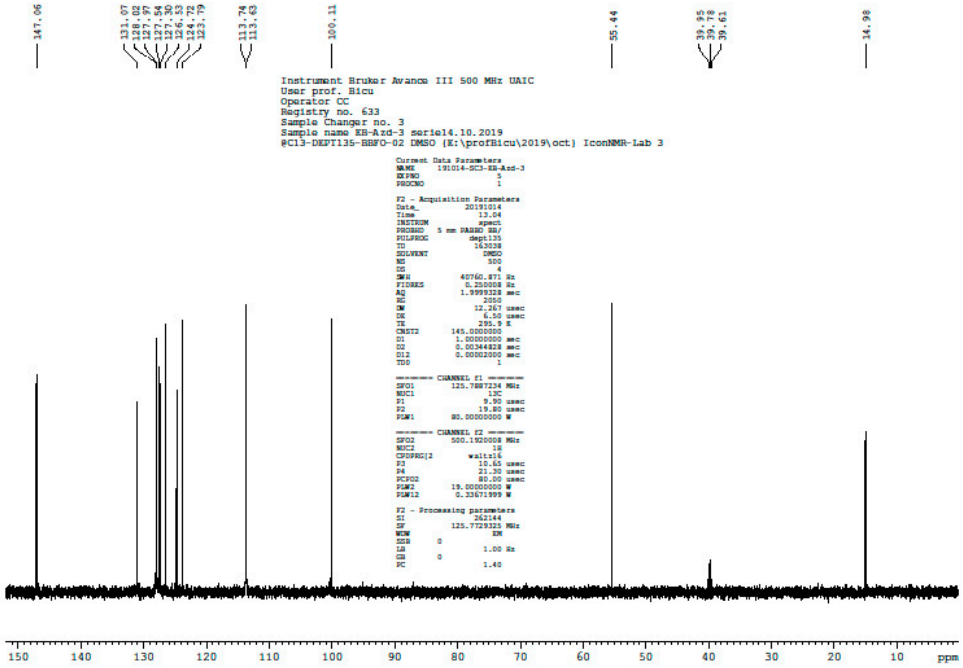
^{1}H NMR (500 MHz, DMSO-d_6)- **2l**



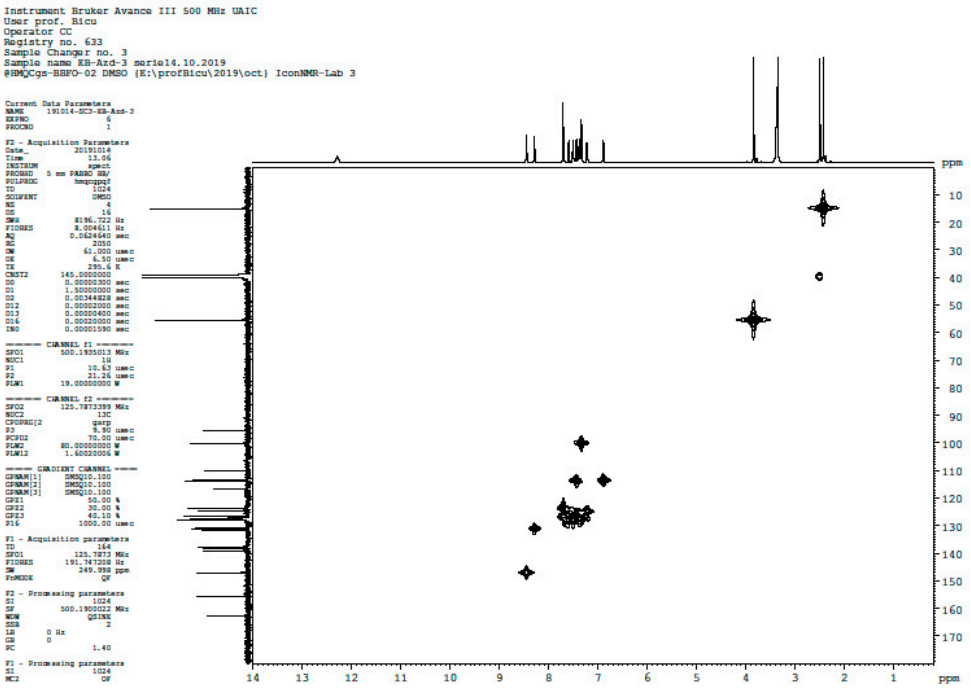
^{13}C NMR (125 MHz, DMSO-d_6)-**2l**



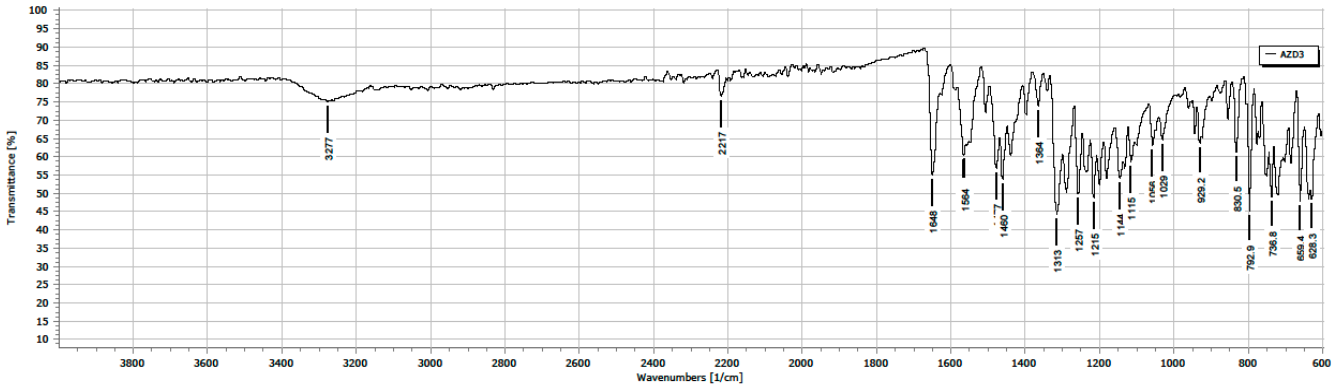
^{13}C-DEPT NMR (125 MHz, DMSO-*d*$_6$)-**2l**



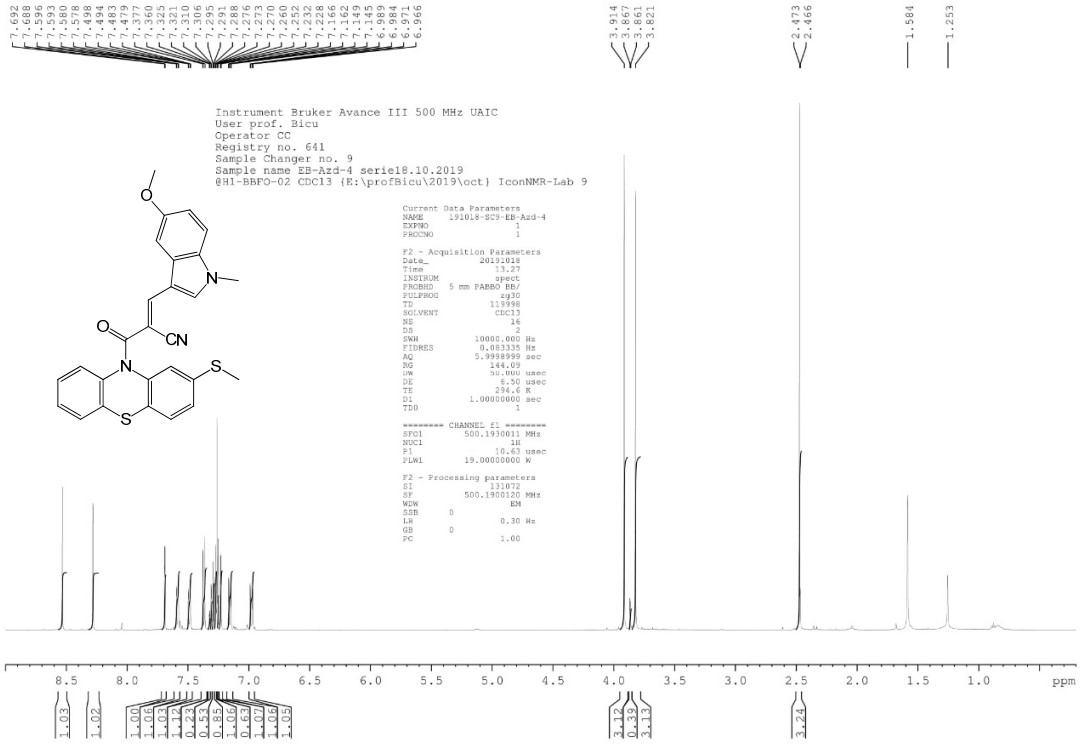
HMQC NMR (500 MHz, DMSO-*d*$_6$)-**2l**



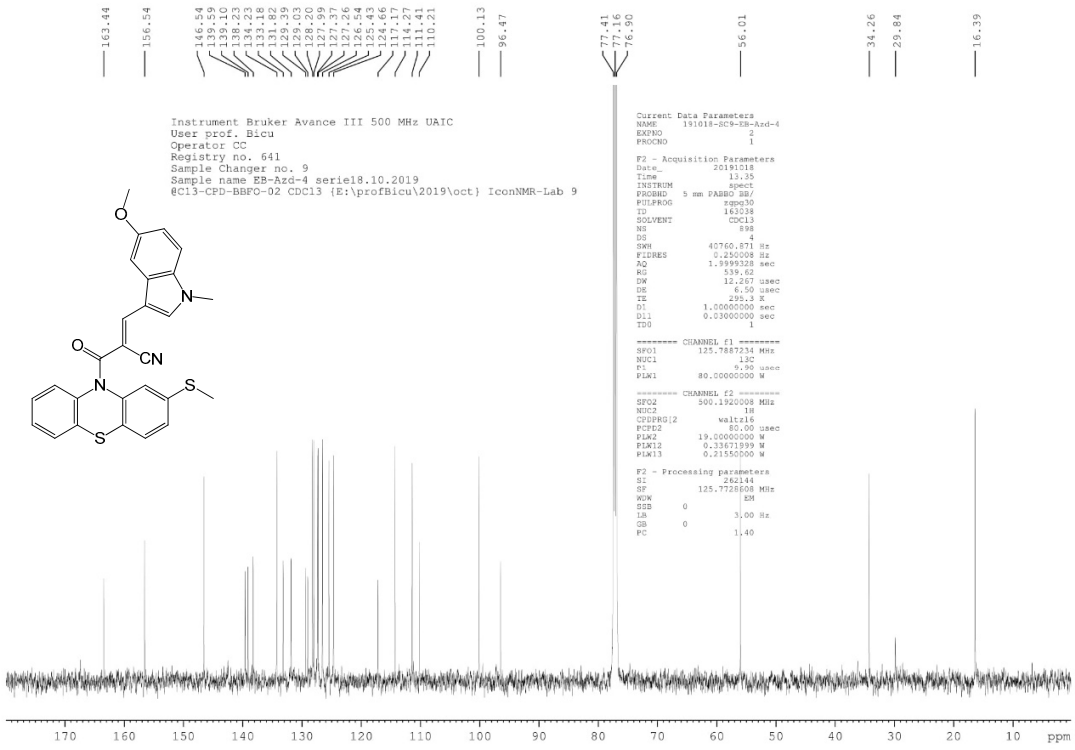
IR-2l



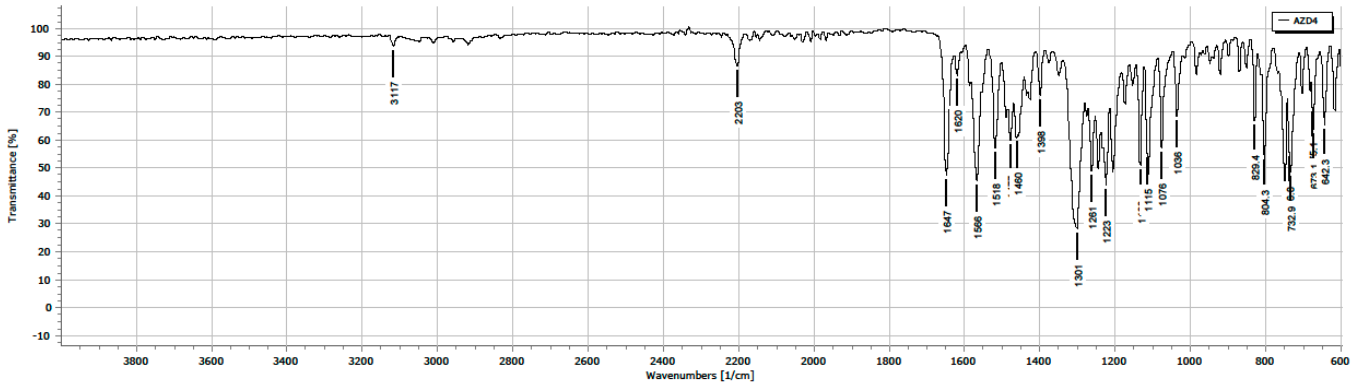
^{1}H NMR (500 MHz, DMSO-*d*$_6$)- **2m**



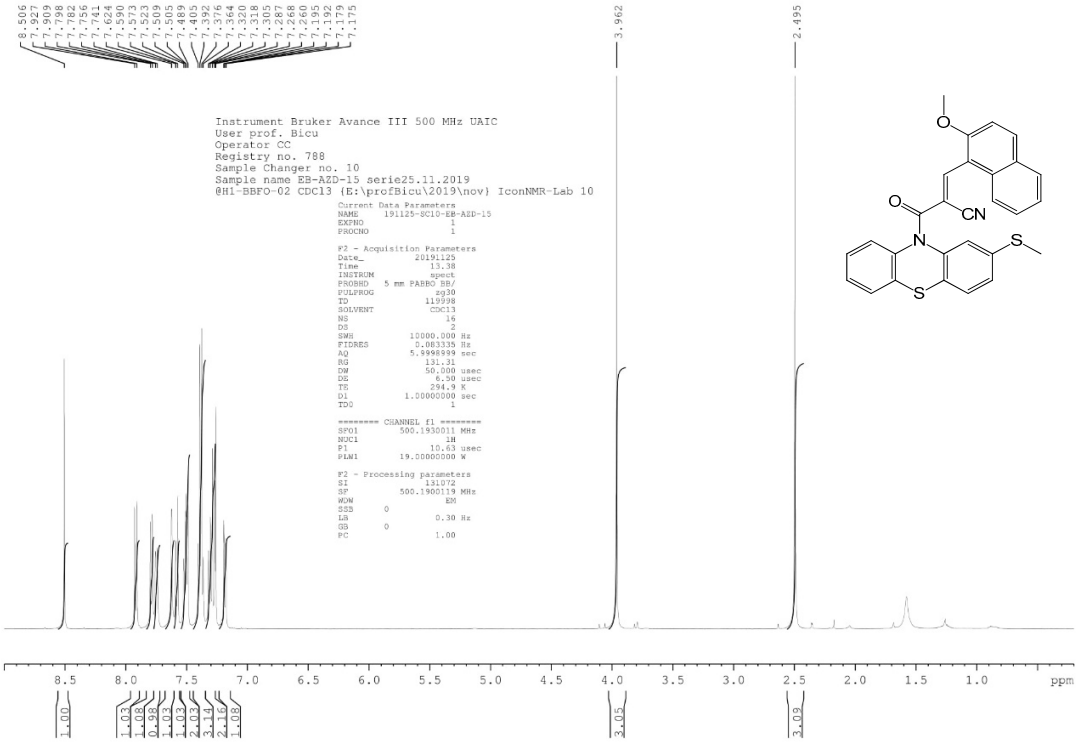
^{13}C NMR (125 MHz, DMSO-d_6)-**2m**



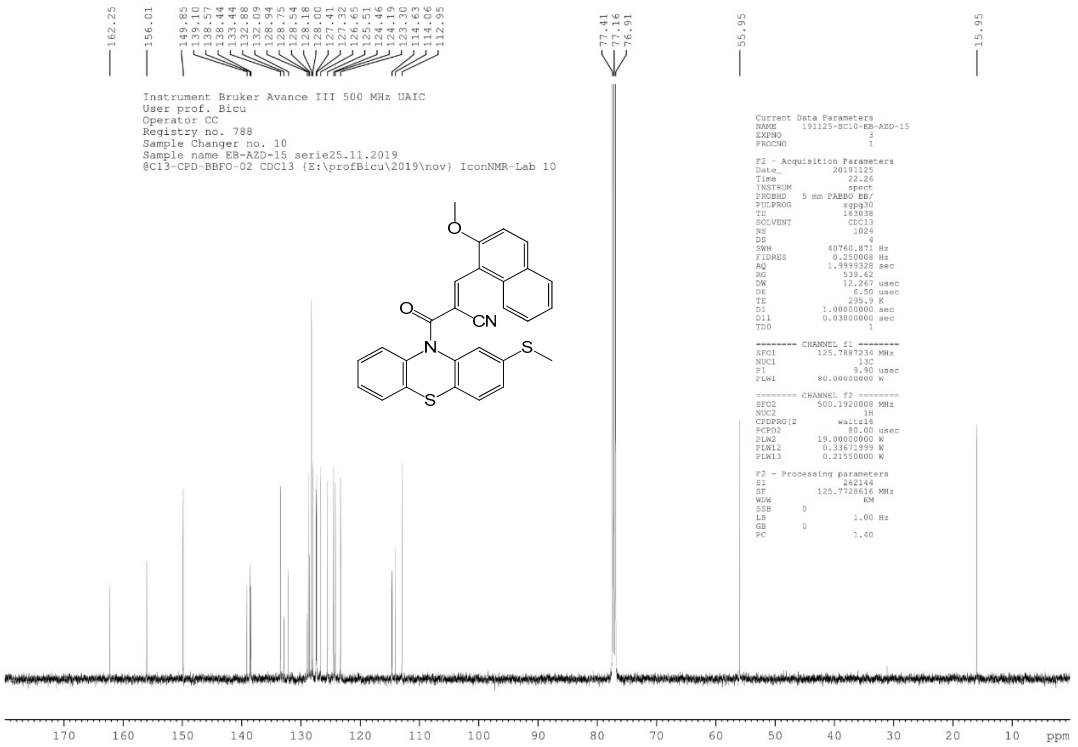
IR-2m



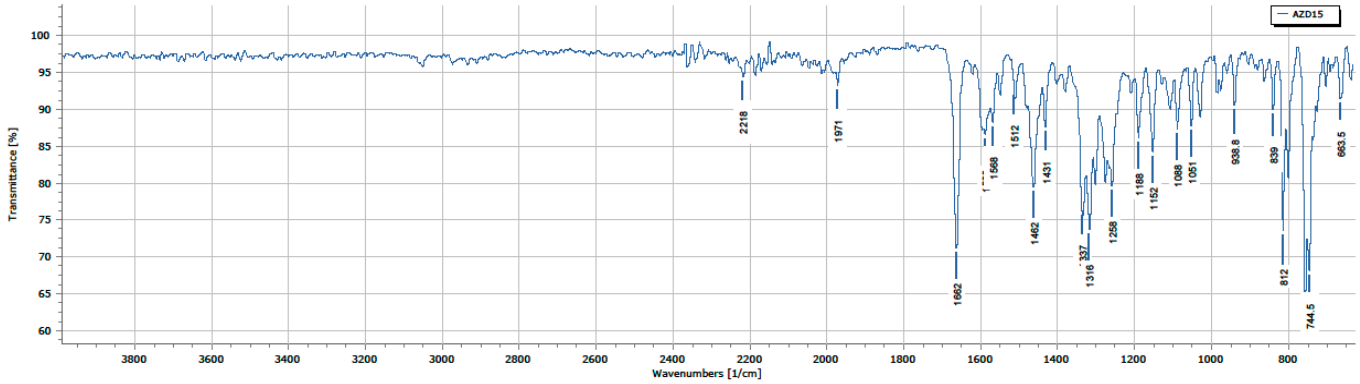
^{1}H NMR (500 MHz, $CDCl_3$)- **2n**



^{13}C NMR (125 MHz, $CDCl_3$)-**2n**



IR-2n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Transmittance [%]
Wavenumbers [1/cm]
2218
1971
1662
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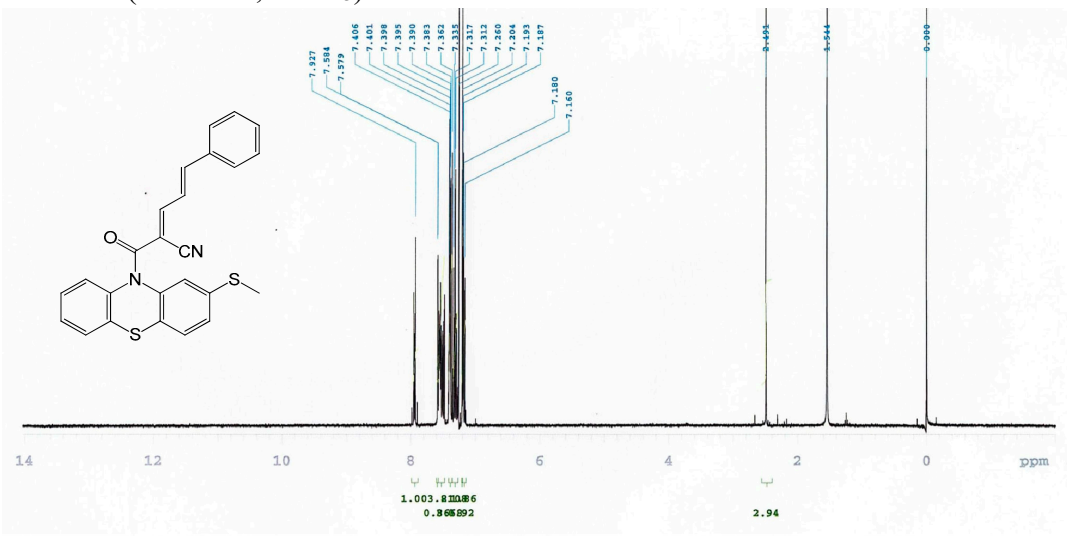
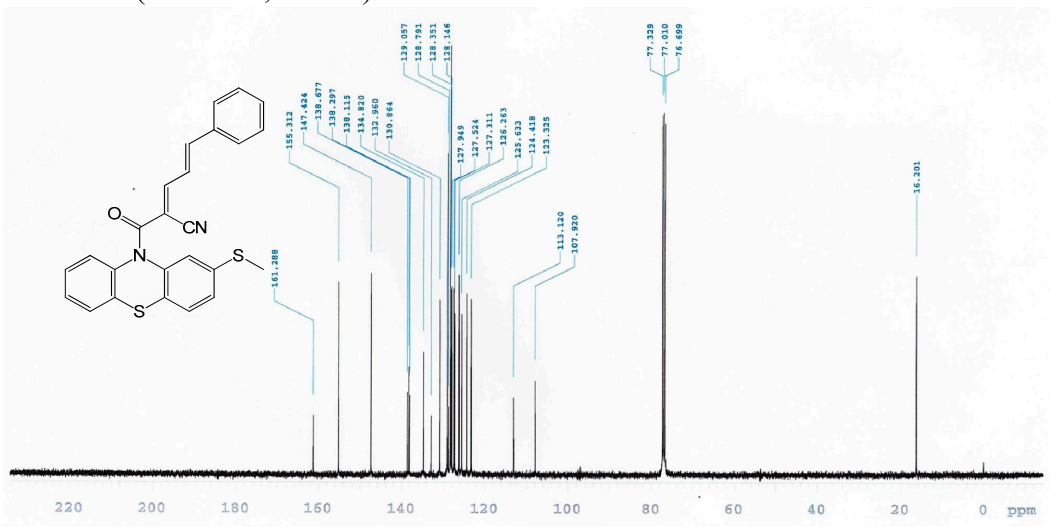
1512
1462
1431
1337
1316
1258
1188
1152
1088
1051
938.8
839
812
744.5
663.5

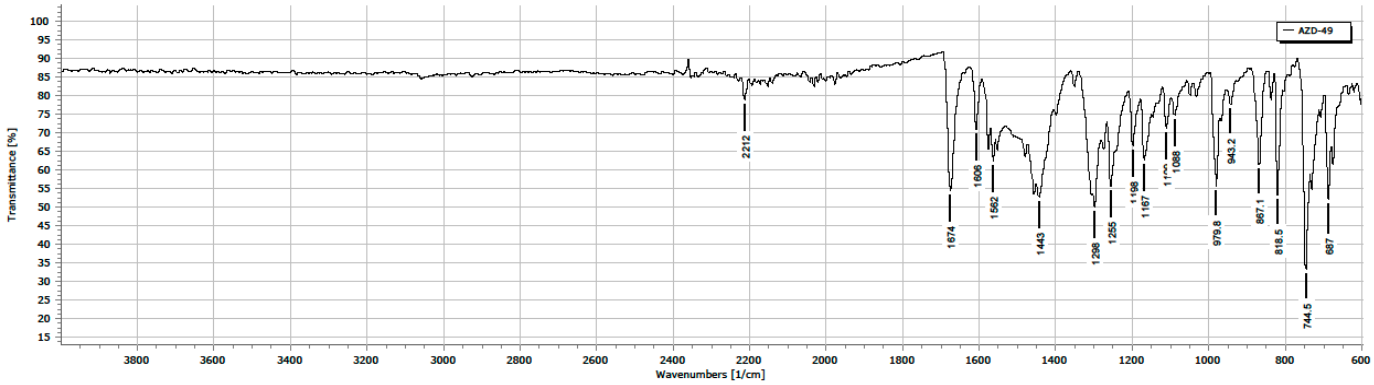
^{1}H NMR (400 MHz, $CDCl_3$)-**2o**



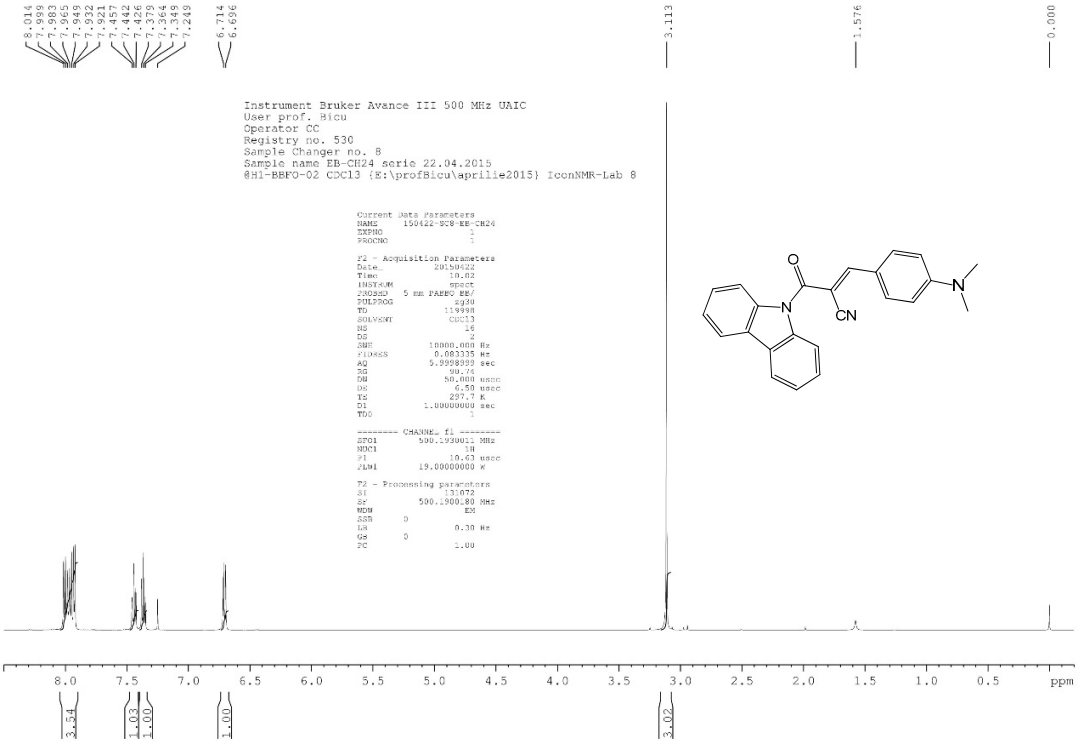
^{13}C NMR (100 MHz, $CDCl_3$)-**2o**



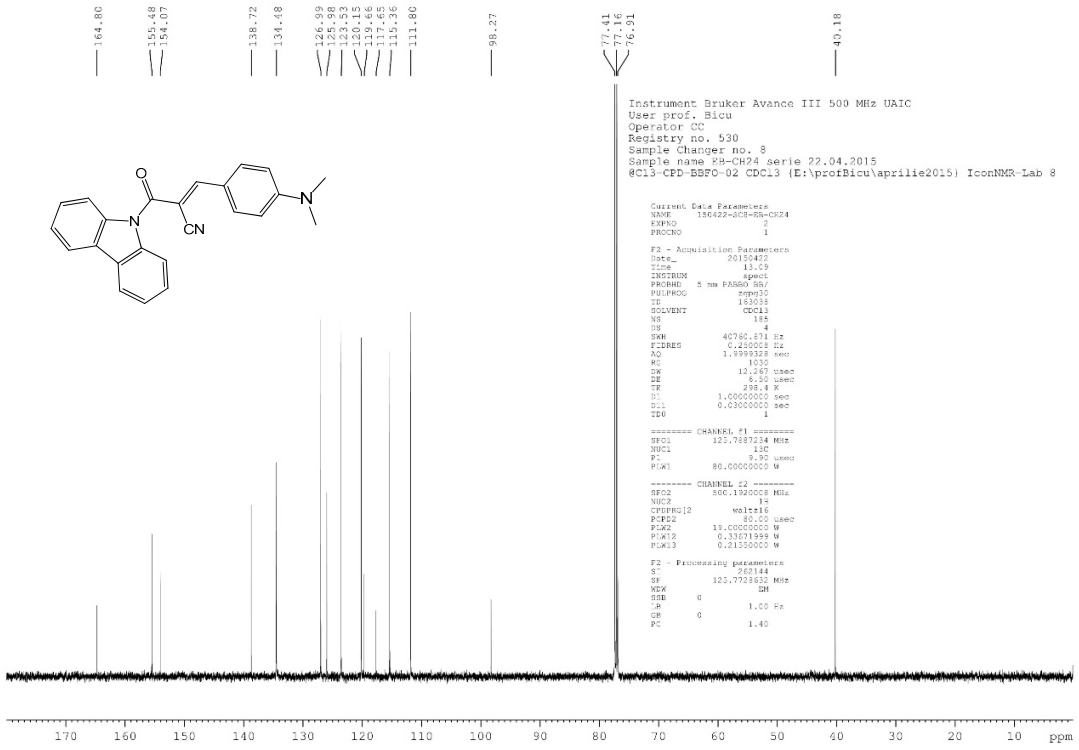
IR-2o



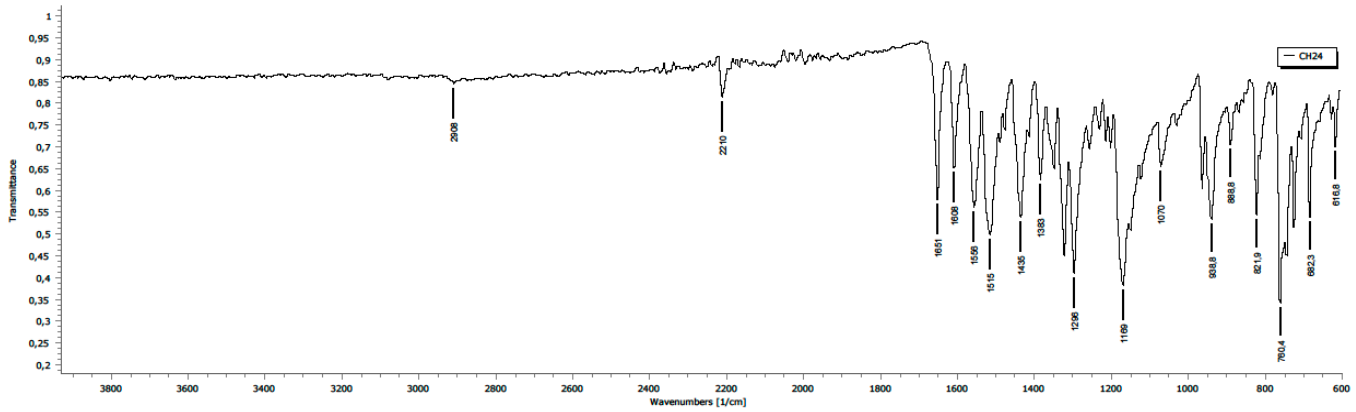
^{1}H NMR (500 MHz, $CDCl_3$)- **3a**



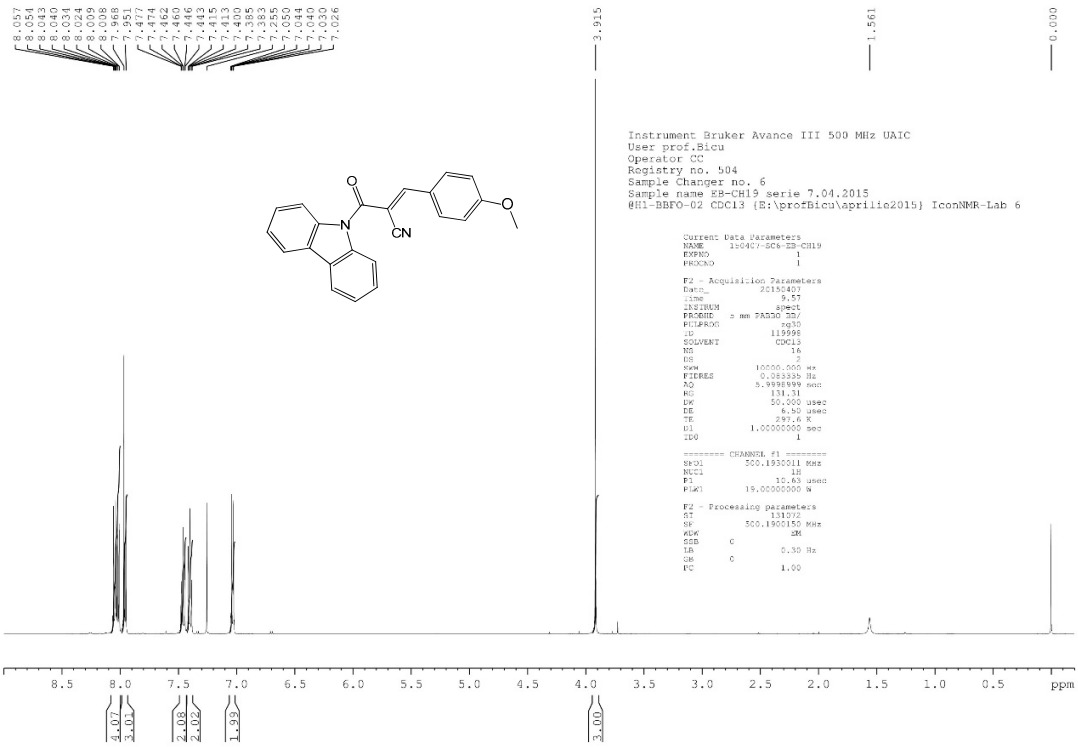
^{13}C NMR (125 MHz, $CDCl_3$)-**3a**



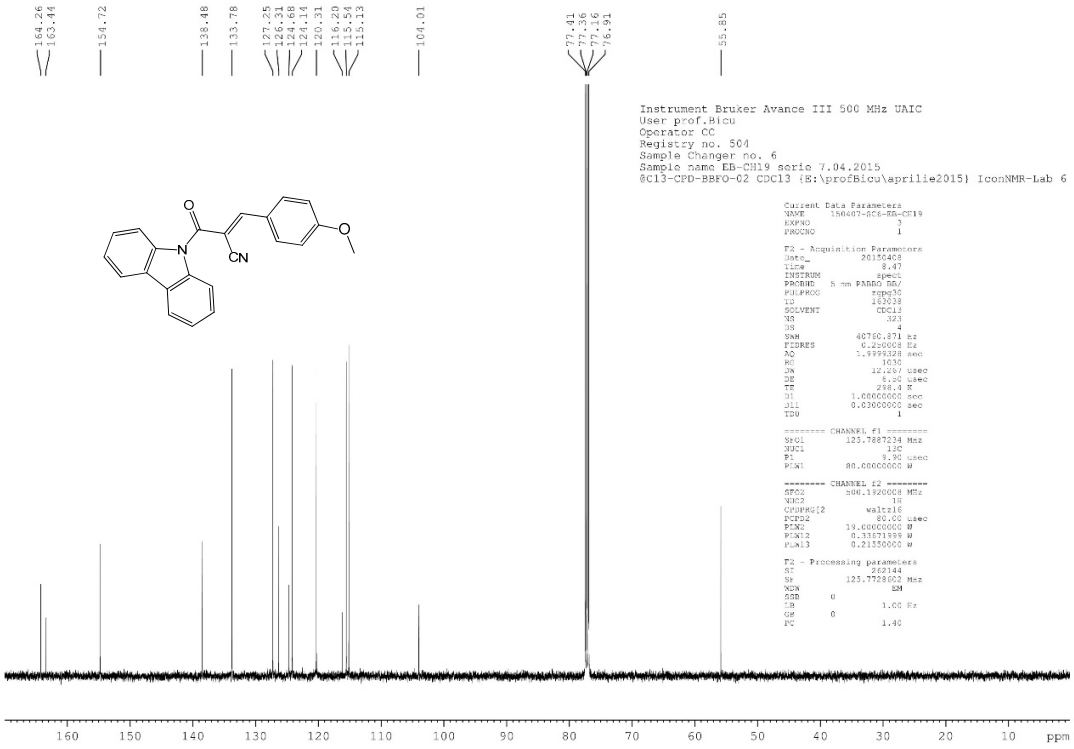
IR-3a



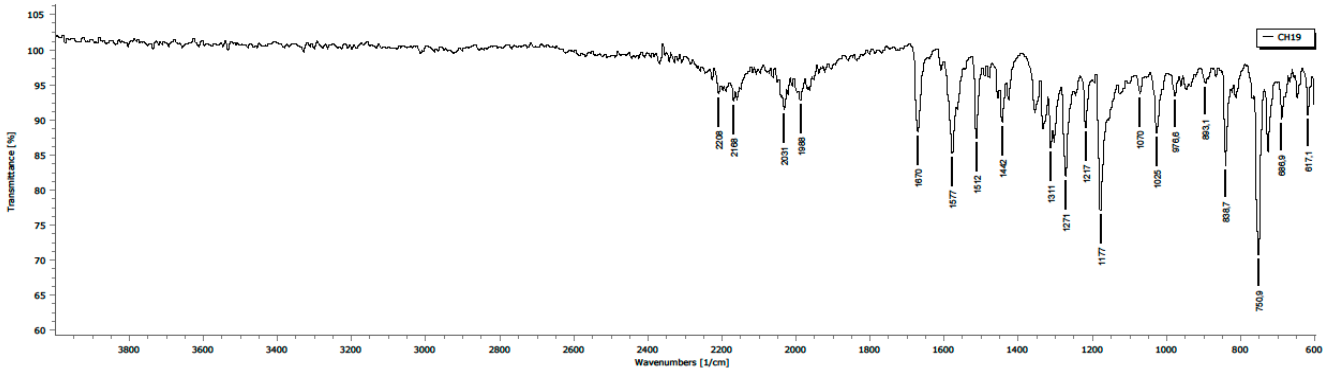
^{1}H NMR (500 MHz, $CDCl_3$)-**3b**



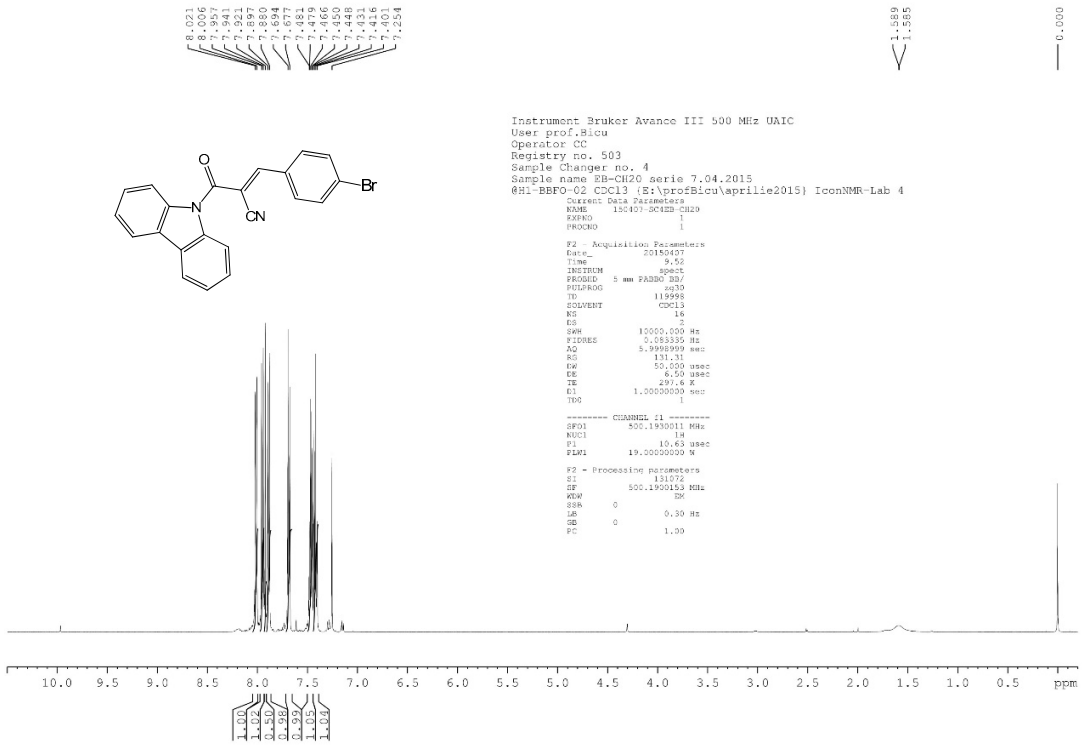
^{13}C NMR (125 MHz, $CDCl_3$)-**3b**



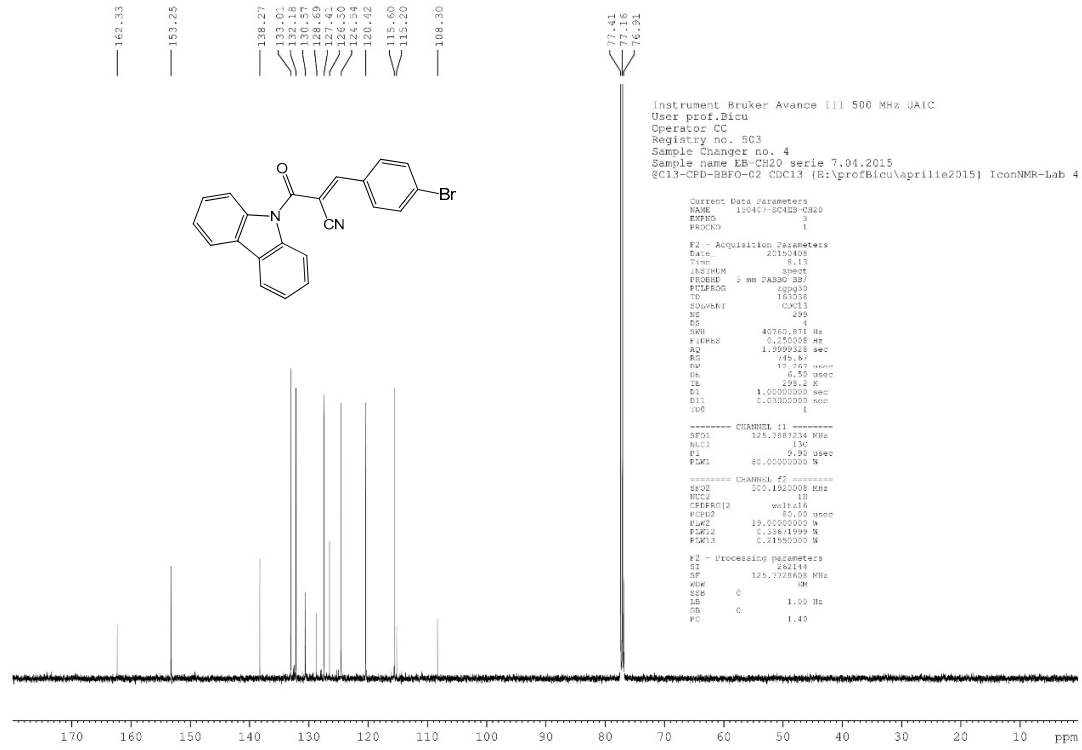
IR-3b



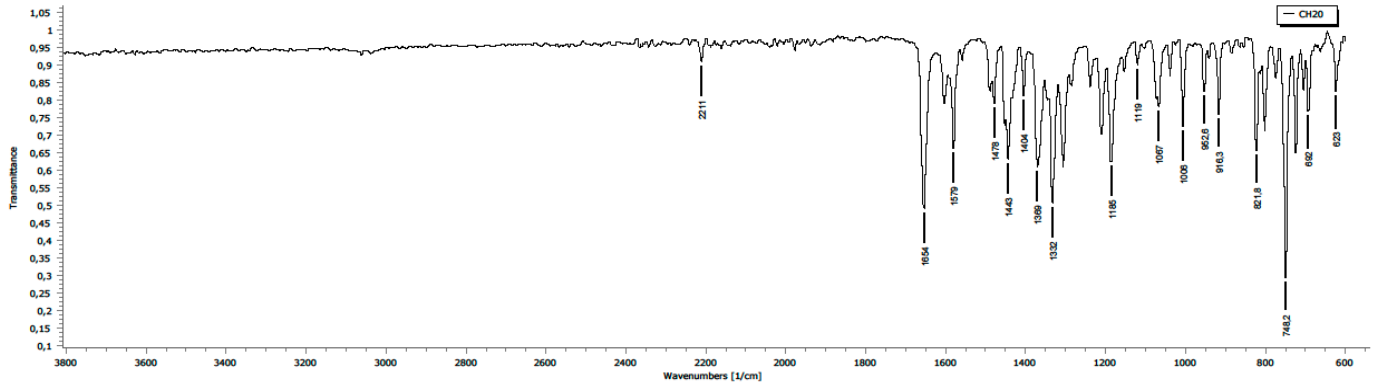
^{1}H NMR (500 MHz, $CDCl_3$)-**3c**



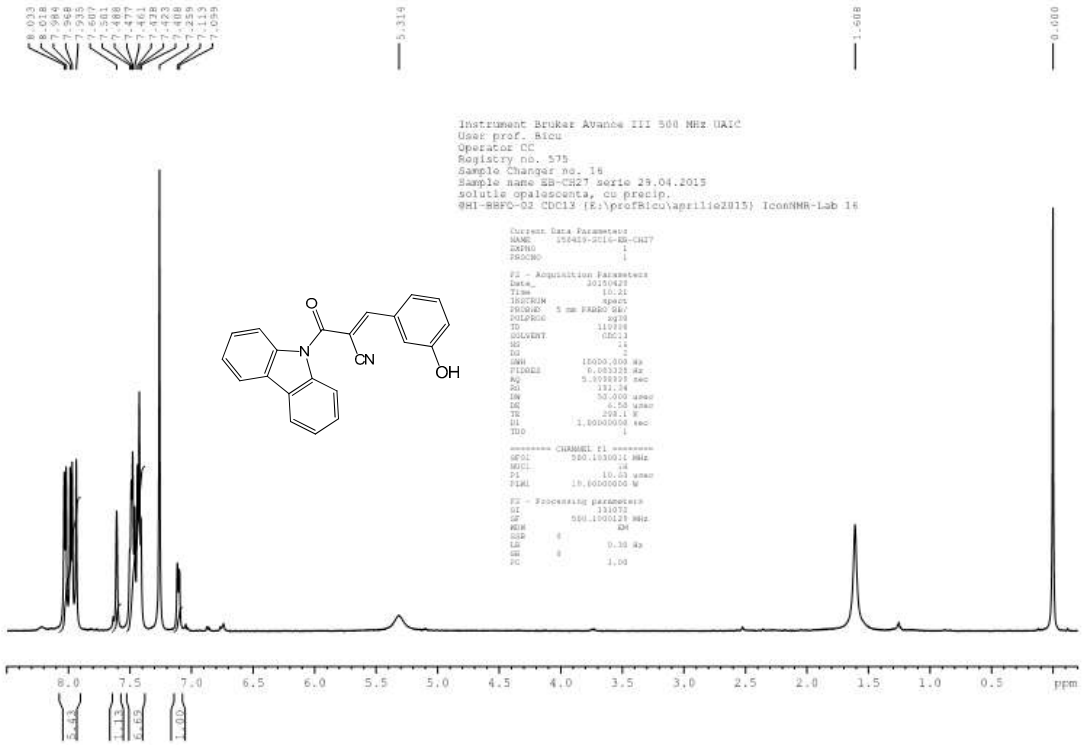
^{13}C NMR (125 MHz, $CDCl_3$)-**3c**



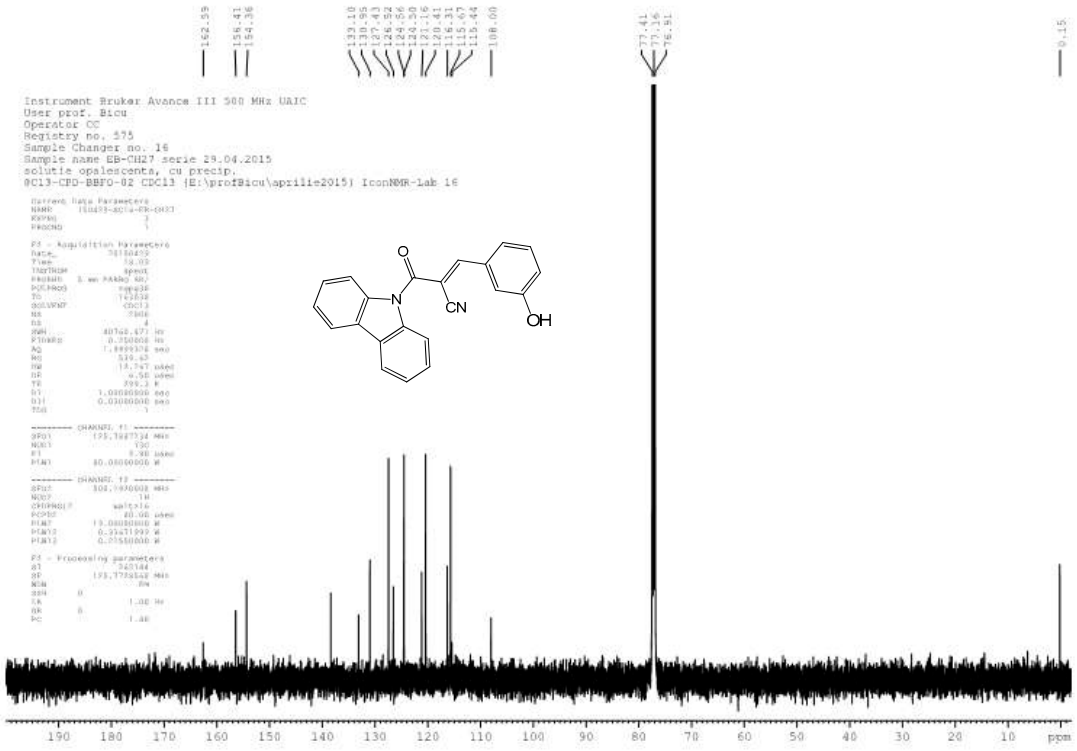
IR-3c



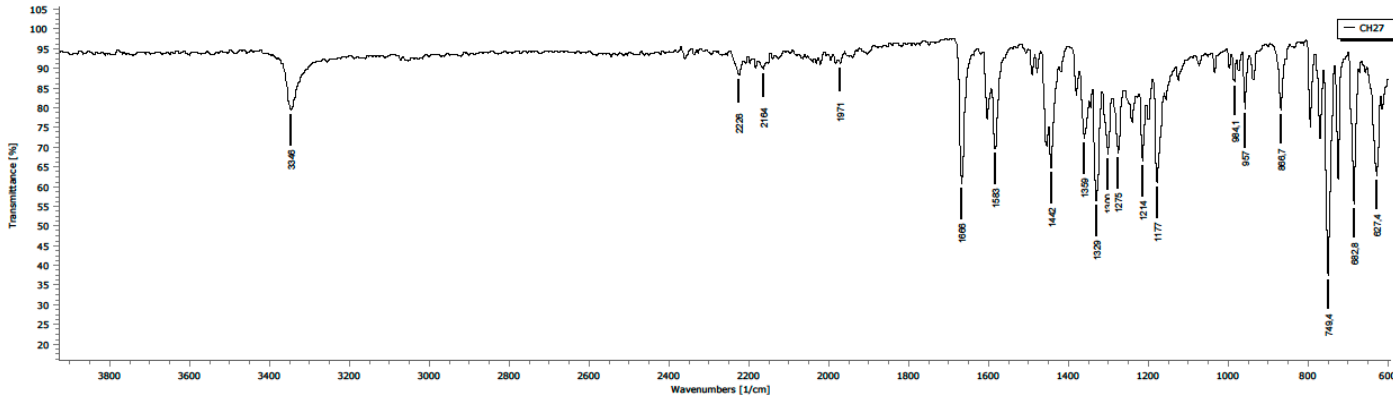
^{1}H NMR (500 MHz, DMSO-d_6)-**3d**



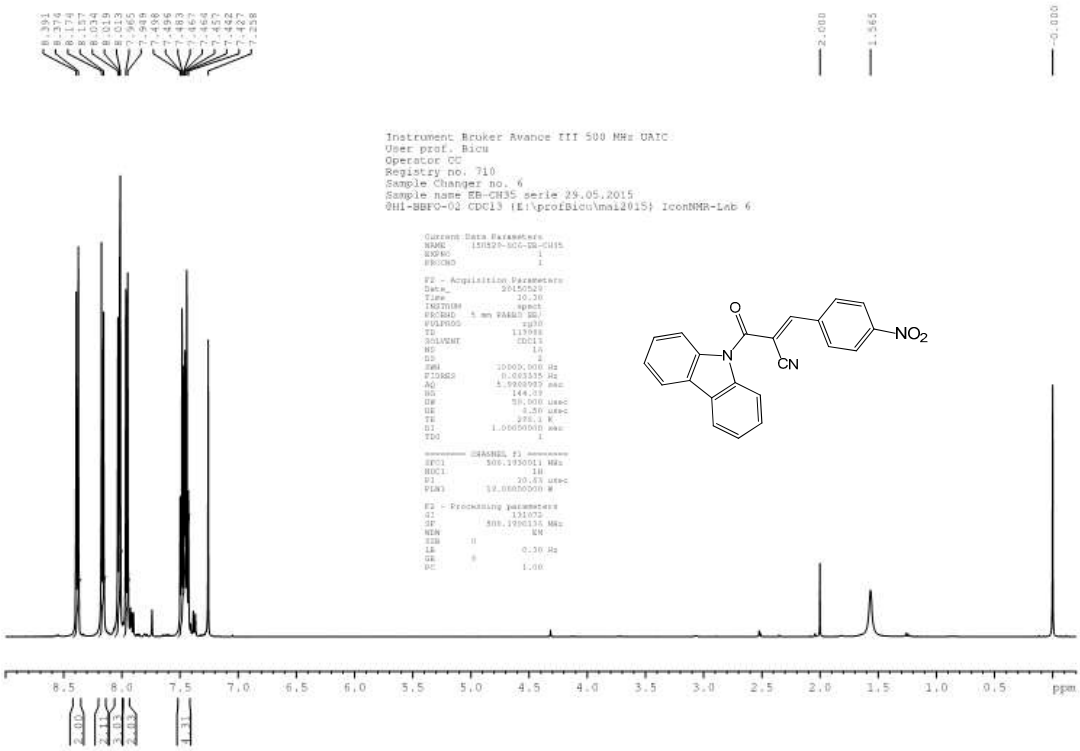
^{13}C NMR (125 MHz, DMSO-d_6)-**3d**



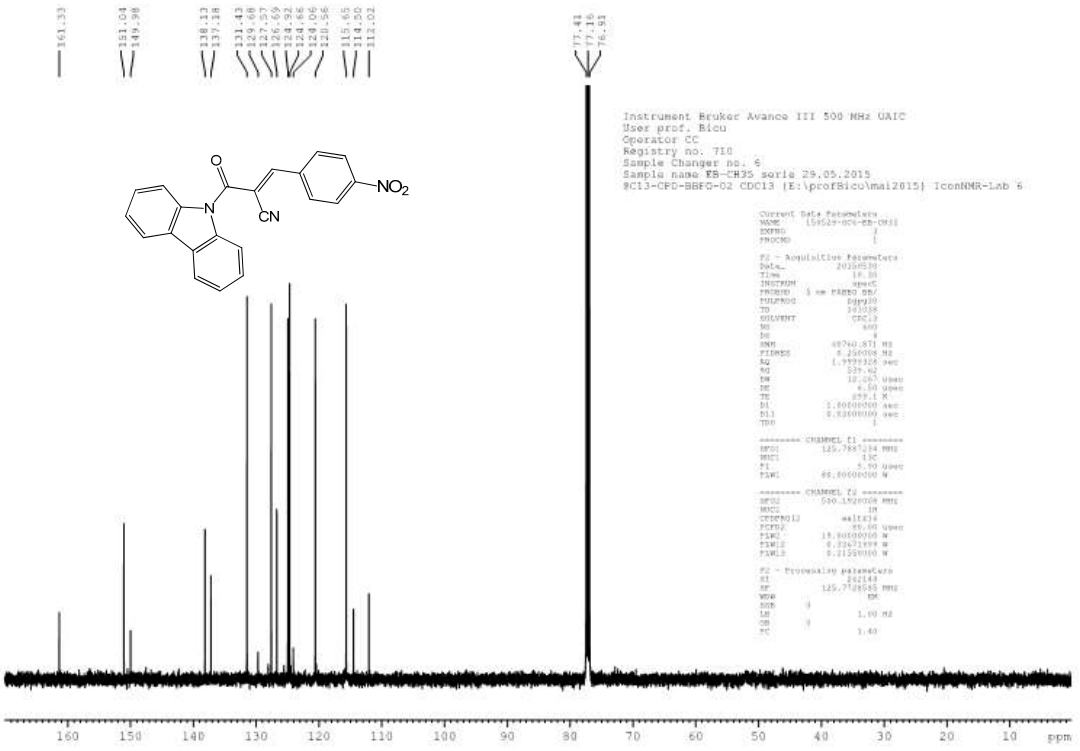
IR-3d



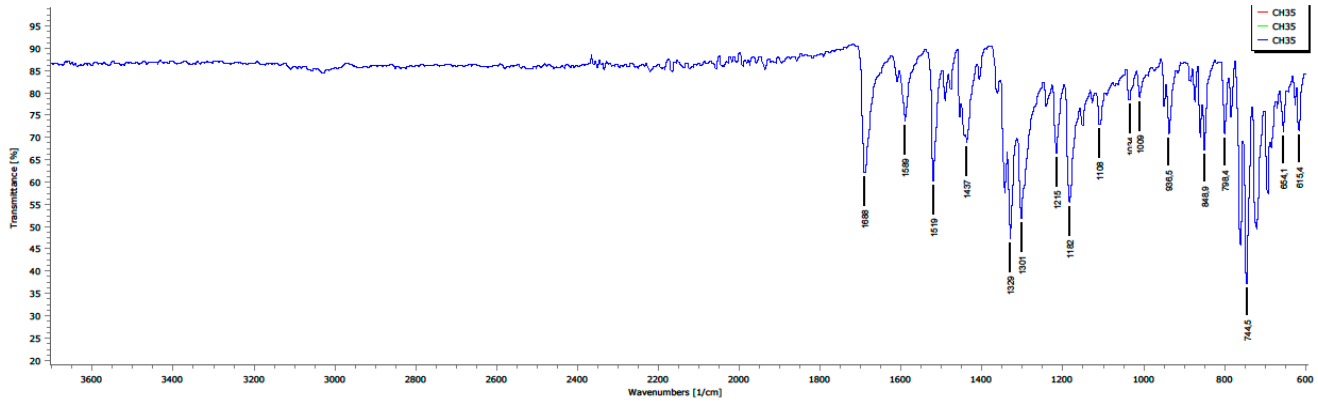
^{1}H NMR (500 MHz, $CDCl_3$)-**3e**



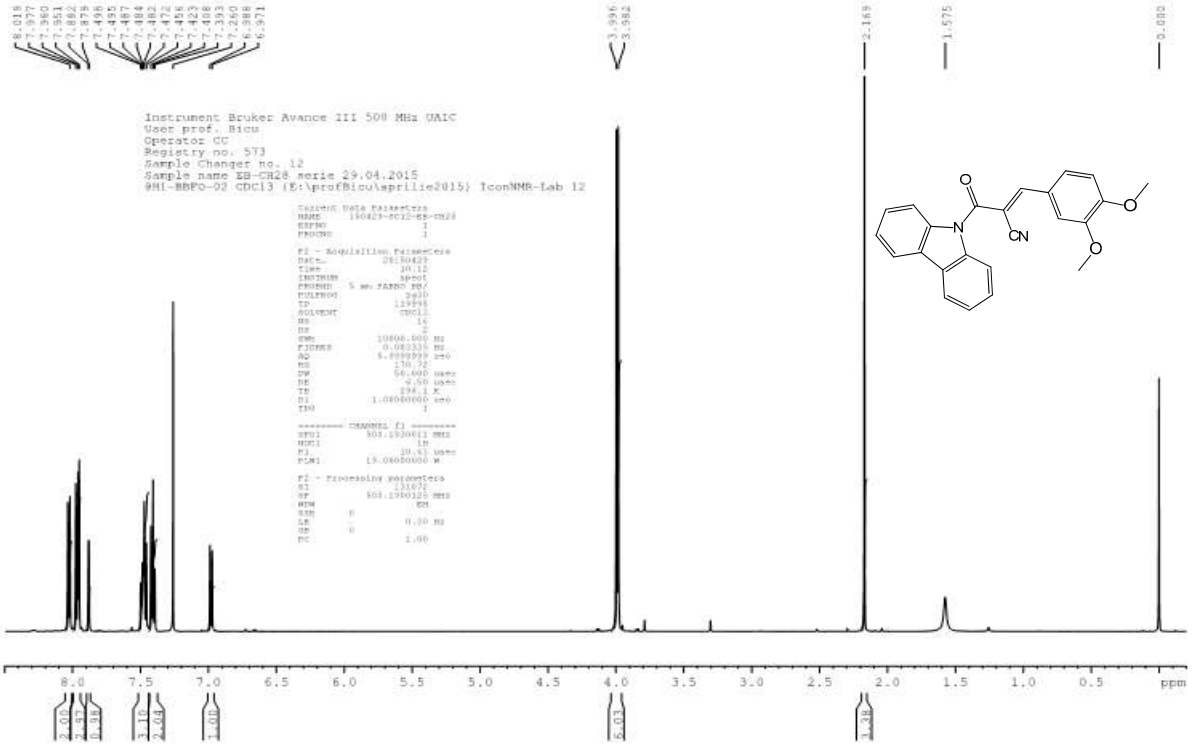
^{13}C NMR (125 MHz, $CDCl_3$)-**3e**



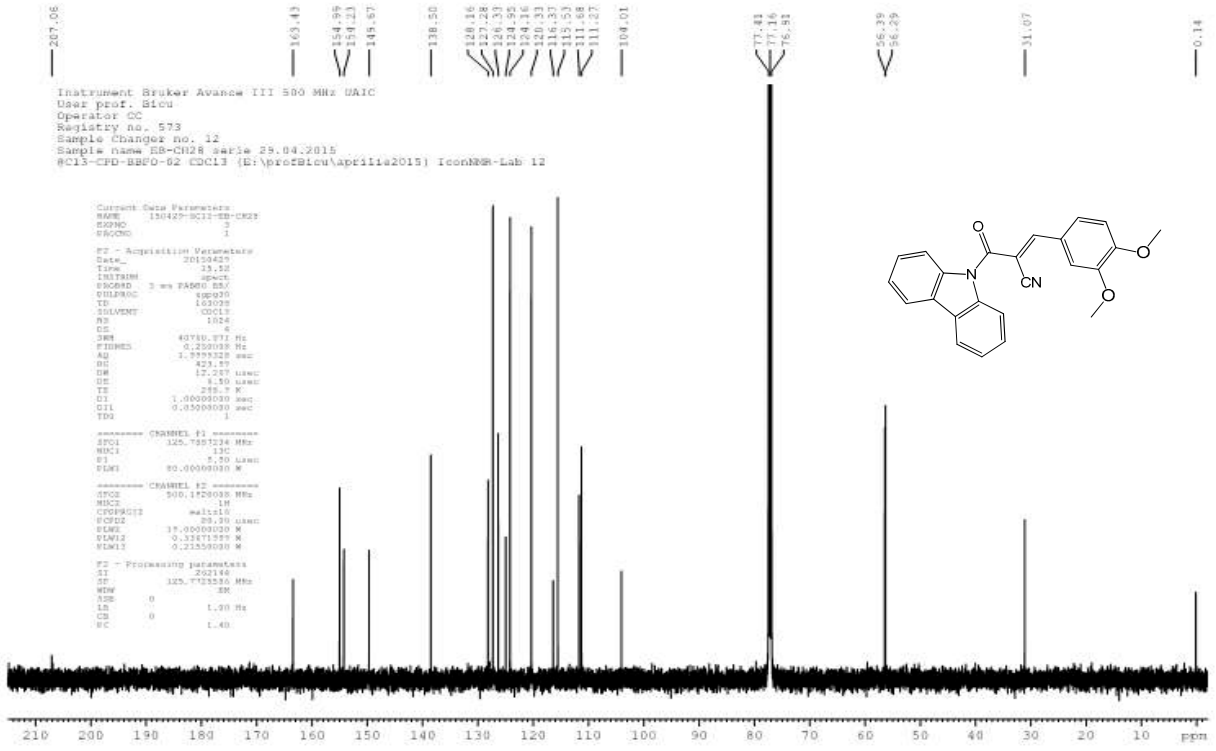
IR-3e



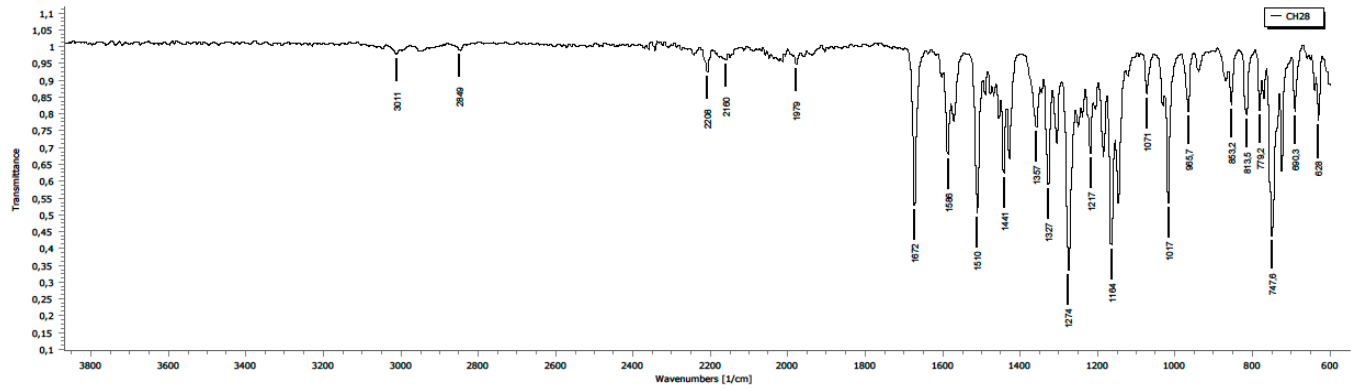
^{1}H NMR (500 MHz, $CDCl_3$)-**3f**



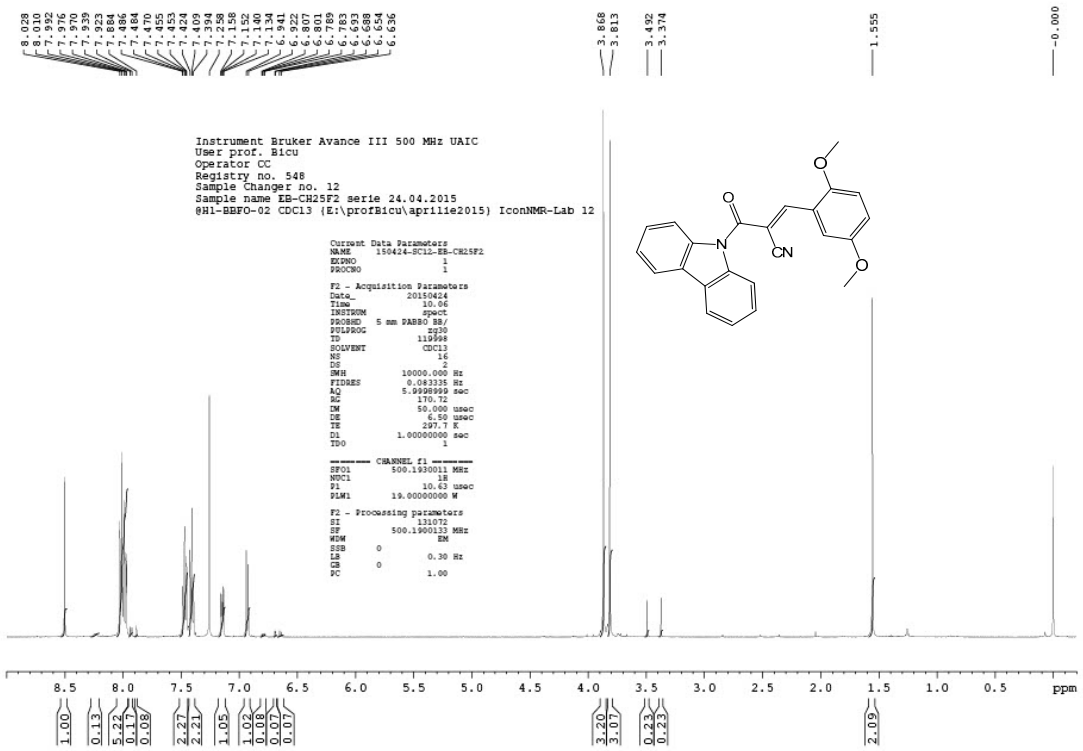
^{13}C NMR (125 MHz, $CDCl_3$)-**3f**



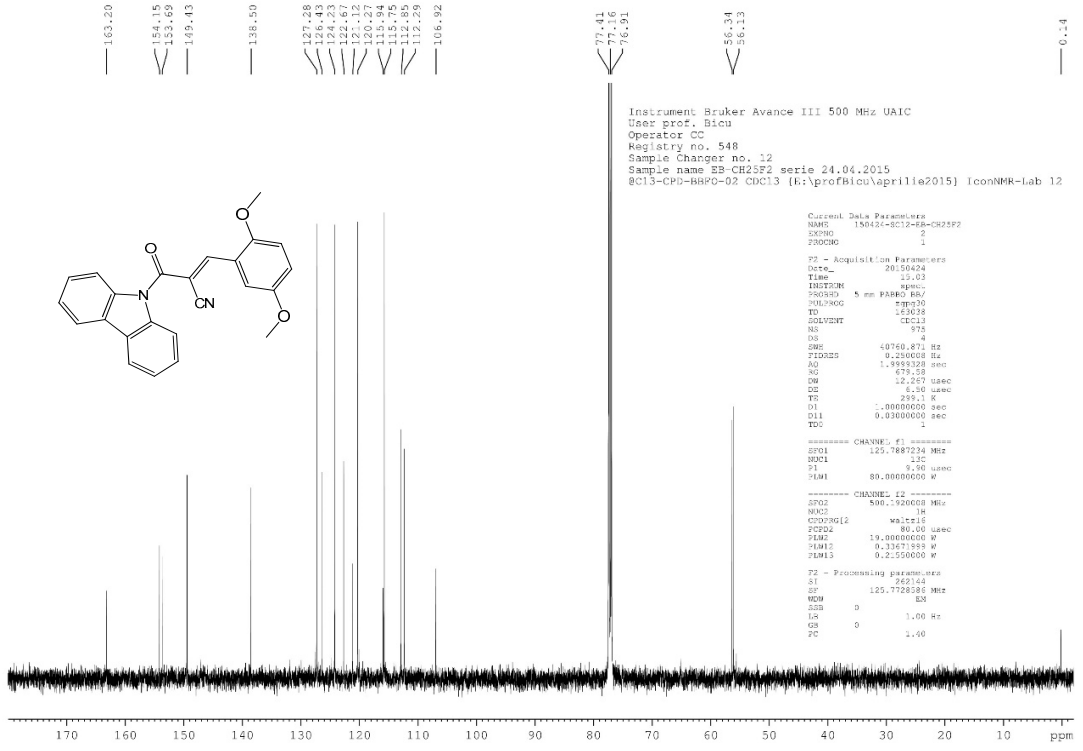
IR-3f



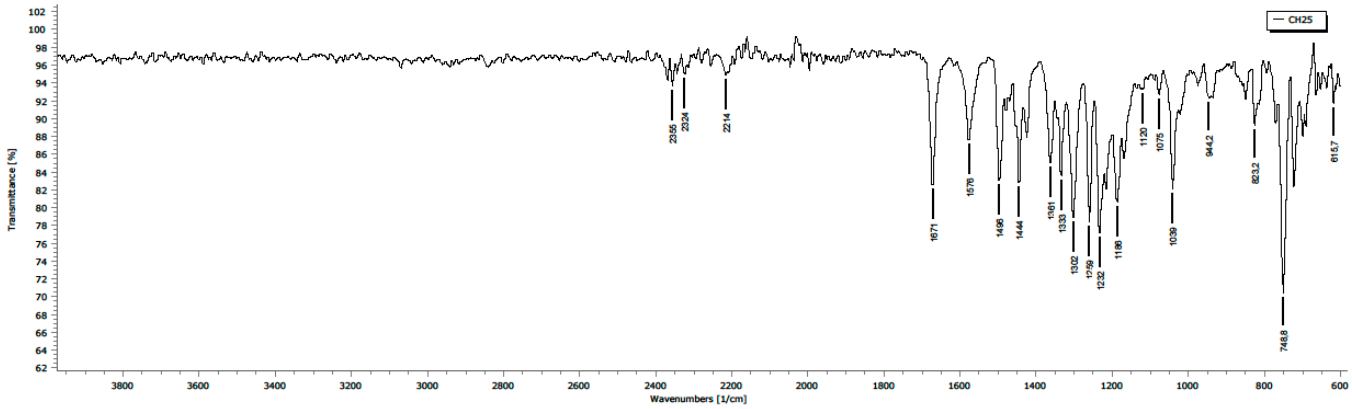
^{1}H NMR (500 MHz, $CDCl_3$)-**3g**



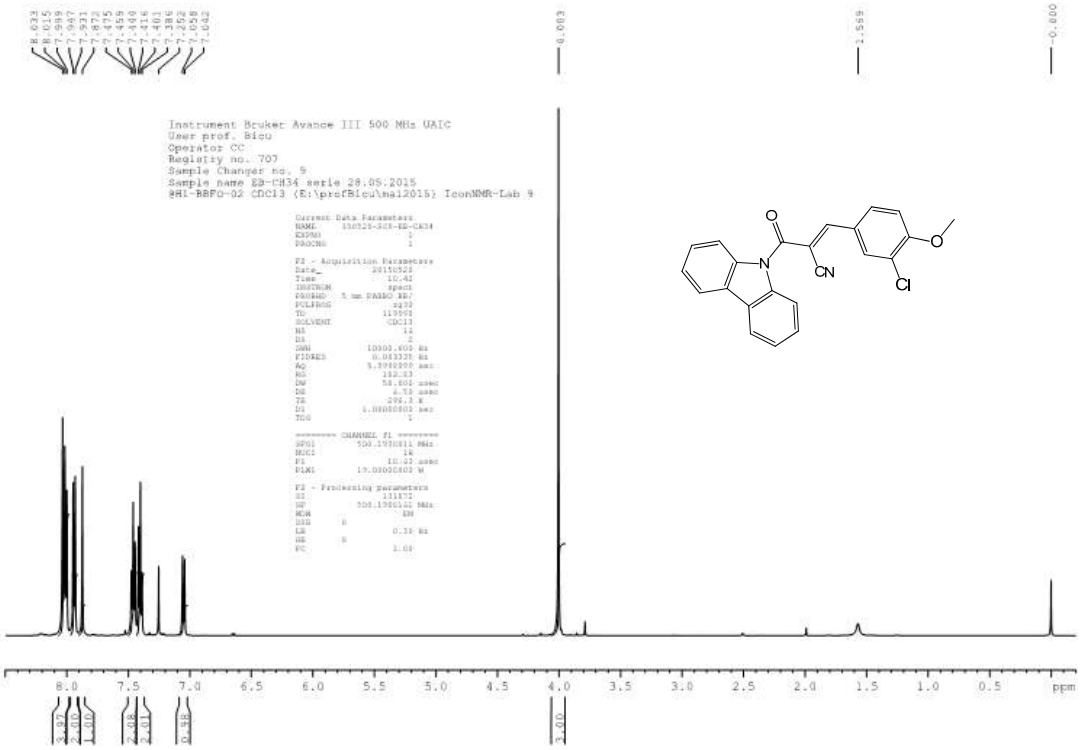
^{13}C NMR (125 MHz, $CDCl_3$)-**3g**



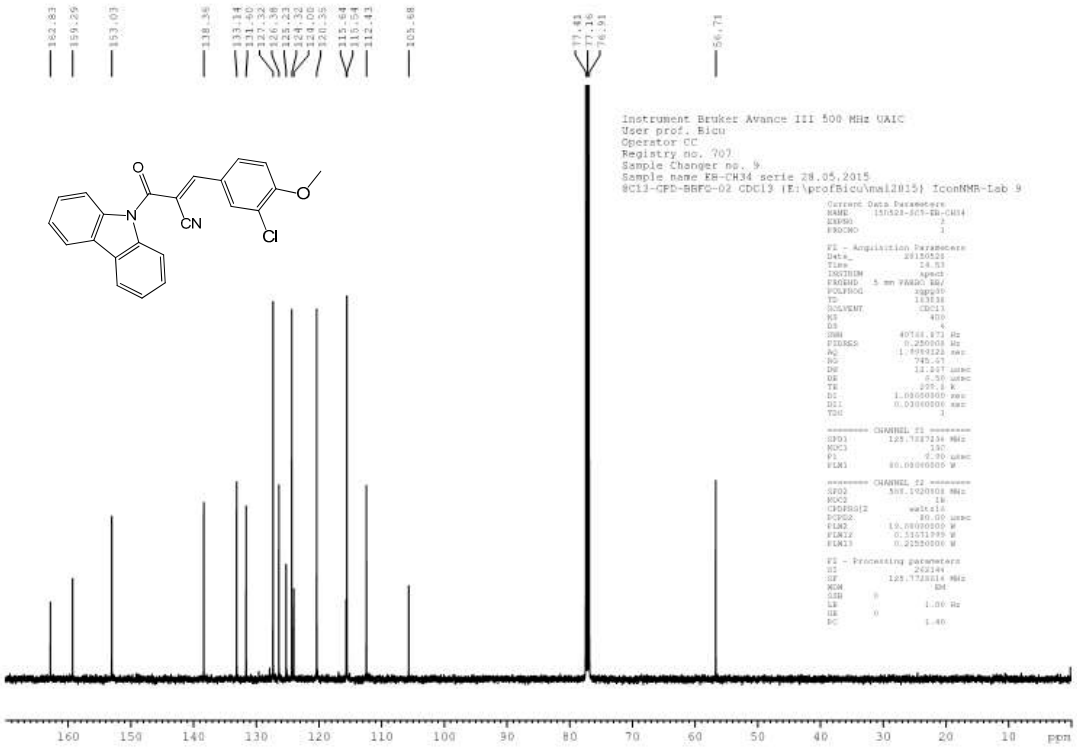
IR-3g



^{1}H NMR (500 MHz, $CDCl_3$)-**3h**



^{13}C NMR (125 MHz, $CDCl_3$)-**3h**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159.29
153.03
138.36
133.14
131.60
127.32
126.38
125.23
124.32
124.00
120.35
115.64
110.54
112.43
105.68
77.41
77.16
76.91
56.71
O
N
CN
O
Cl
Instrument Bruker Avance III 500 MHz UAIC
User prof. Bicu
Operator CC
Registry no. 707
Sample Changer no. 9
Sample name EB-CH34 serie 28.05.2015
8C13-GFD-BBFO-02 CDCl3 (E:\profBicu\nmr12015) TconNMR-Lab 9
Current Data Parameters
NAME 150528-8C5-EB-CH34
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Data... 20150528
Time 14.53
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 113838
SOLVENT CDCl3
NS 400
DS 4
SWH 40768.871 Hz
FIDRES 0.358008 Hz
AQ 1.6999123 sec
RG 745.67
DW 12.267 usec
DE 6.50 usec
TE 297.1 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7337234 MHz
NUC1 13C
P1 8.00 usec
PLW1 80.00000000 W
======== CHANNEL f2 ========
SFO2 500.1020008 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 19.08000000 W
PLW12 0.51071999 W
PLW13 0.21550000 W
F2 - Processing parameters
SI 262144
SF 125.7720214 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
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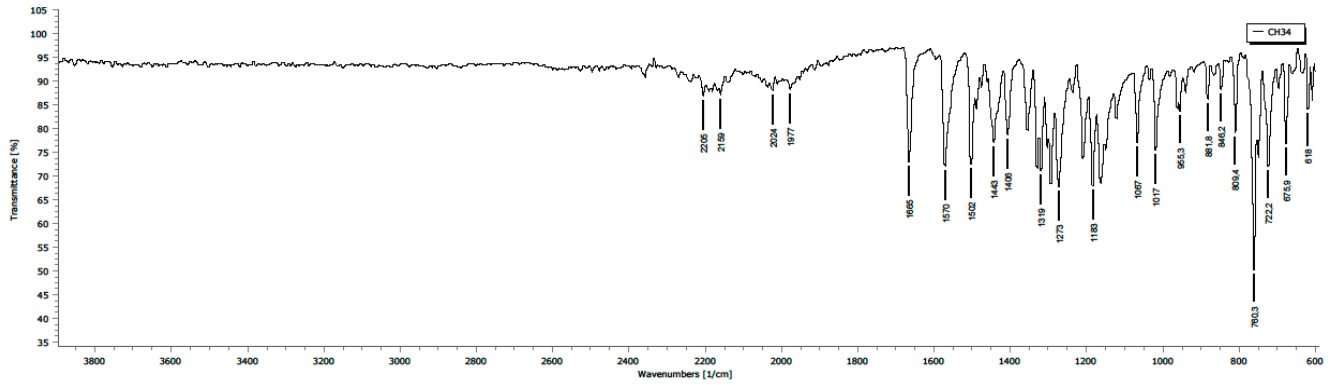
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

IR-3h


CH34
Transmittance [%]
Wavenumbers [1/cm]
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2024
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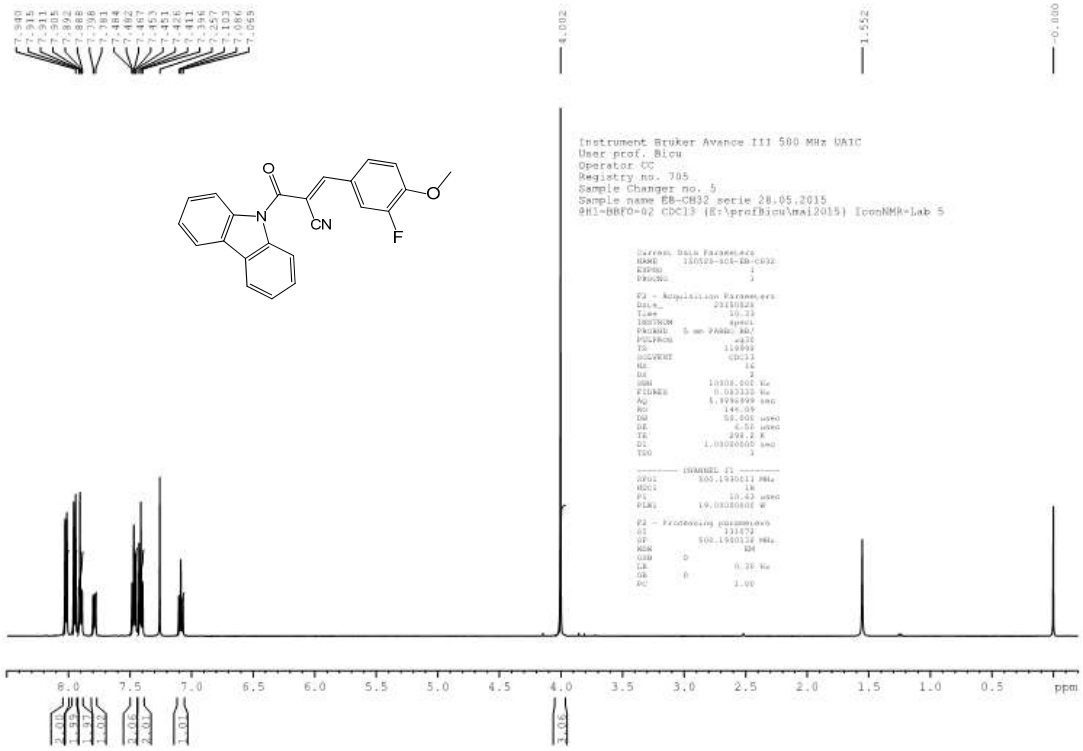
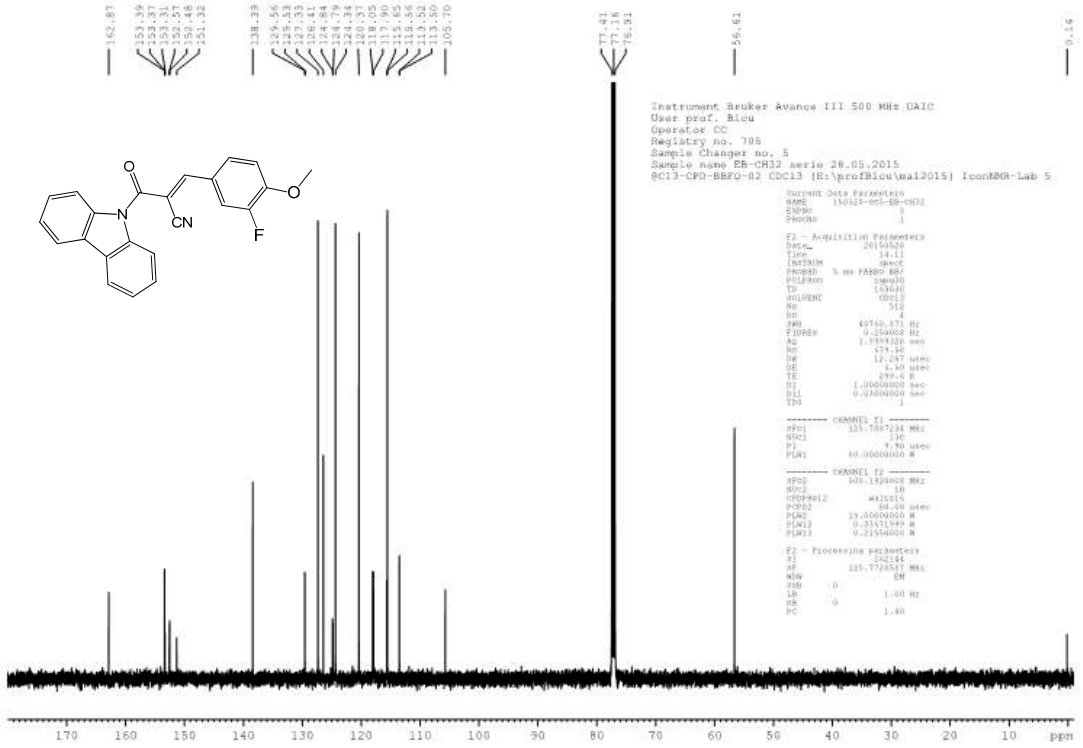
1443
1406
1319
1273
1180
1097
1017
953
881.8
846.2
809.4
760.3
722.2
675.9
618

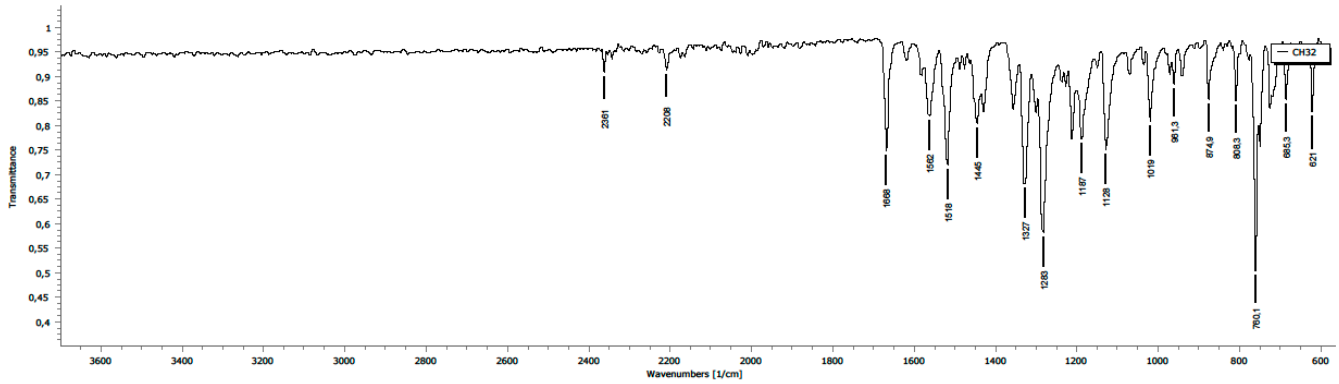
^{1}H NMR (500 MHz, $CDCl_3$)-**3i**



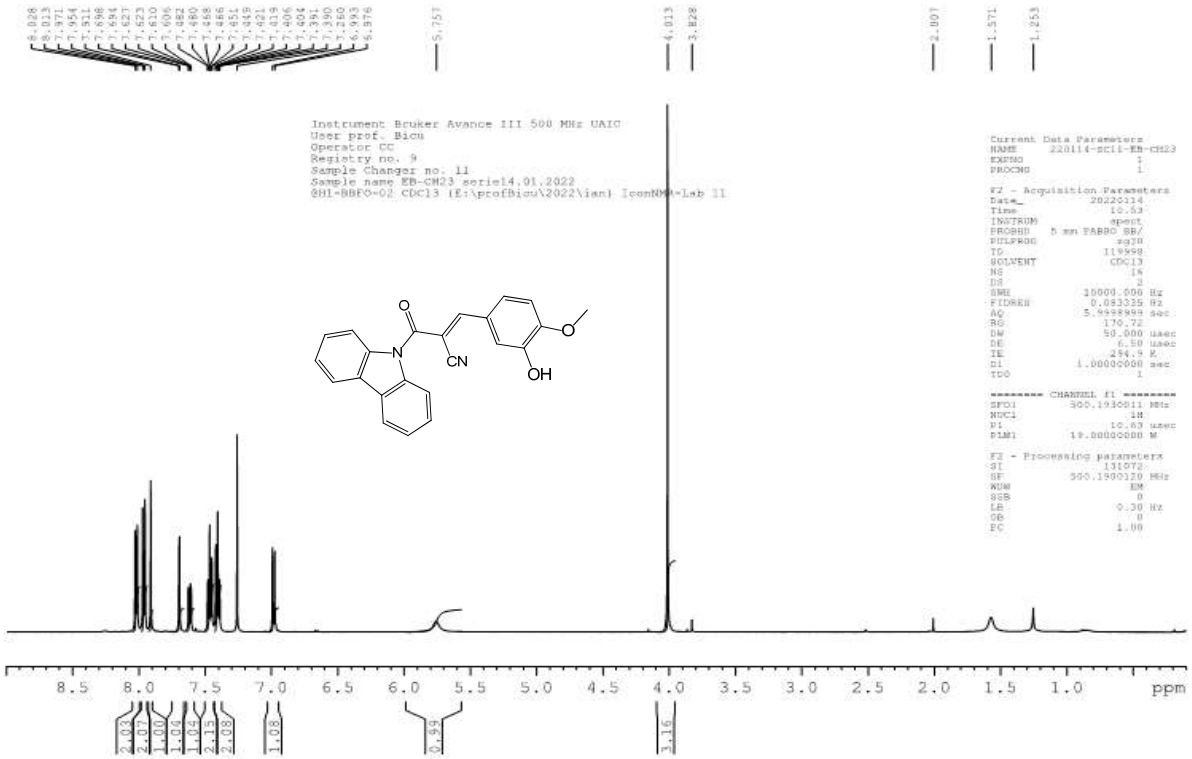
^{13}C NMR (125 MHz, $CDCl_3$)-**3i**



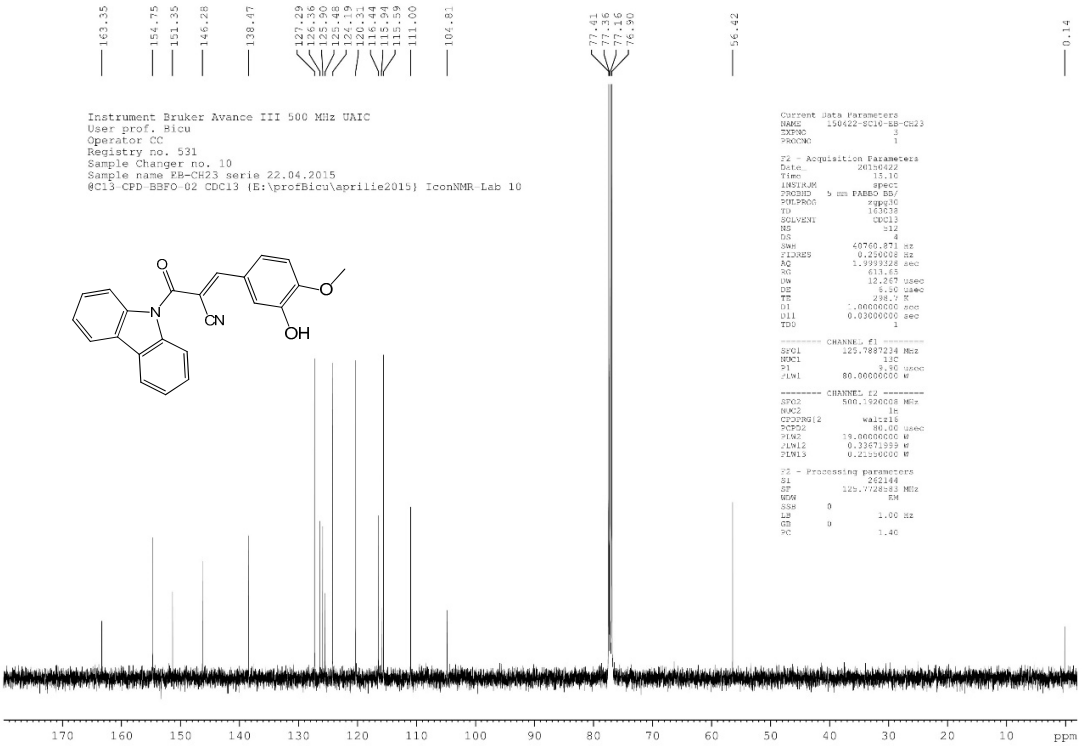
IR-3i



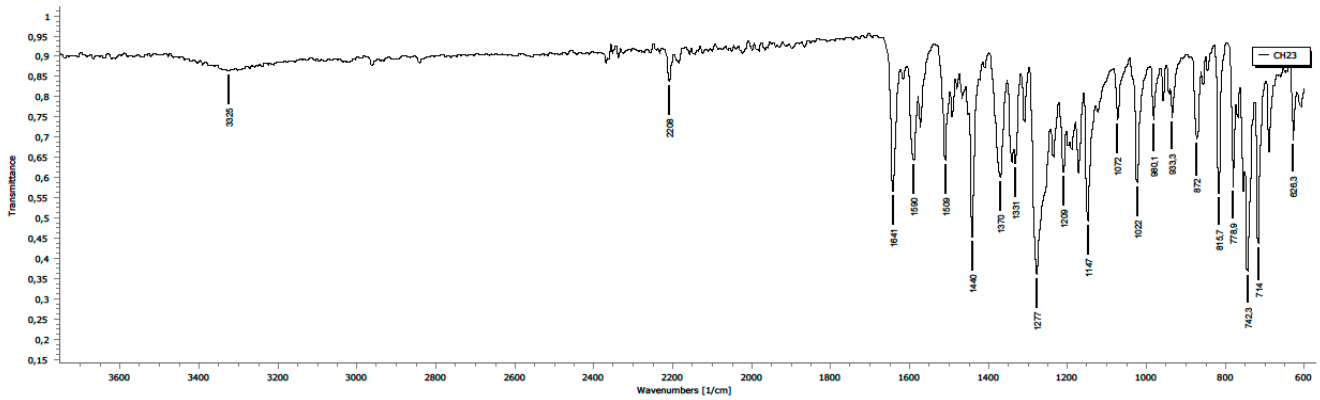
^{1}H NMR (500 MHz, $CDCl_3$)-**3j**



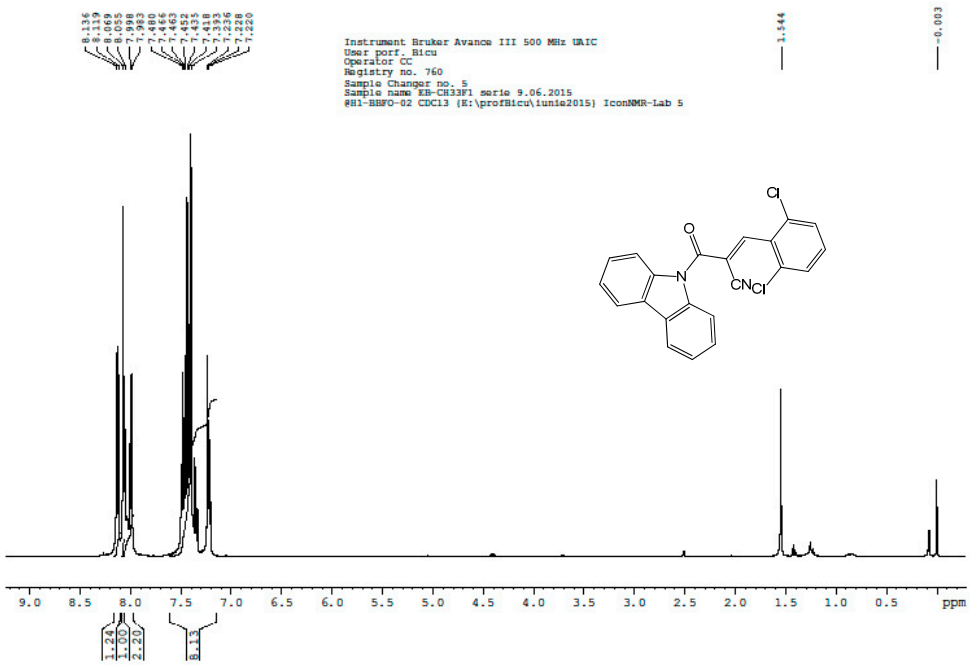
^{13}C NMR (125 MHz, $CDCl_3$)-**3j**



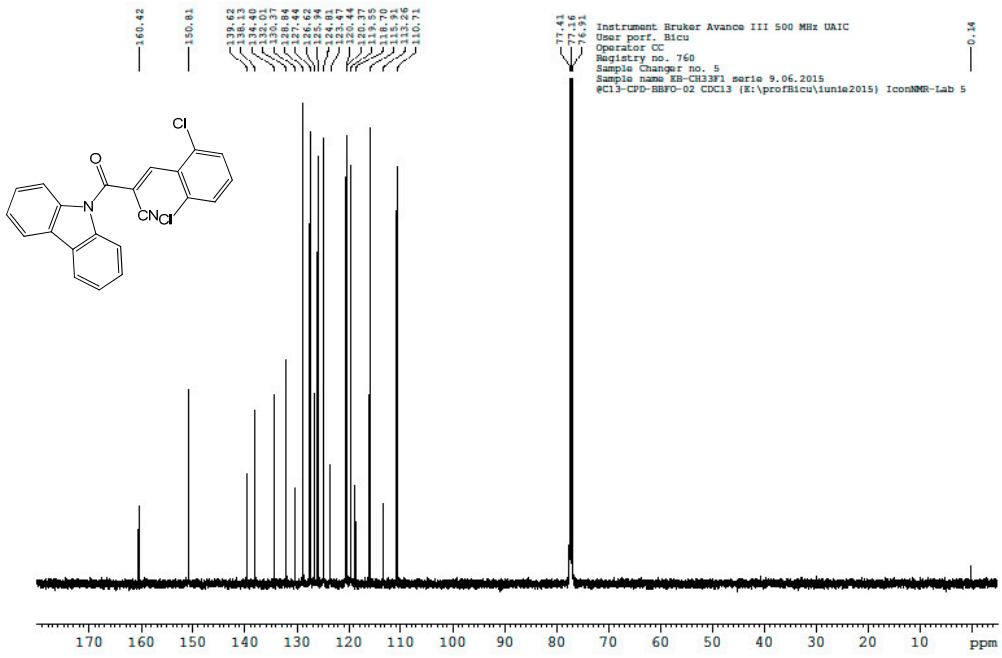
IR-3j



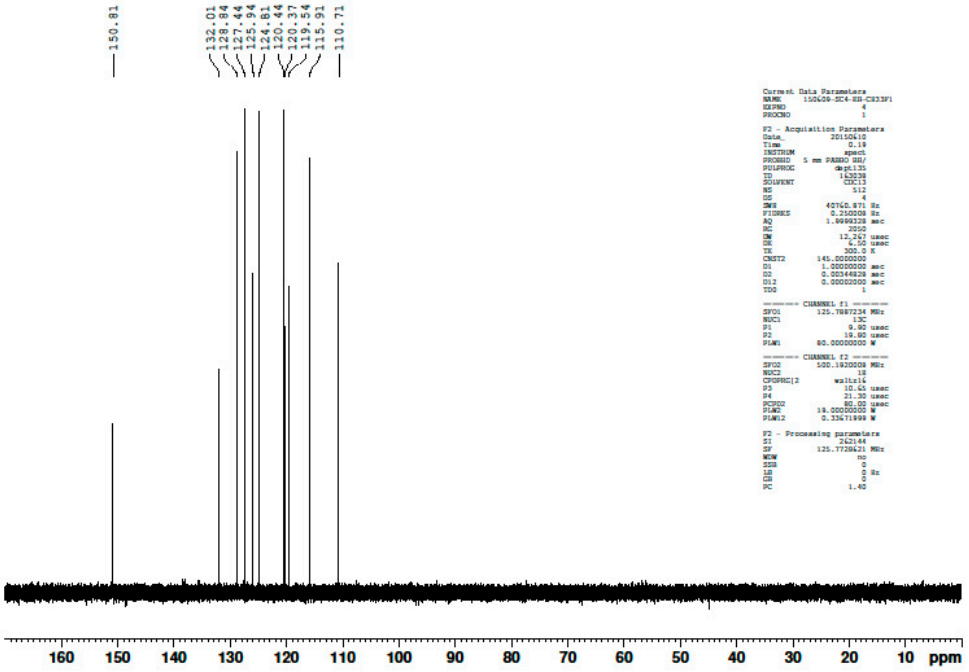
^{1}H NMR (500 MHz, $CDCl_3$)-**3k**



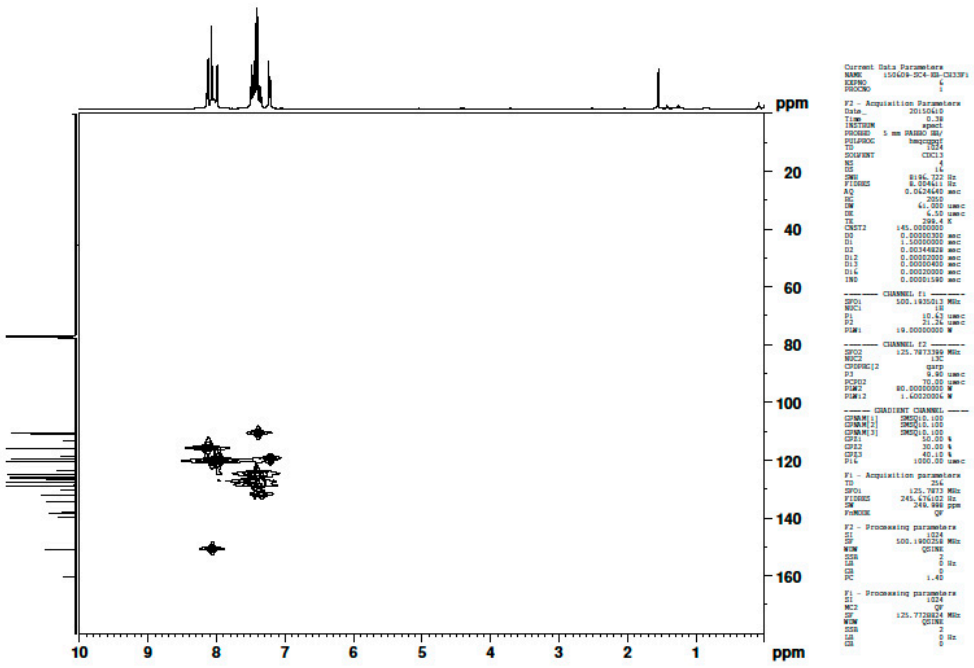
^{13}C NMR (125 MHz, $CDCl_3$)-**3k**



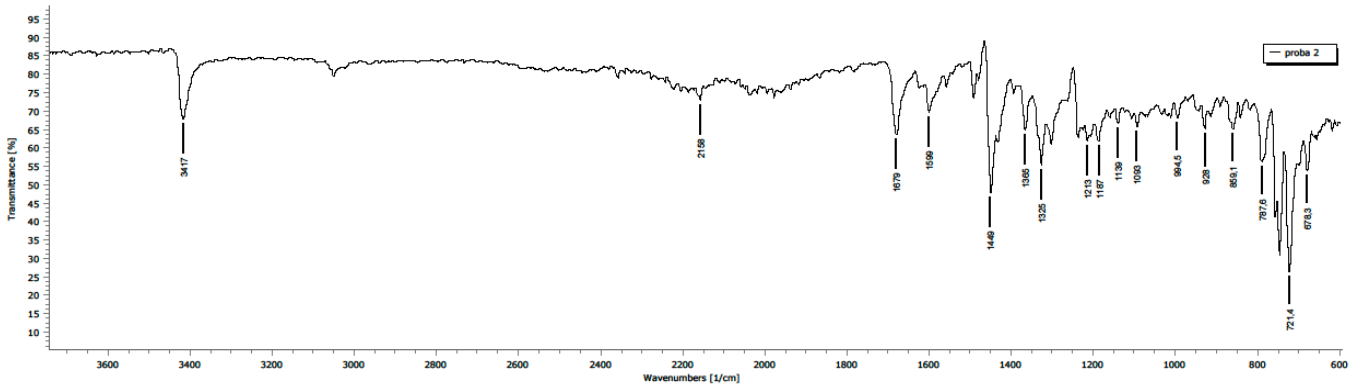
^{13}C-DEPT NMR (125 MHz, $CDCl_3$)-**3k**



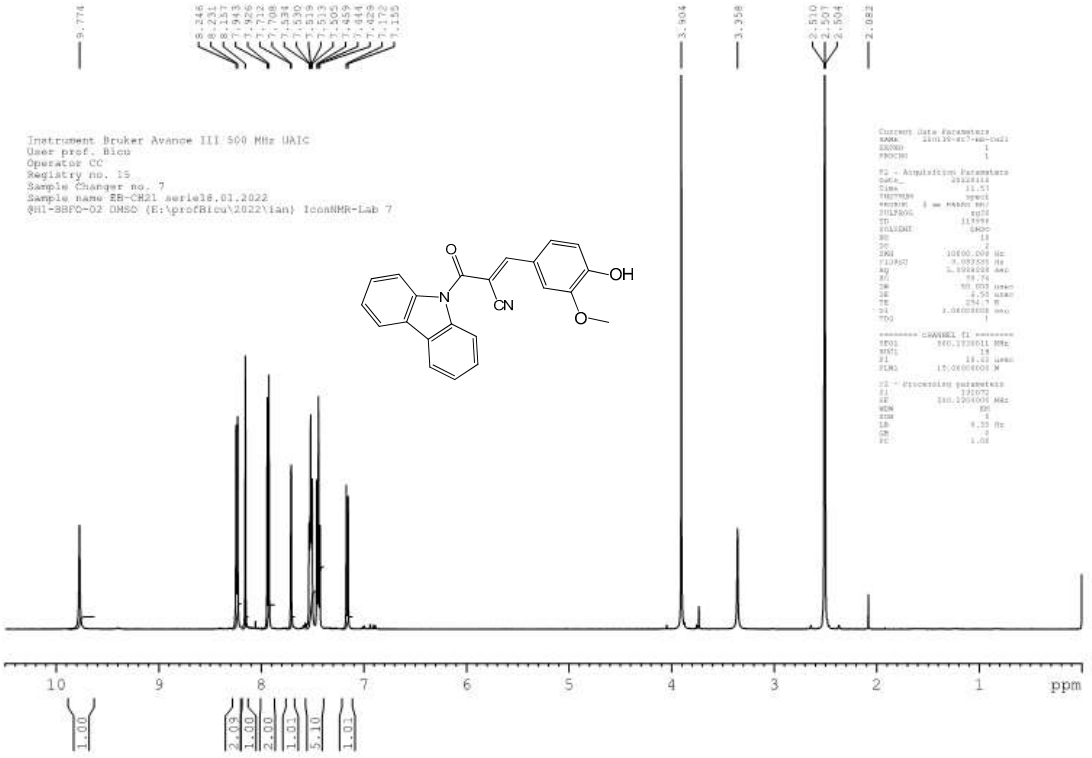
HMQC NMR (500 MHz, $CDCl_3$)-**3k**



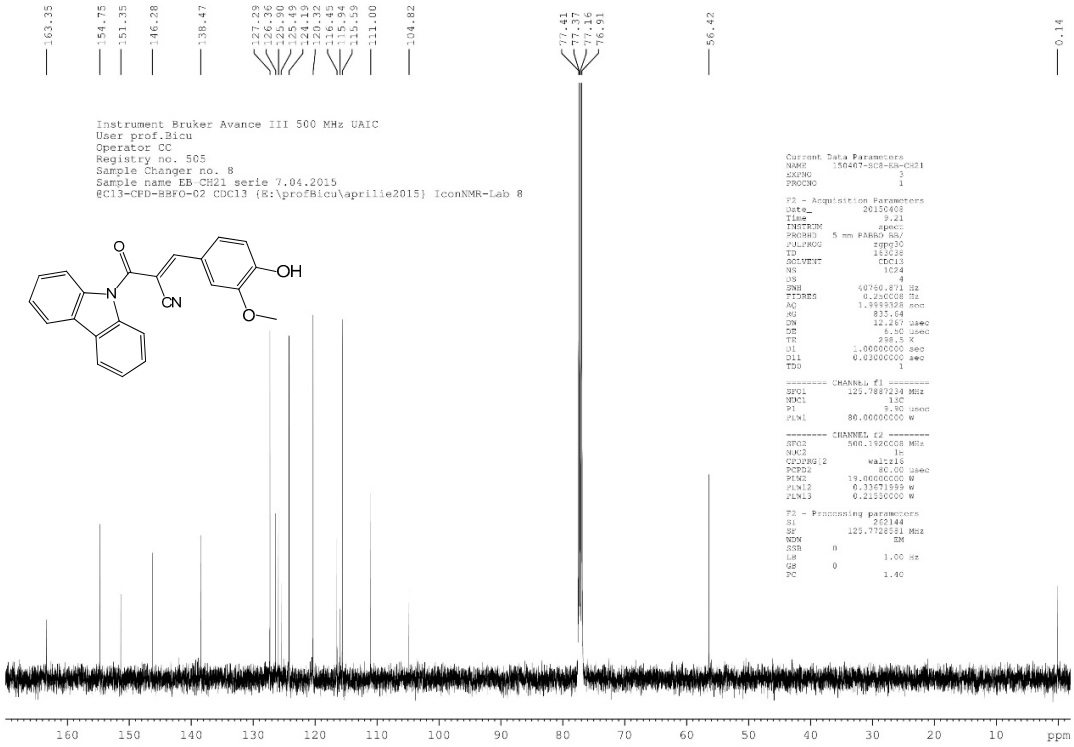
IR-3k



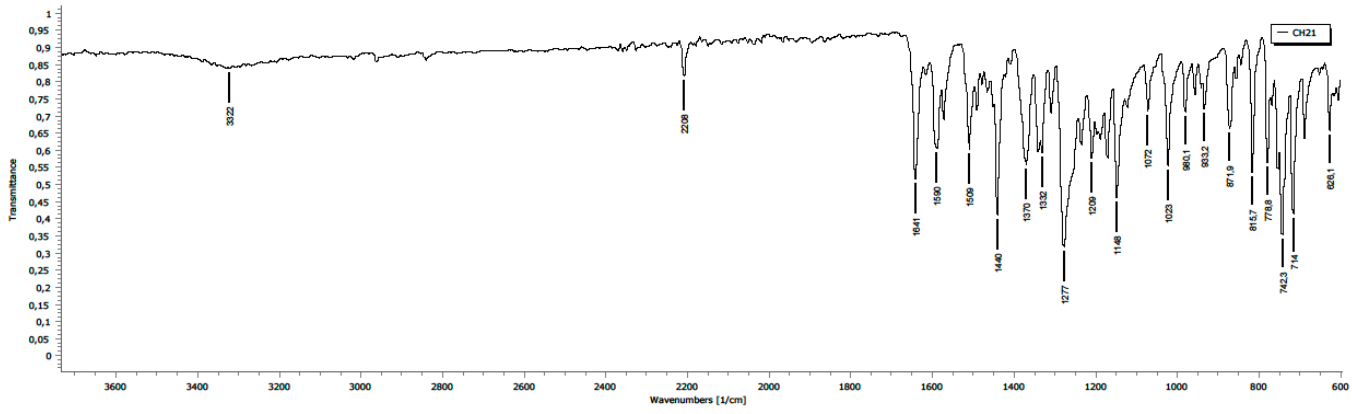
^{1}H NMR (500 MHz, DMSO-*d*$_6$)**-3l**



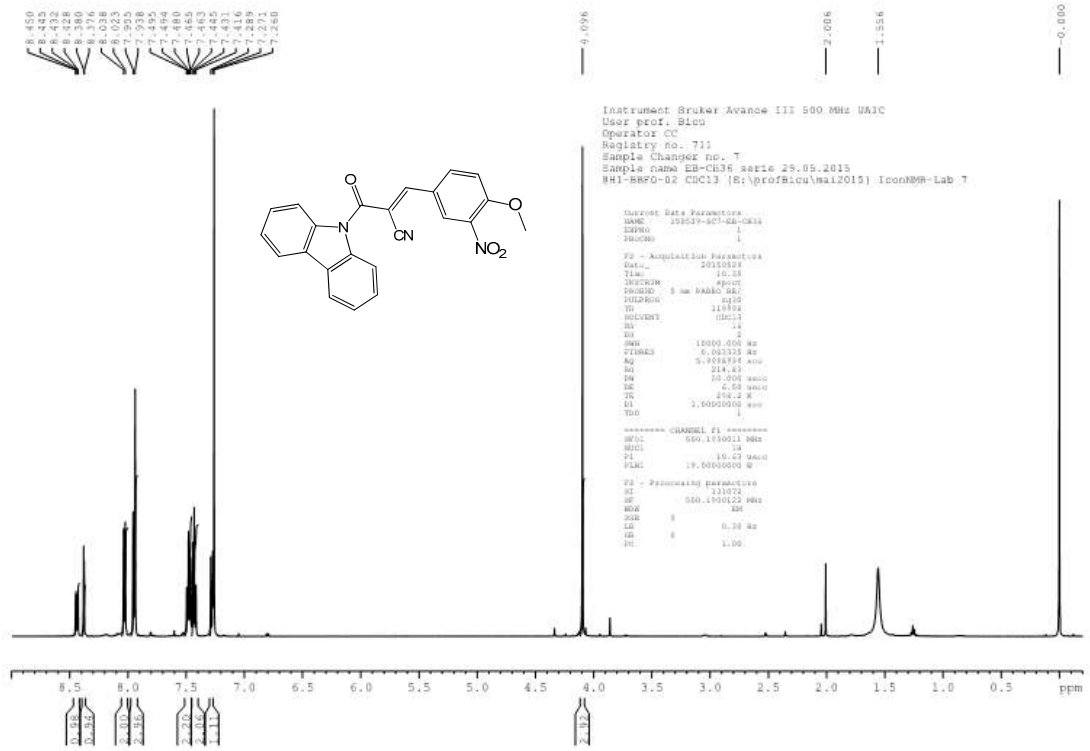
^{13}C NMR (125 MHz, DMSO-d_6)- **3l**



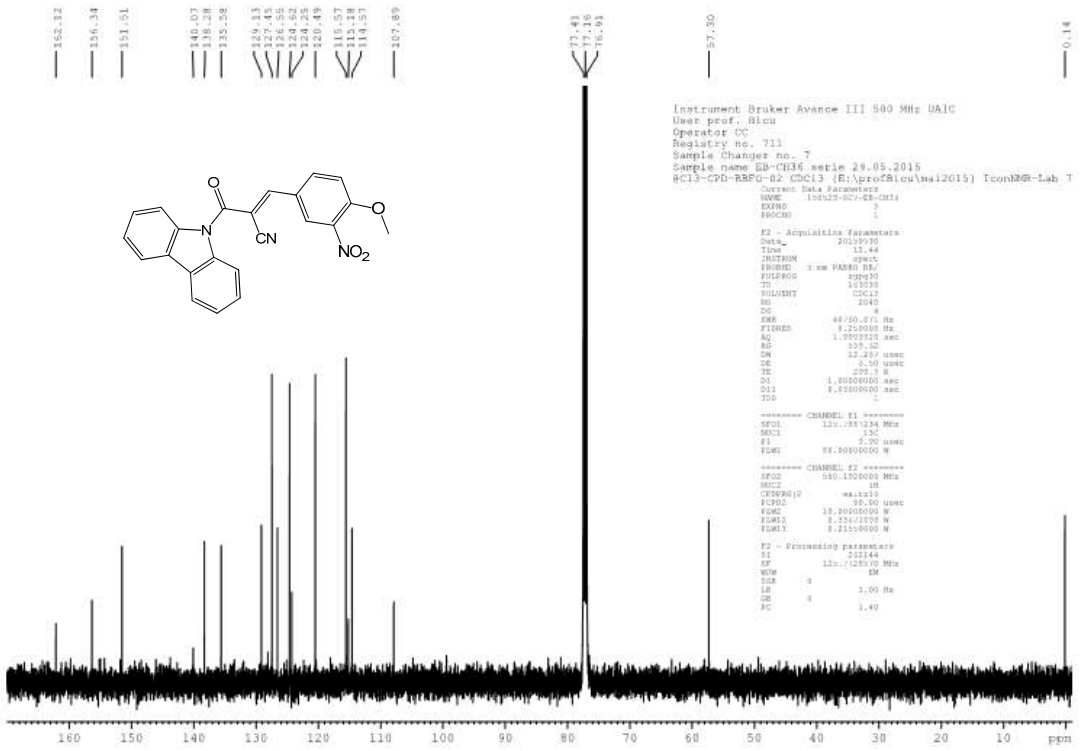
IR-3l



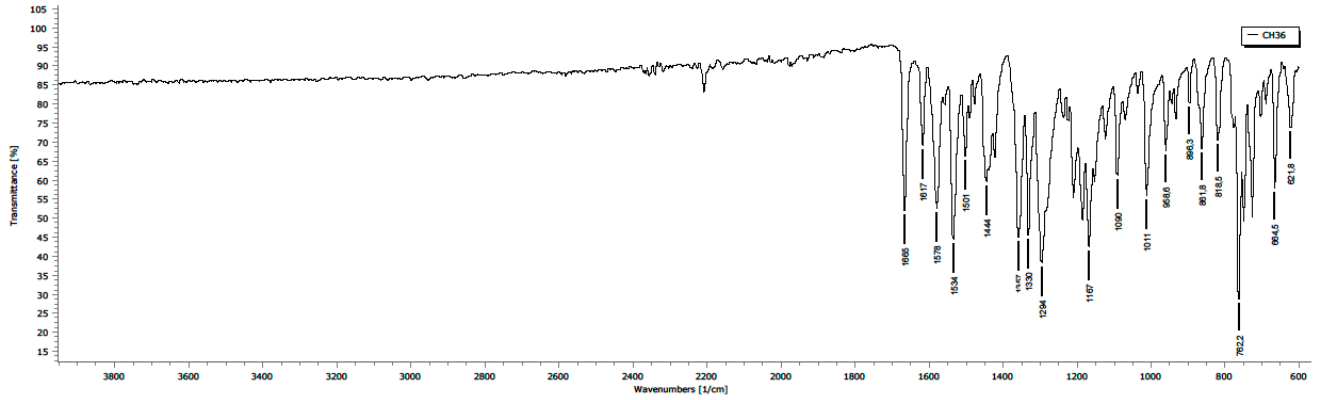
^{1}H NMR (500 MHz, $CDCl_3$)-**3m**



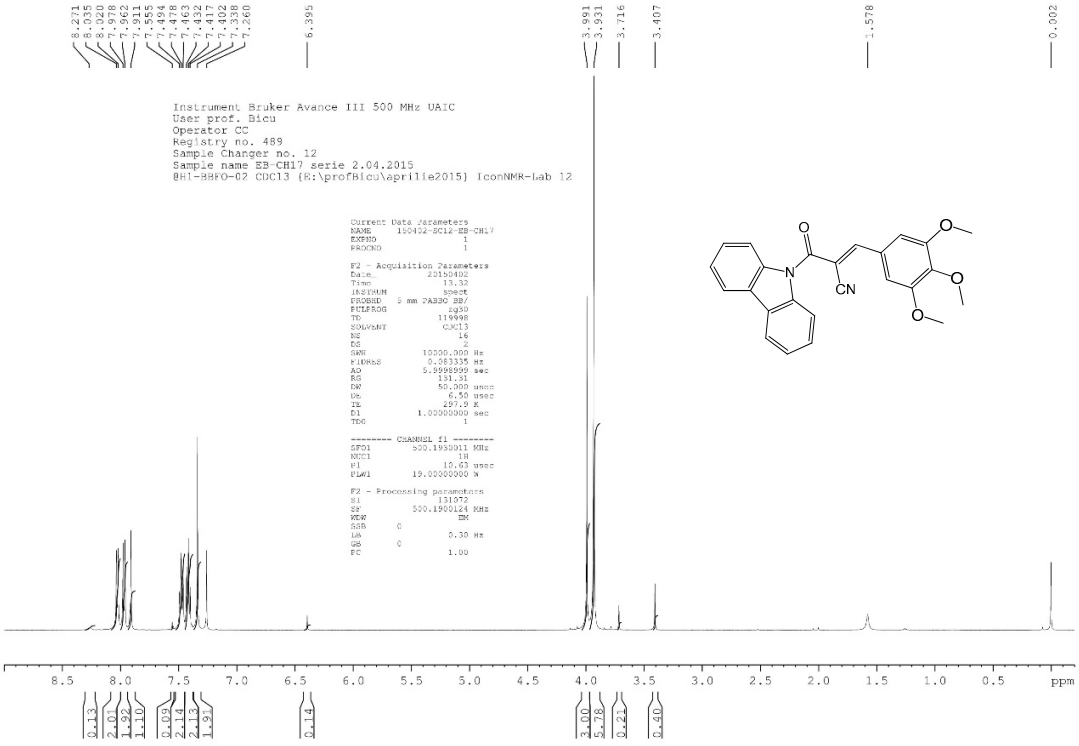
^{13}C NMR (125 MHz, $CDCl_3$)- **3m**



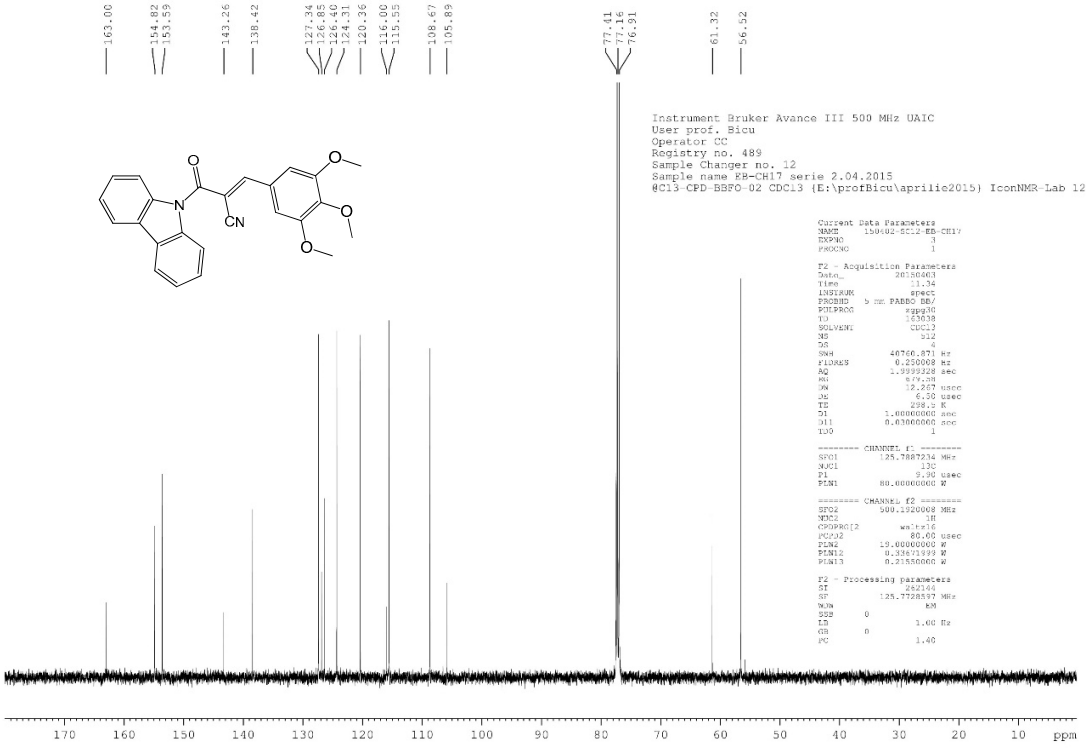
IR-3m



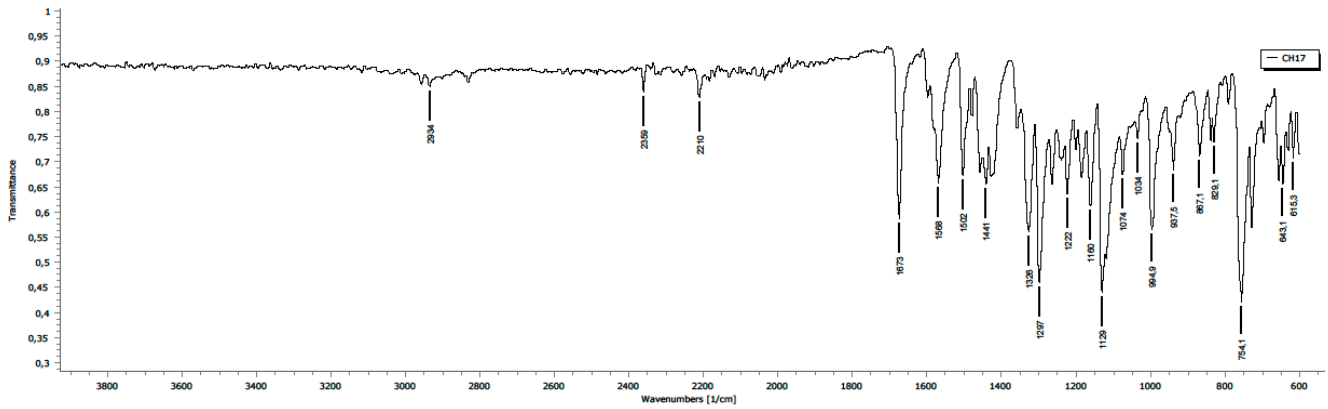
^{1}H NMR (500 MHz, $CDCl_3$)-**3n**



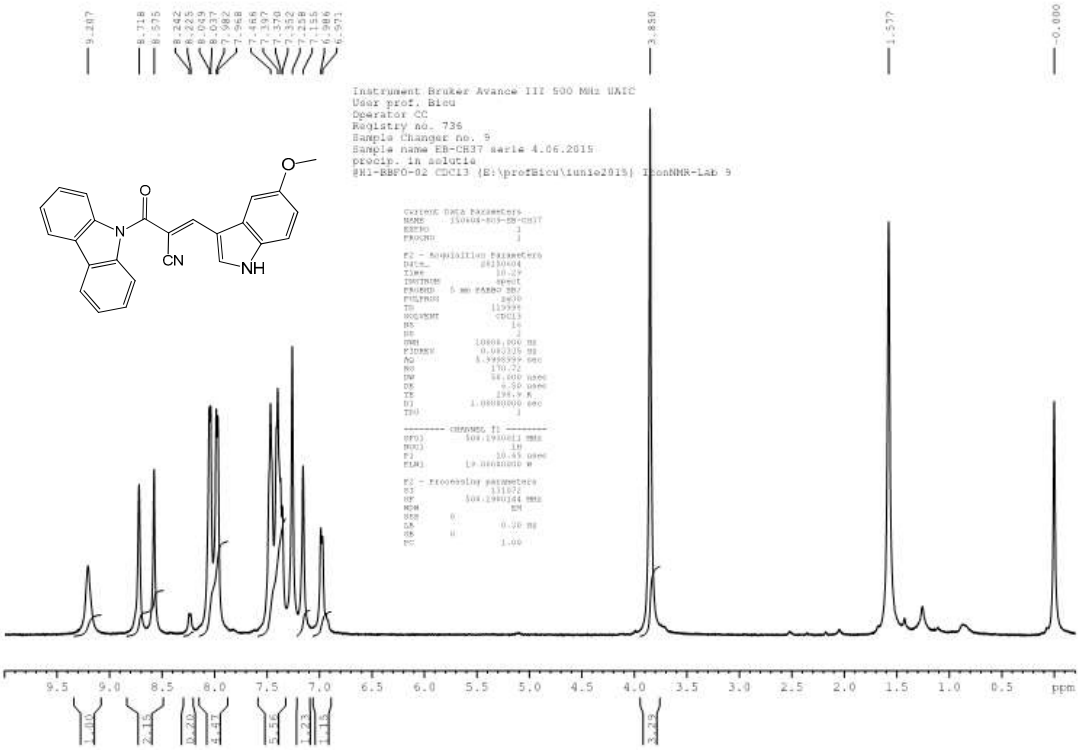
^{13}C NMR (125 MHz, $CDCl_3$)- **3n**



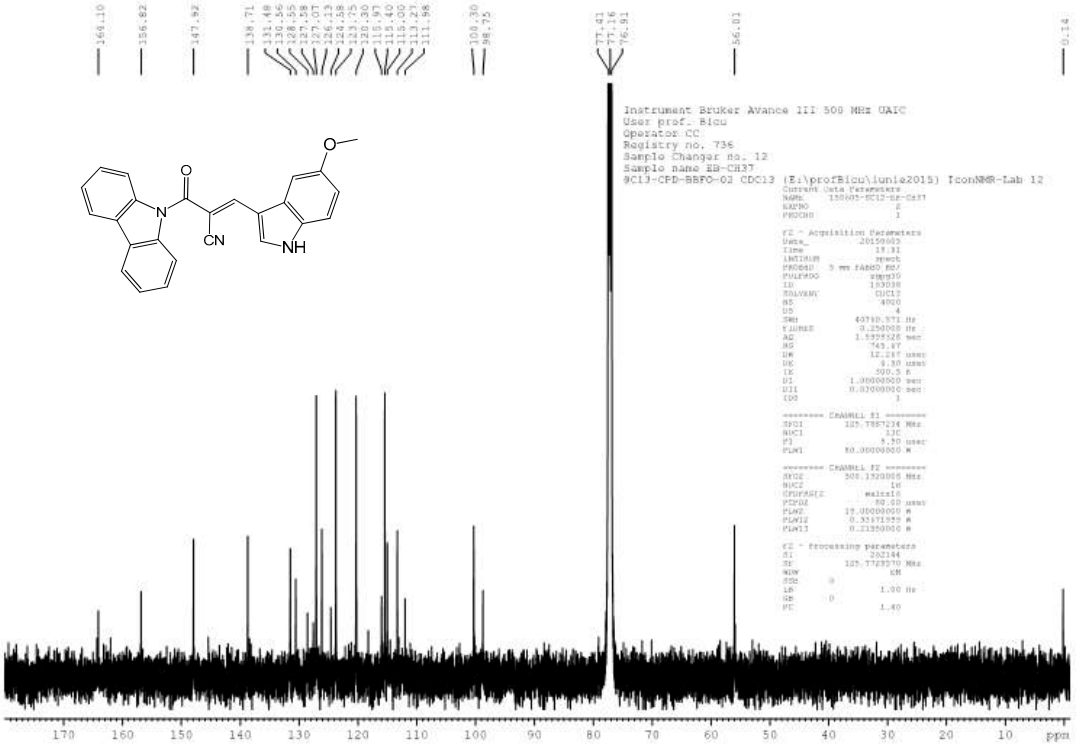
IR-3n



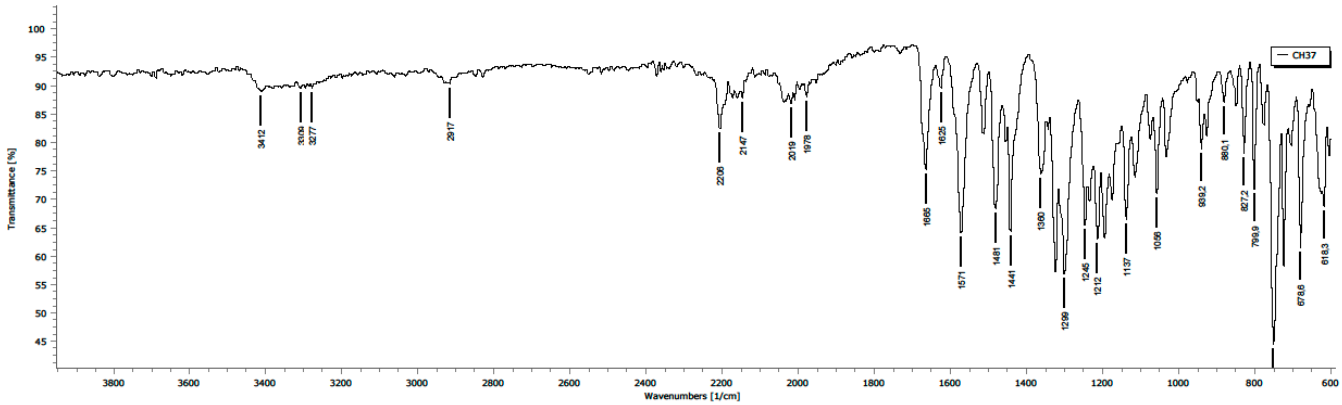
^{1}H NMR (500 MHz, $CDCl_3$)-**3o**



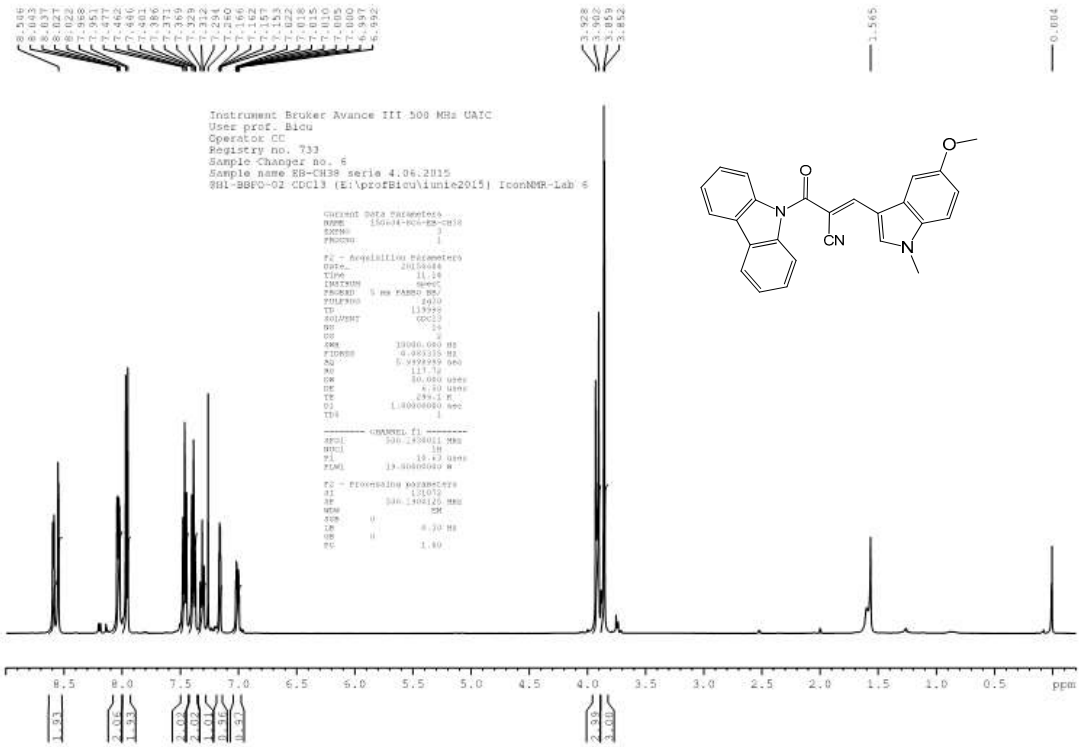
^{13}C NMR (125 MHz, $CDCl_3$)- **3o**



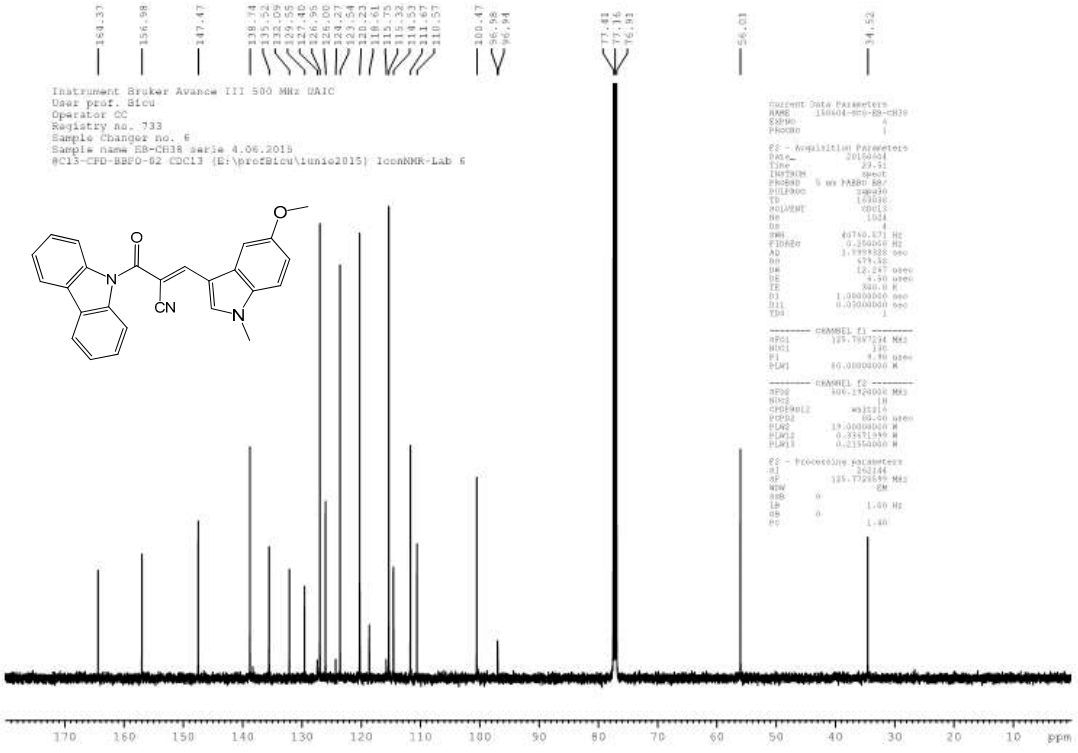
IR-3o



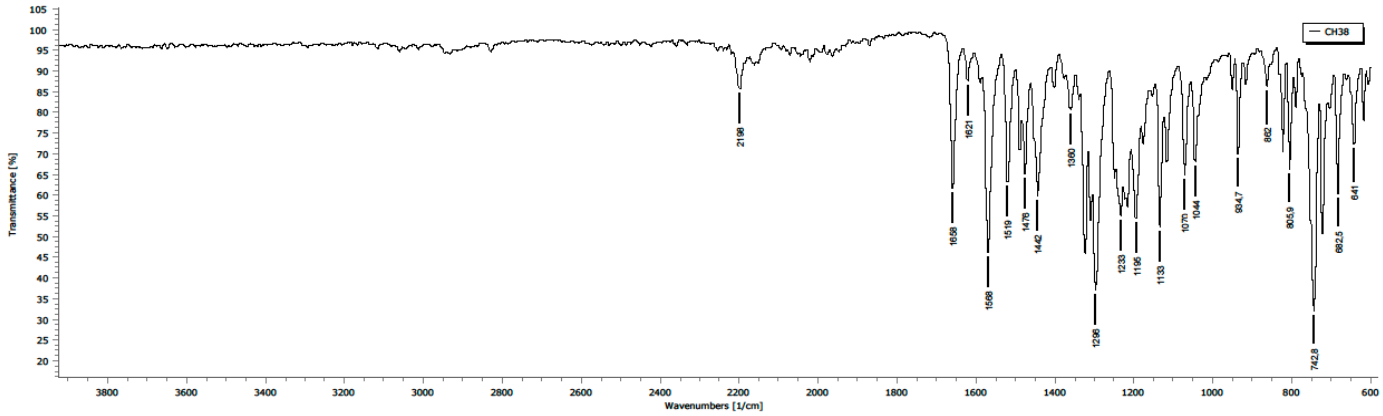
^{1}H NMR (500 MHz, $CDCl_3$)**-3p**



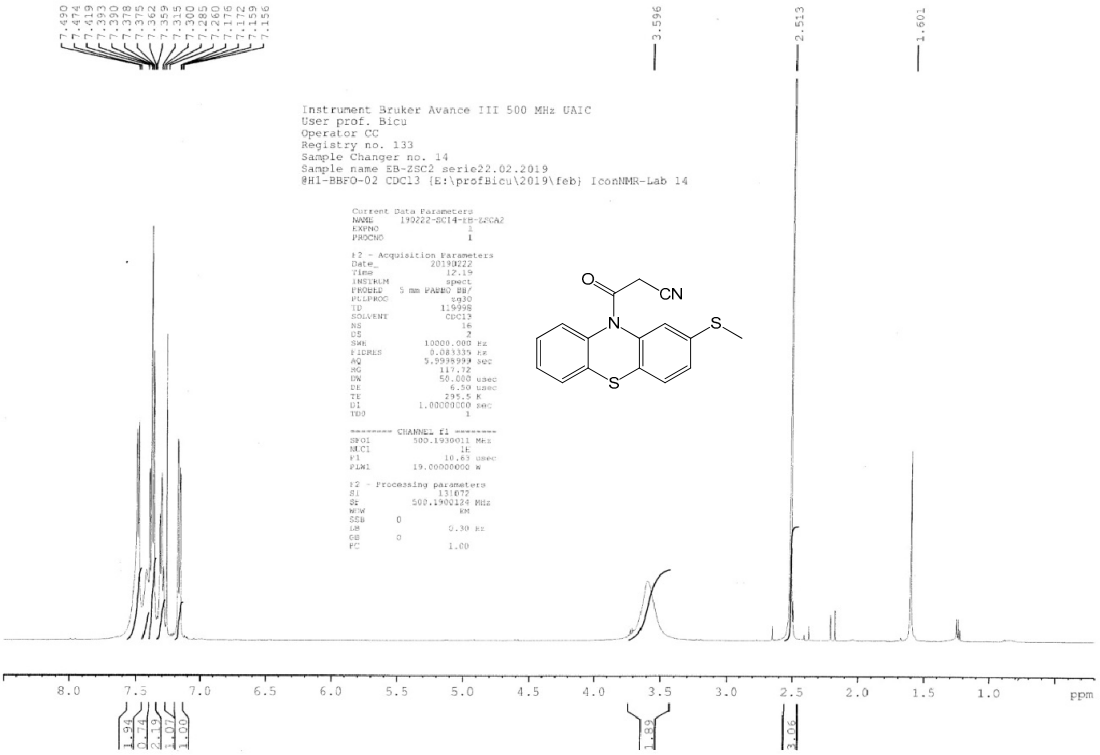
^{13}C NMR (125 MHz, $CDCl_3$)-**3p**



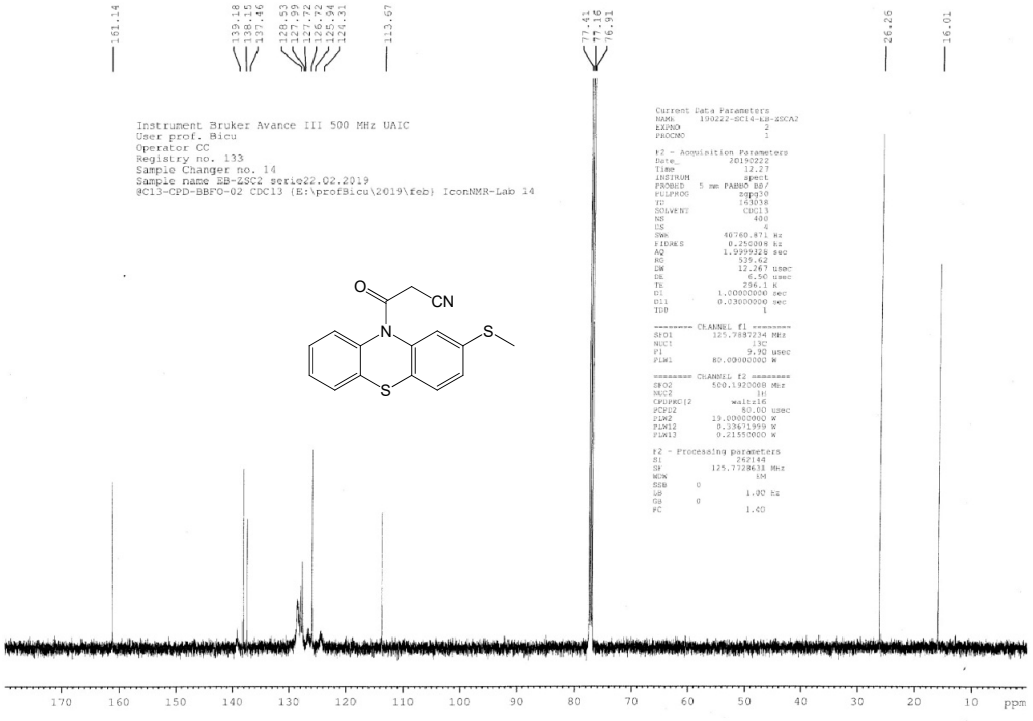
IR-3p



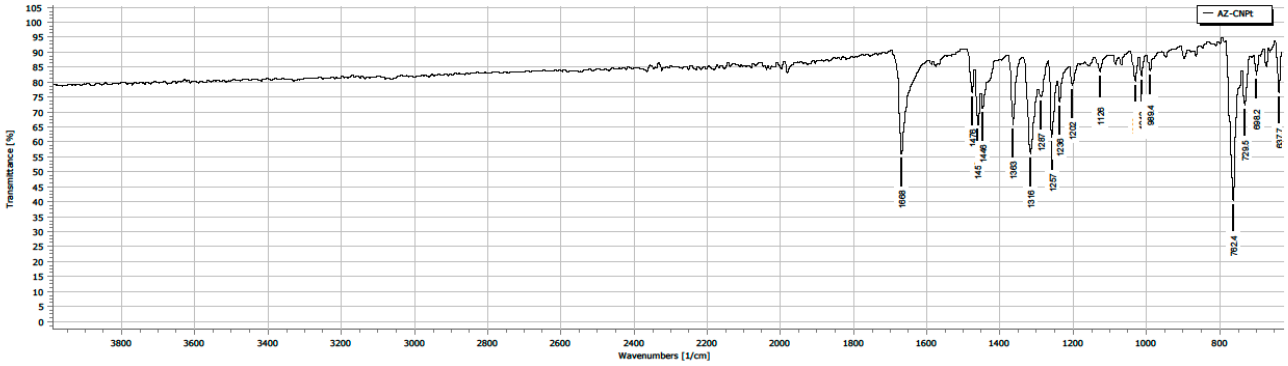
^{1}H NMR (500 MHz, $CDCl_3$)-**4b**



^{13}C NMR (125 MHz, $CDCl_3$)-**4b**

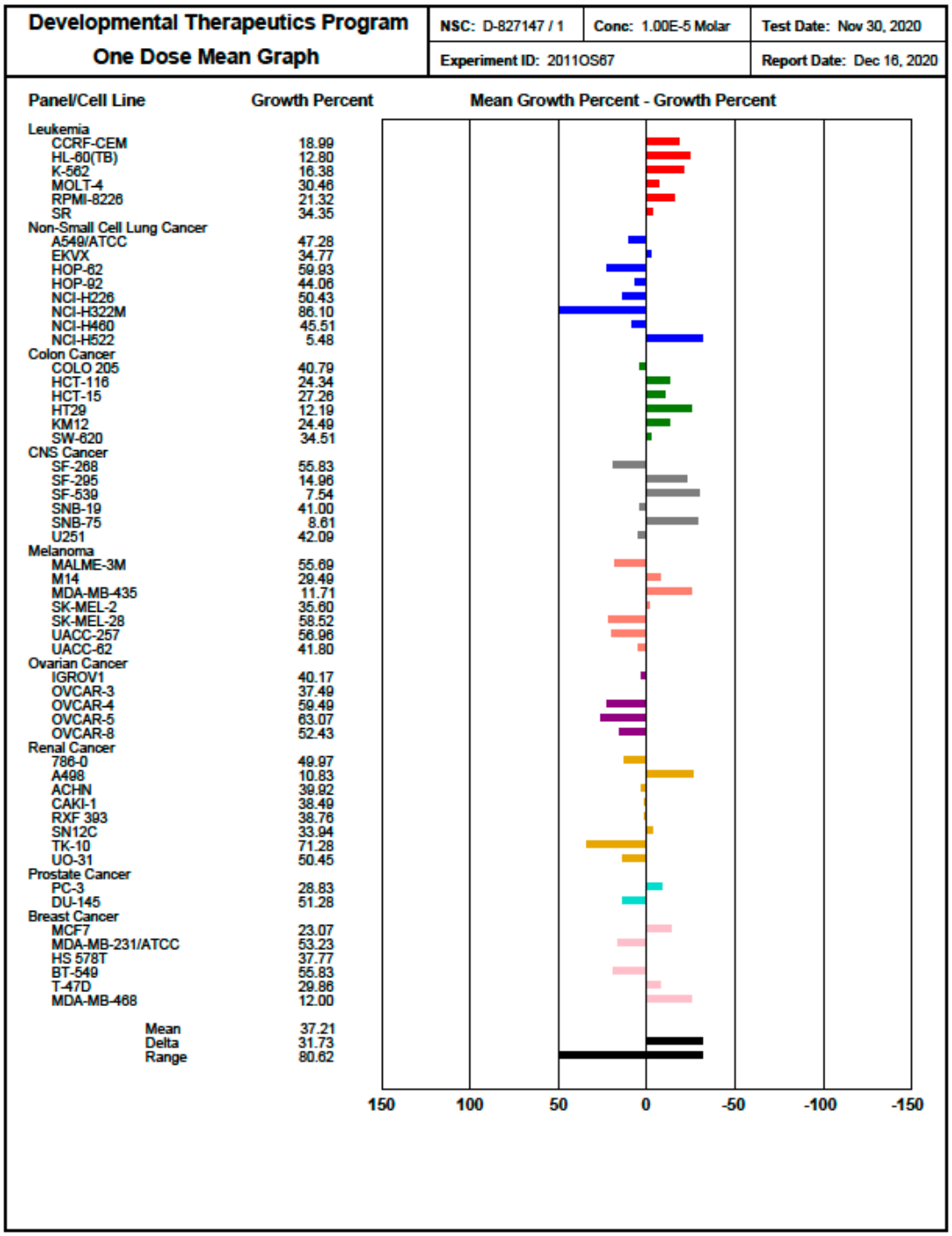


IR-4b


AZ-CNPt
Transmittance [%]
Wavenumbers [1/cm]
1668
1476
1446
1363
1316
1287
1257
1236
1202
1128
999.4
762.4
729.5
698.2
637.7

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

Compound 2k

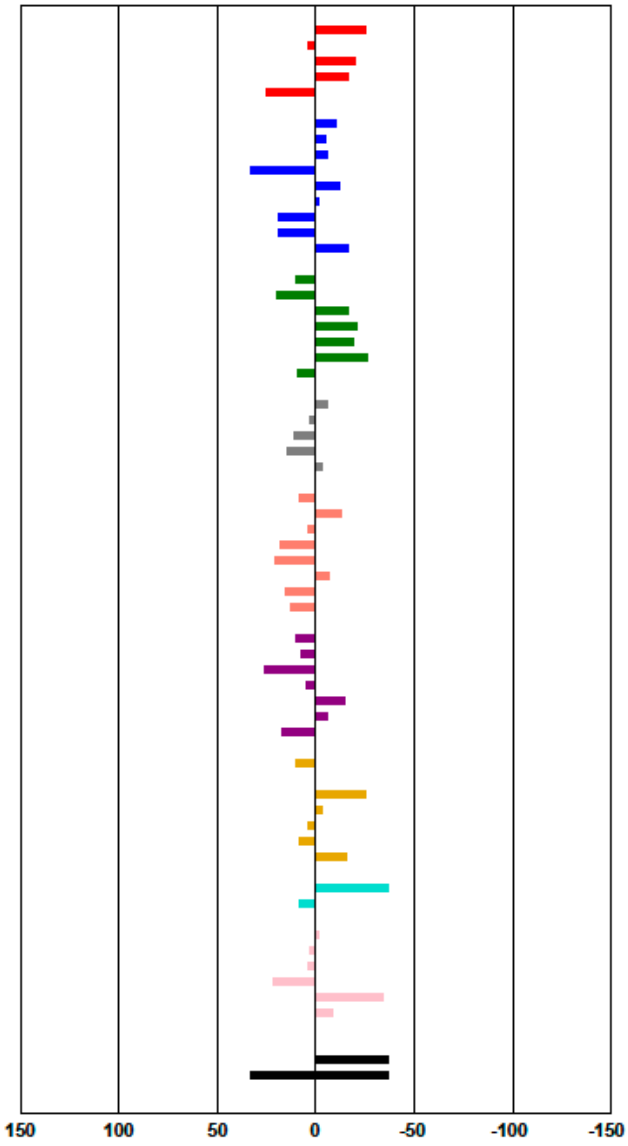


Compound 2l

Developmental Therapeutics Program
One Dose Mean Graph

NSC: D-826472 / 1	Conc: 1.00E-5 Molar	Test Date: Oct 26, 2020
Experiment ID: 2010OS59		Report Date: Dec 02, 2020

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	51.35
HL-60(TB)	80.79
K-562	56.82
MOLT-4	60.08
SR	101.63
Non-Small Cell Lung Cancer	
A549/ATCC	66.11
EKVX	71.42
HOP-62	70.62
HOP-92	109.28
NCI-H226	64.54
NCI-H23	75.15
NCI-H322M	95.35
NCI-H460	95.46
NCI-H522	60.62
Colon Cancer	
COLO 205	86.61
HCC-2998	96.25
HCT-116	59.81
HCT-15	55.49
HT29	57.67
KM12	50.69
SW-620	85.43
CNS Cancer	
SF-268	70.97
SF-295	79.40
SF-539	87.65
SNB-19	91.14
U251	73.15
Melanoma	
MALME-3M	84.81
M14	64.12
MDA-MB-435	80.36
SK-MEL-2	94.37
SK-MEL-28	96.92
SK-MEL-5	69.56
UACC-257	92.25
UACC-62	89.12
Ovarian Cancer	
IGROV1	86.39
OVCAR-3	83.95
OVCAR-4	102.58
OVCAR-5	81.30
OVCAR-8	61.92
NCI/ADR-RES	71.20
SK-OV-3	93.59
Renal Cancer	
786-0	86.54
ACHN	76.55
CAKI-1	51.01
RXF 393	73.39
SN12C	80.34
TK-10	84.49
UO-31	60.69
Prostate Cancer	
PC-3	39.92
DU-145	85.09
Breast Cancer	
MCF7	75.30
MDA-MB-231/ATCC	80.04
HS 578T	80.12
BT-549	98.43
T-47D	42.87
MDA-MB-468	68.29
Mean	76.59
Delta	36.67
Range	69.36



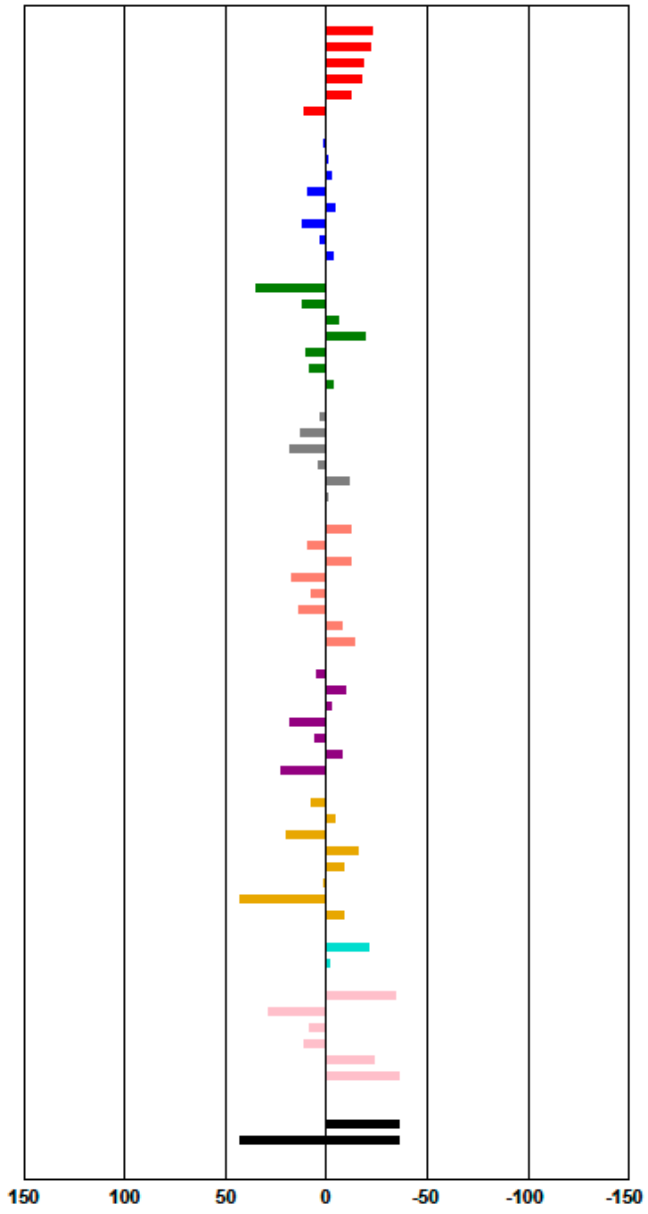
Compound 2o

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-826274 / 1	Conc: 1.00E-5 Molar	Test Date: Oct 19, 2020
Experiment ID: 2010OS56		Report Date: Nov 12, 2020

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	53.54
HL-60(TB)	54.06
K-562	58.15
MOLT-4	58.85
RPMI-8226	64.14
SR	86.86
Non-Small Cell Lung Cancer	
A549/ATCC	77.02
EKVX	75.36
HOP-62	73.85
NCI-H226	85.58
NCI-H23	72.43
NCI-H322M	87.82
NCI-H460	79.54
NCI-H522	73.44
Colon Cancer	
COLO 205	111.11
HCC-2998	87.66
HCT-116	69.98
HCT-15	57.47
HT29	86.06
KM12	84.77
SW-620	72.74
CNS Cancer	
SF-268	78.87
SF-295	88.98
SF-539	94.57
SNB-19	79.80
SNB-75	64.95
U251	75.90
Melanoma	
LOX IMVI	63.77
M14	85.24
MDA-MB-435	64.49
SK-MEL-2	93.50
SK-MEL-28	83.87
SK-MEL-5	89.45
UACC-257	88.87
UACC-62	62.40
Ovarian Cancer	
IGROV1	80.95
OVCAR-3	66.62
OVCAR-4	73.76
OVCAR-5	94.35
OVCAR-8	82.26
NCI/ADR-RES	68.71
SK-OV-3	99.01
Renal Cancer	
786-0	83.46
A498	71.88
ACHN	95.92
CAKI-1	60.42
RXF 393	67.90
SN12C	77.21
TK-10	119.10
UO-31	67.87
Prostate Cancer	
PC-3	55.14
DU-145	75.06
Breast Cancer	
MCF7	41.74
MDA-MB-231/ATCC	104.82
HS 578T	84.83
BT-549	87.30
T-47D	53.12
MDA-MB-468	40.50
Mean	76.16
Delta	35.66
Range	78.60



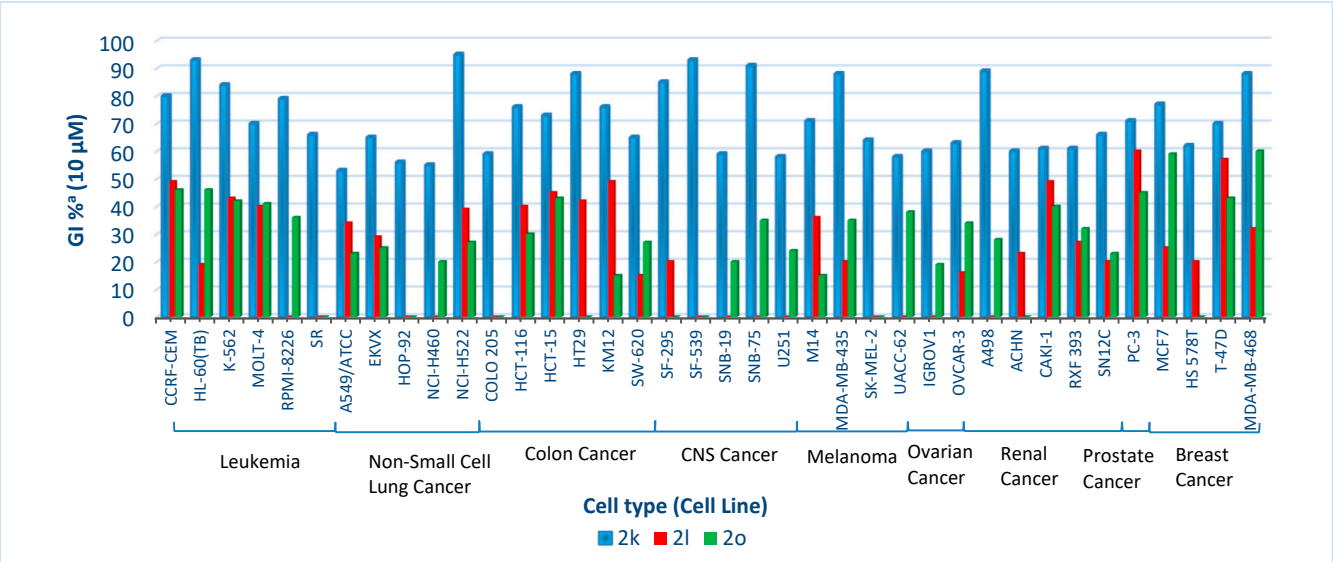
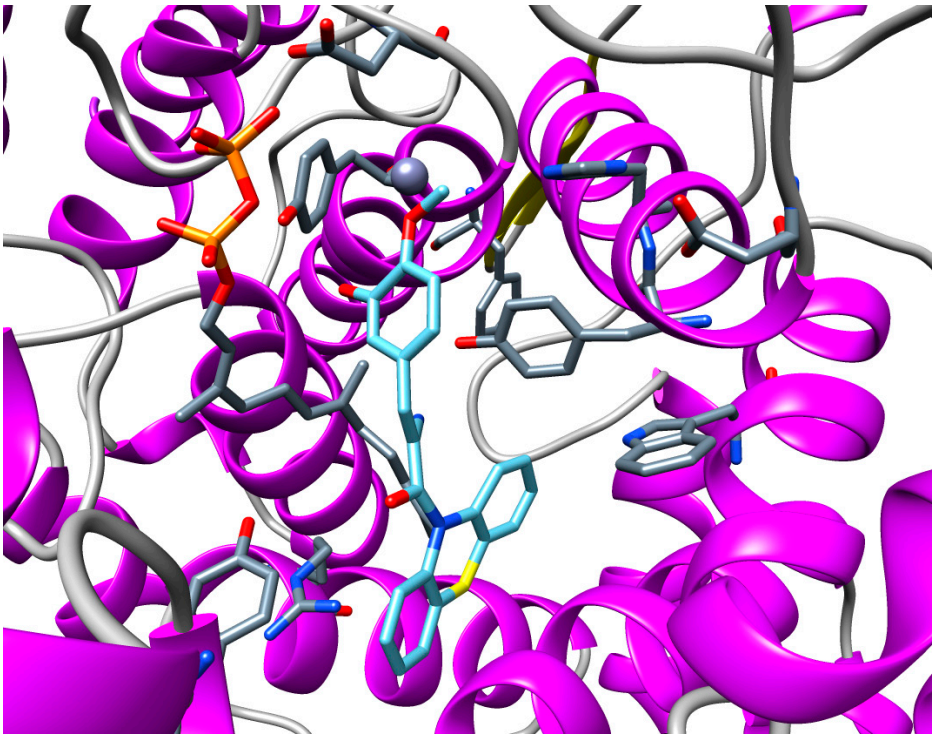


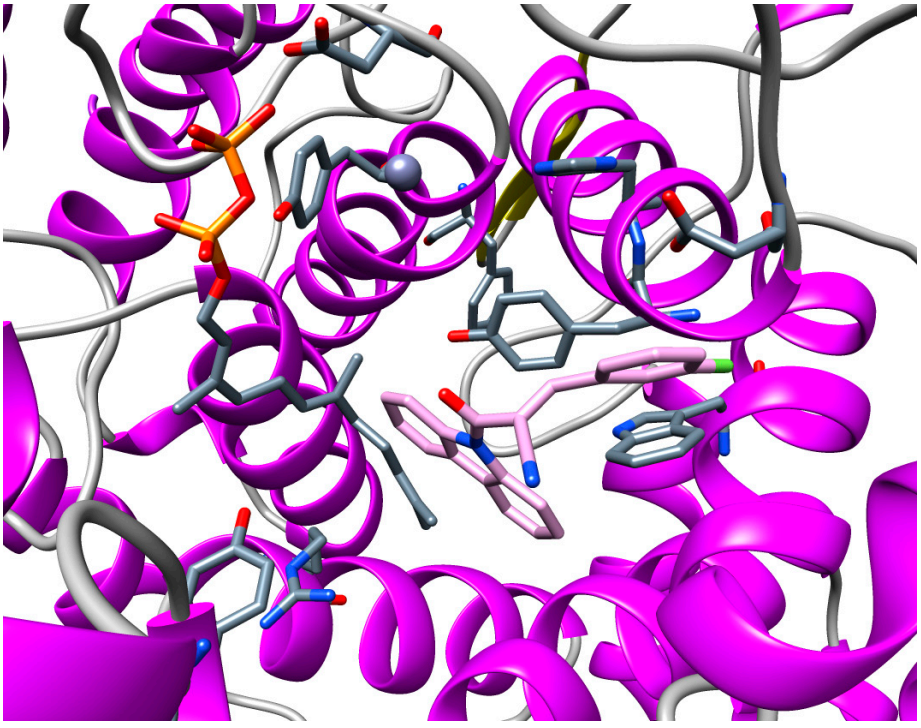
Figure S1. Results of the *in vitro* human cancer cell growth inhibition for selected compounds **2k, 2l** and **2o**.

Docking FTase

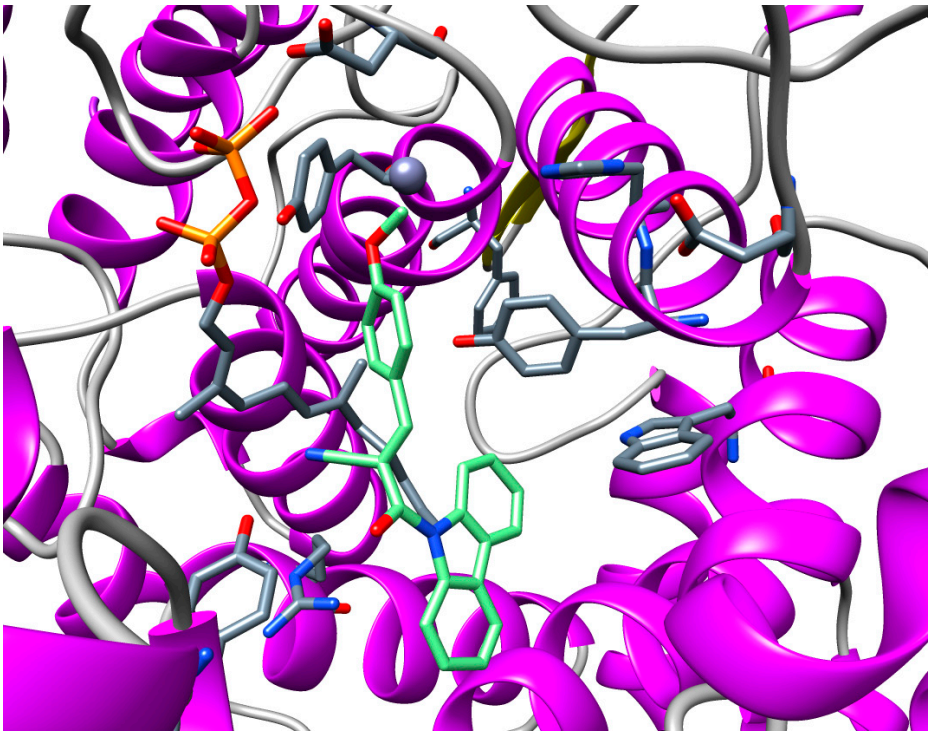
Compound 1l



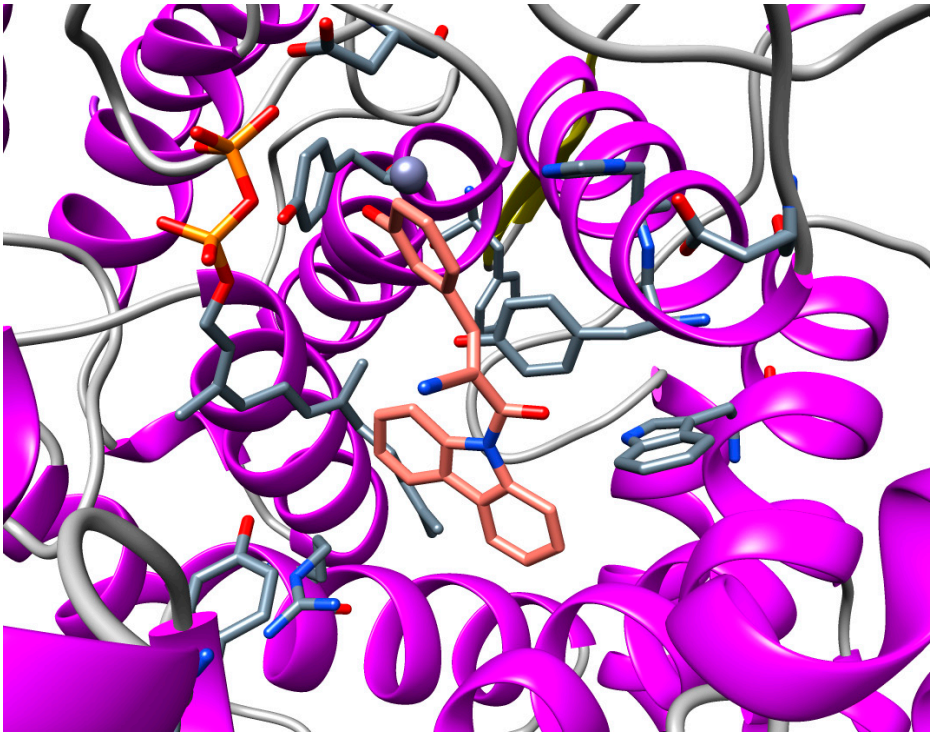
Compound 3a



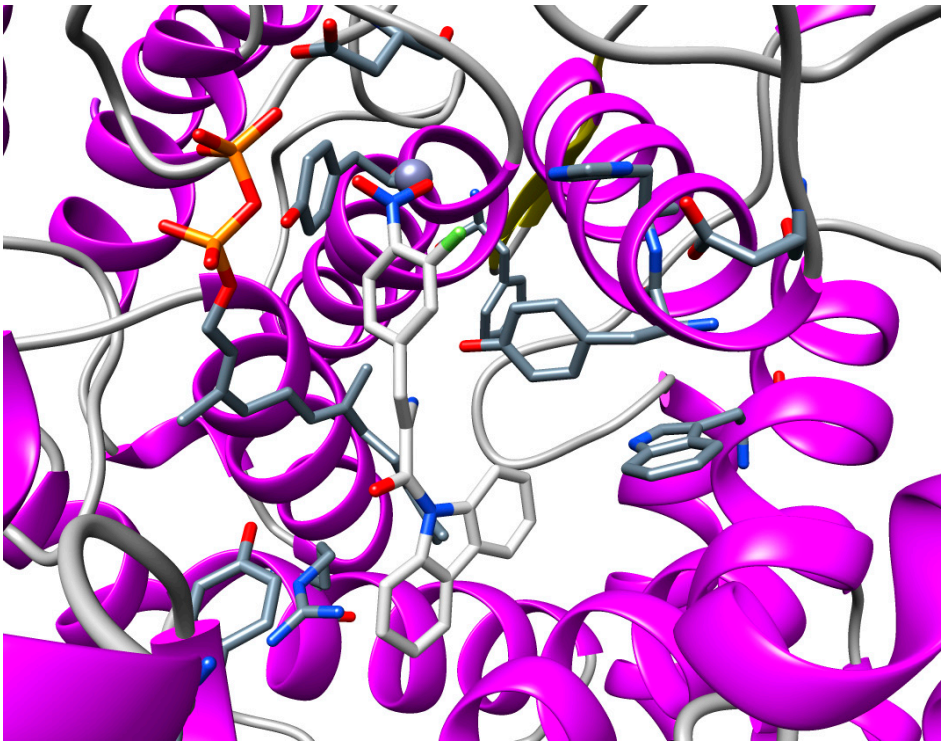
Compound 3b



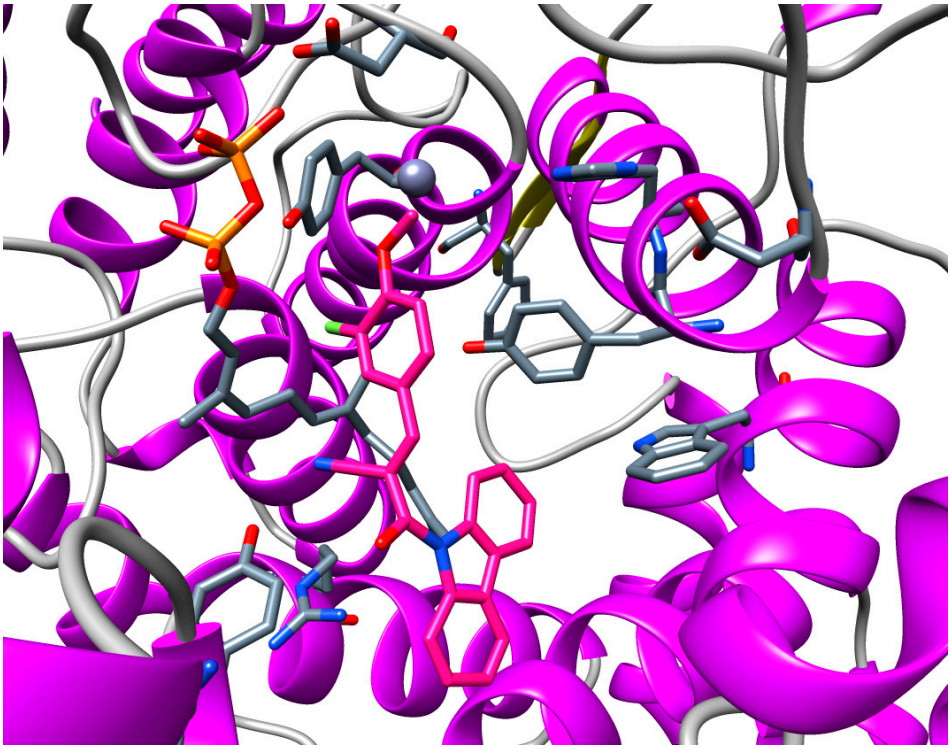
Compound 3d



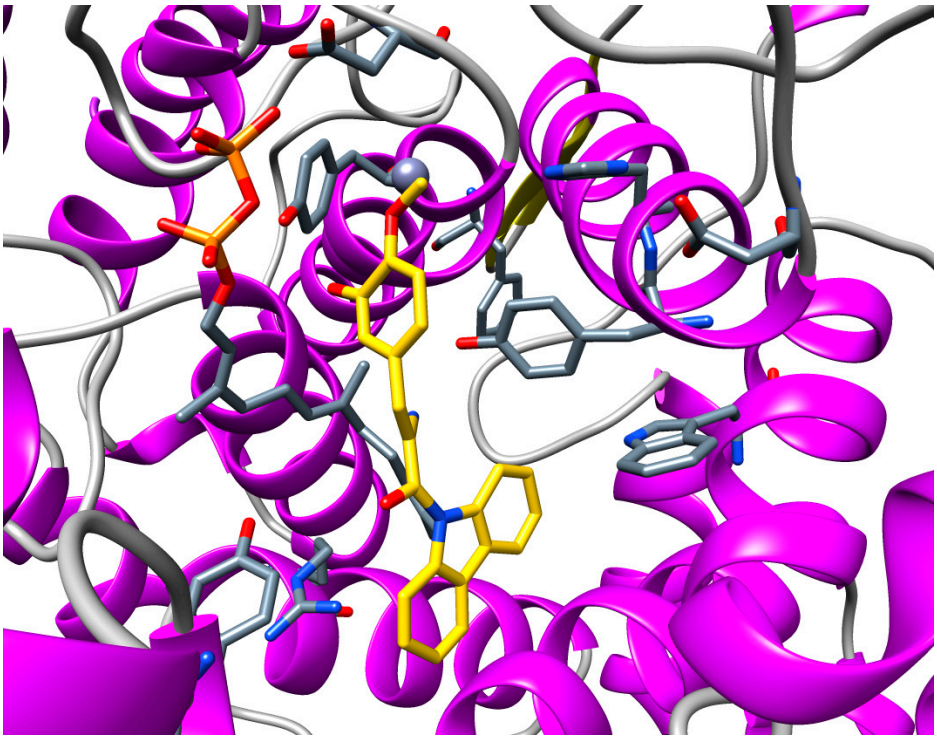
Compound 3e



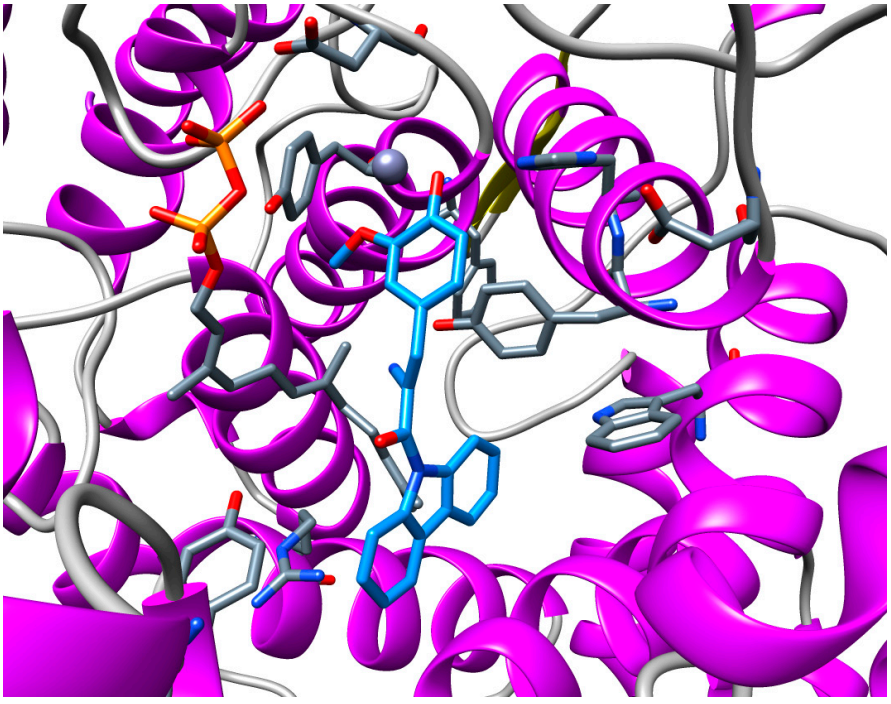
Compound 3i



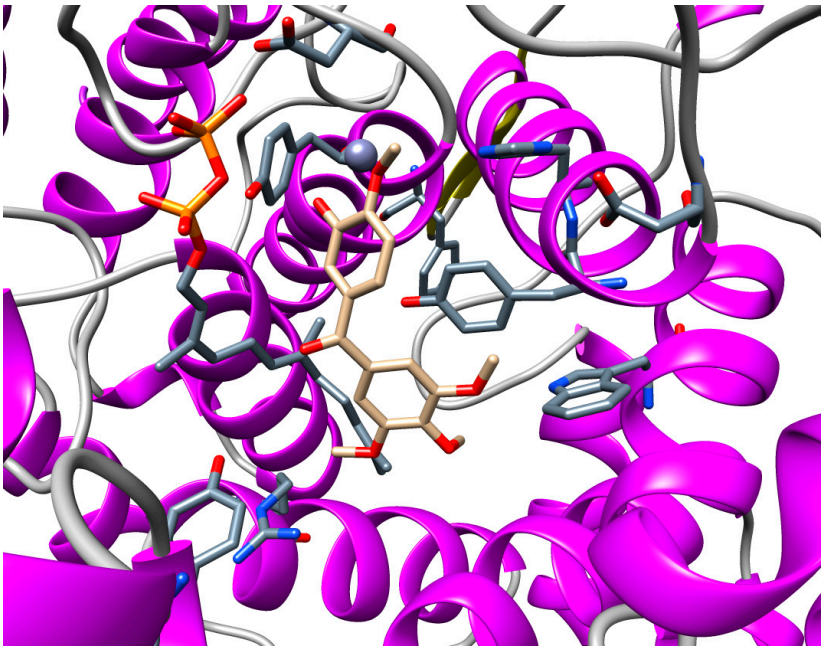
Compound 3j



Compound 3l

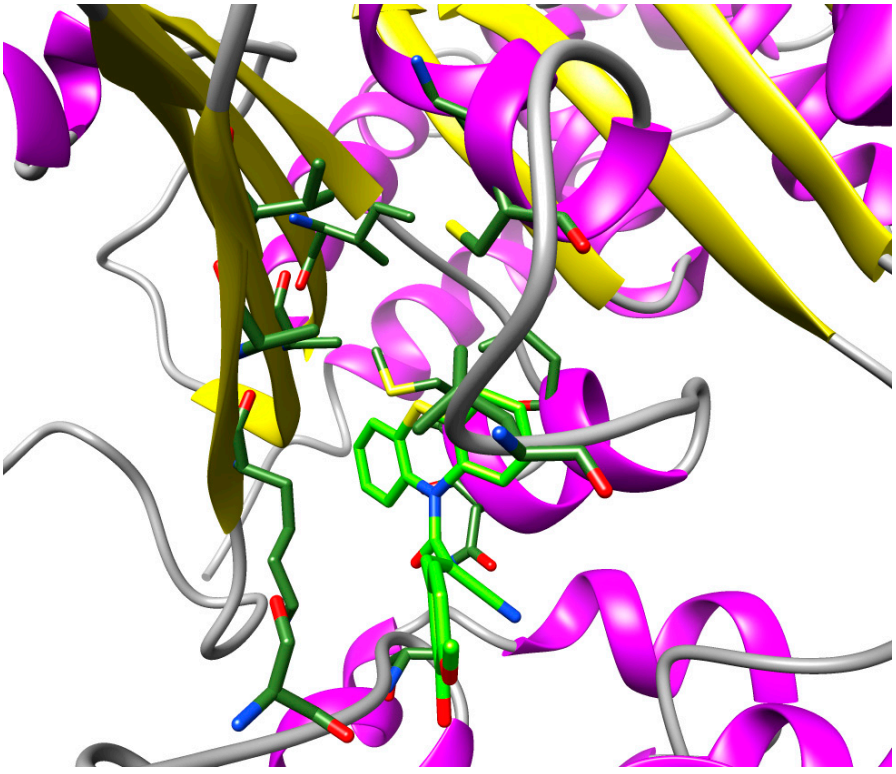


Phenstatin

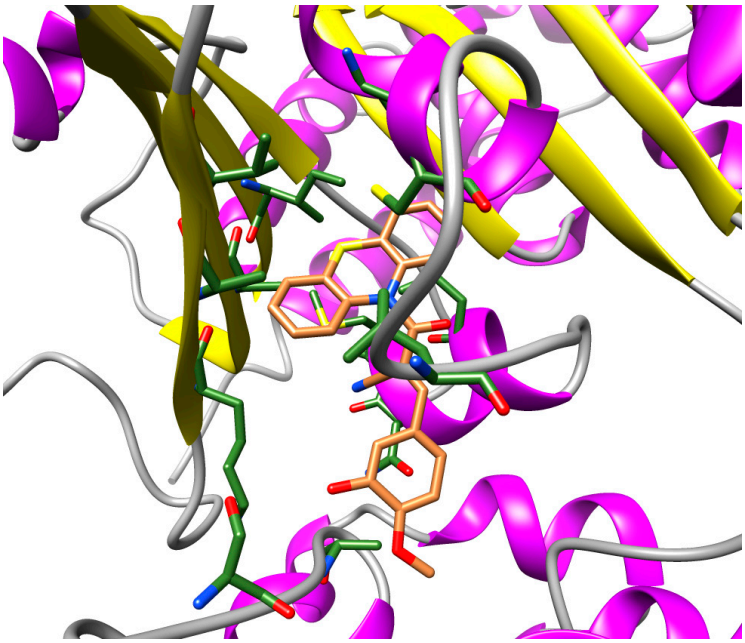


Docking tubulin (colchicine binding site)

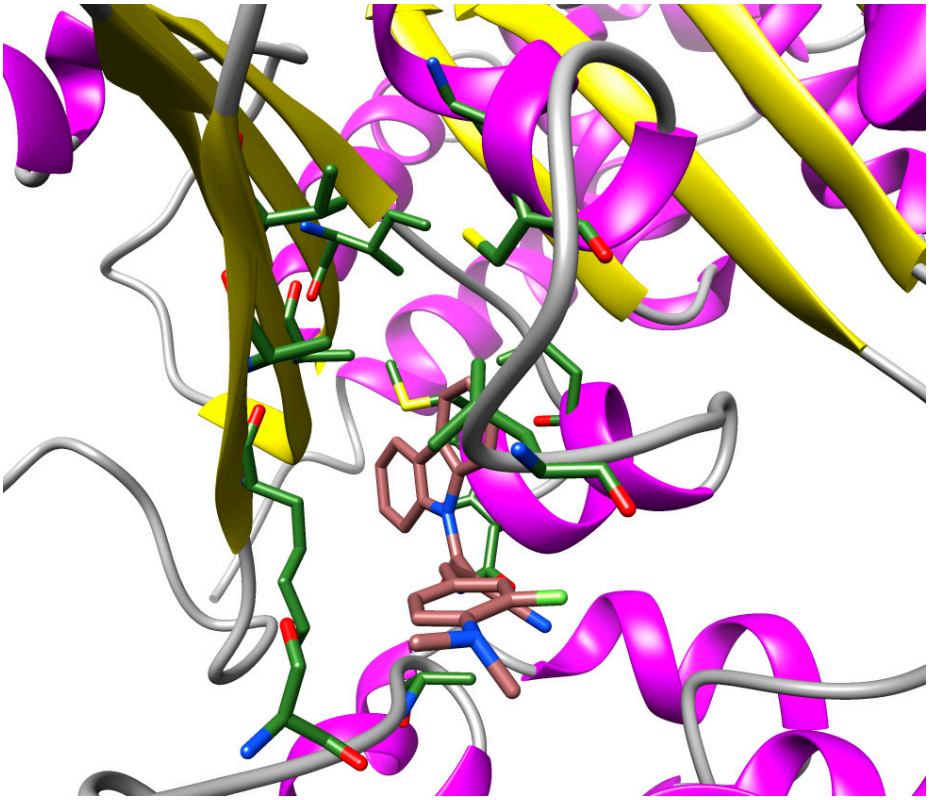
Compound 1l (40% of the solutions)



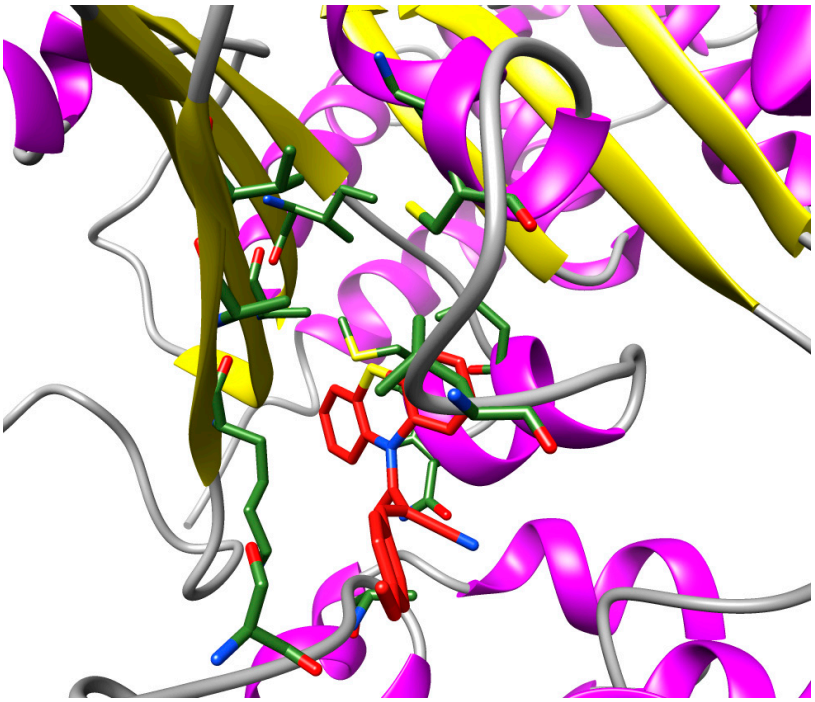
Compound 1l (60% of the solutions)



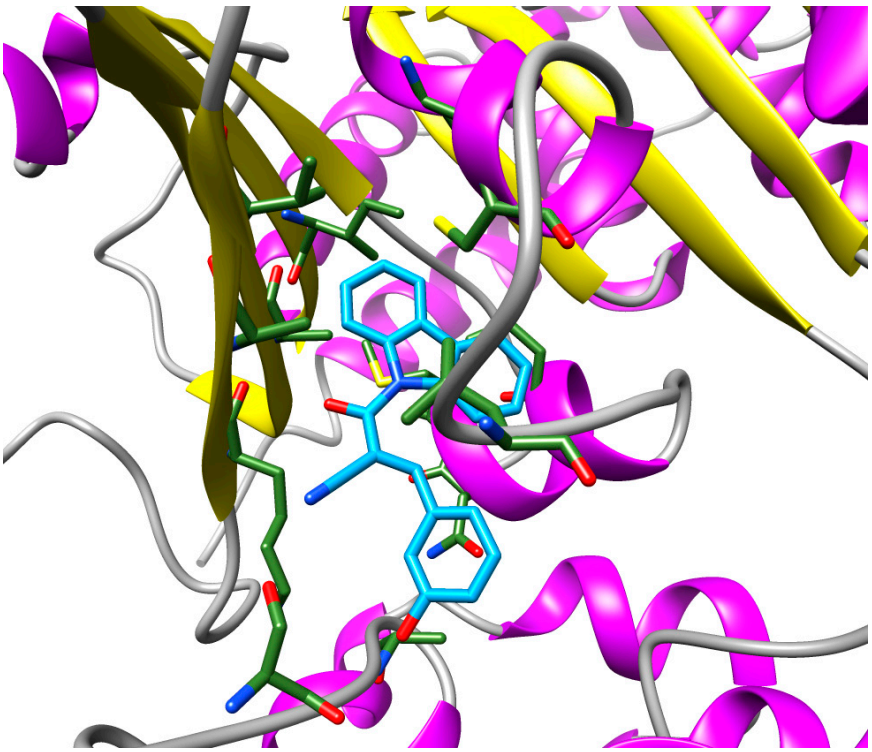
Compound 3a



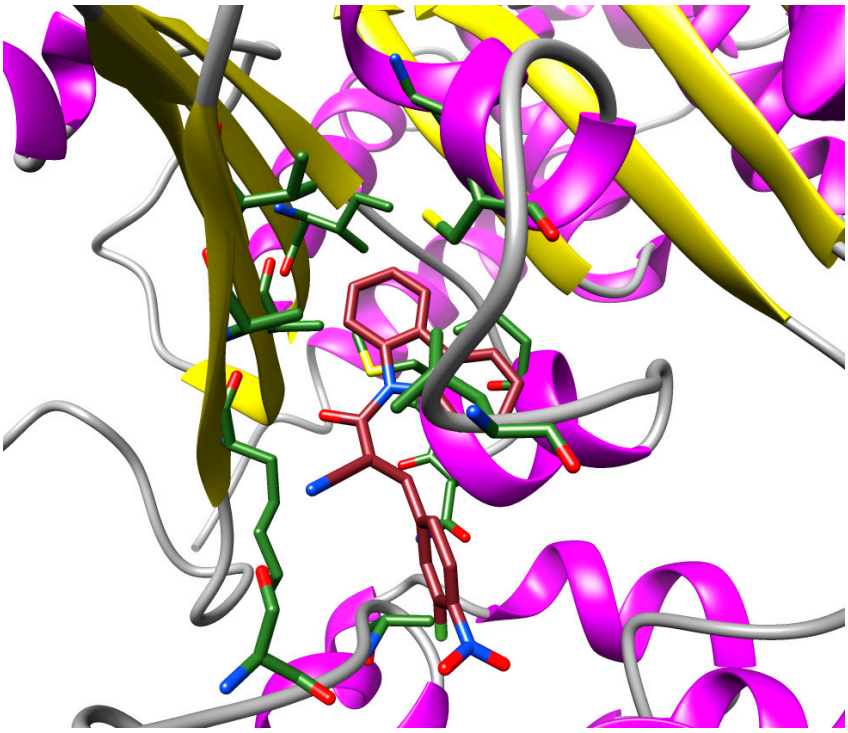
Compound 3b



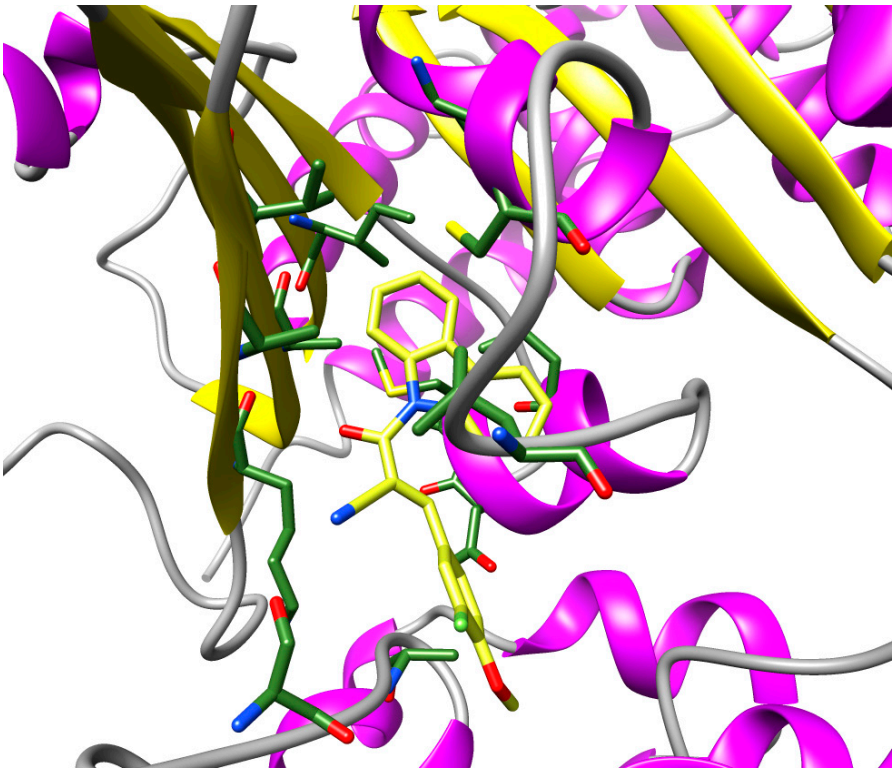
Compound 3d



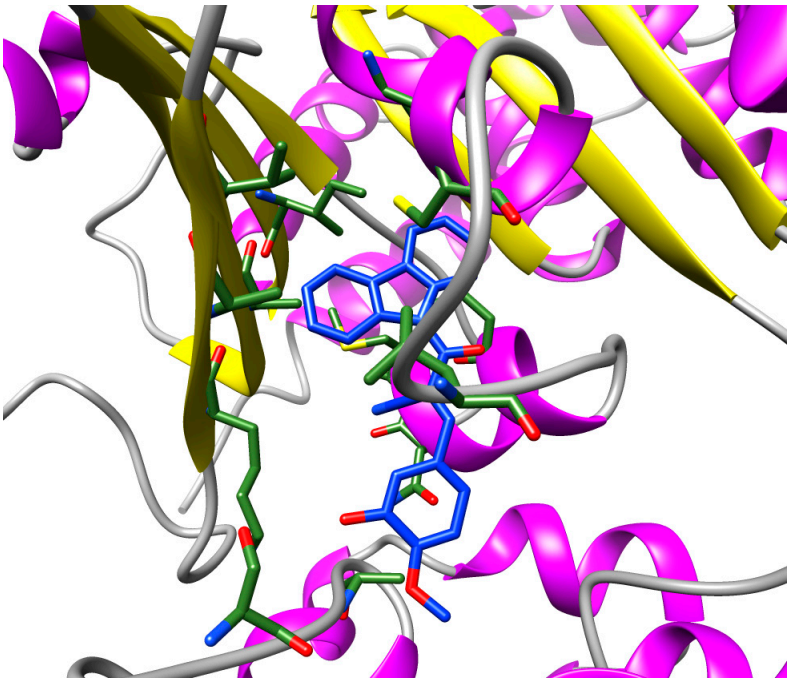
Compound 3e



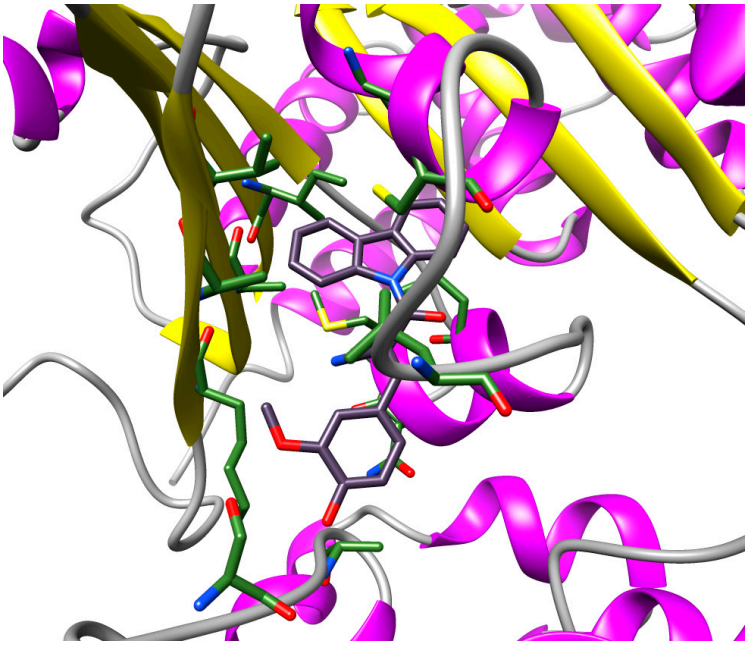
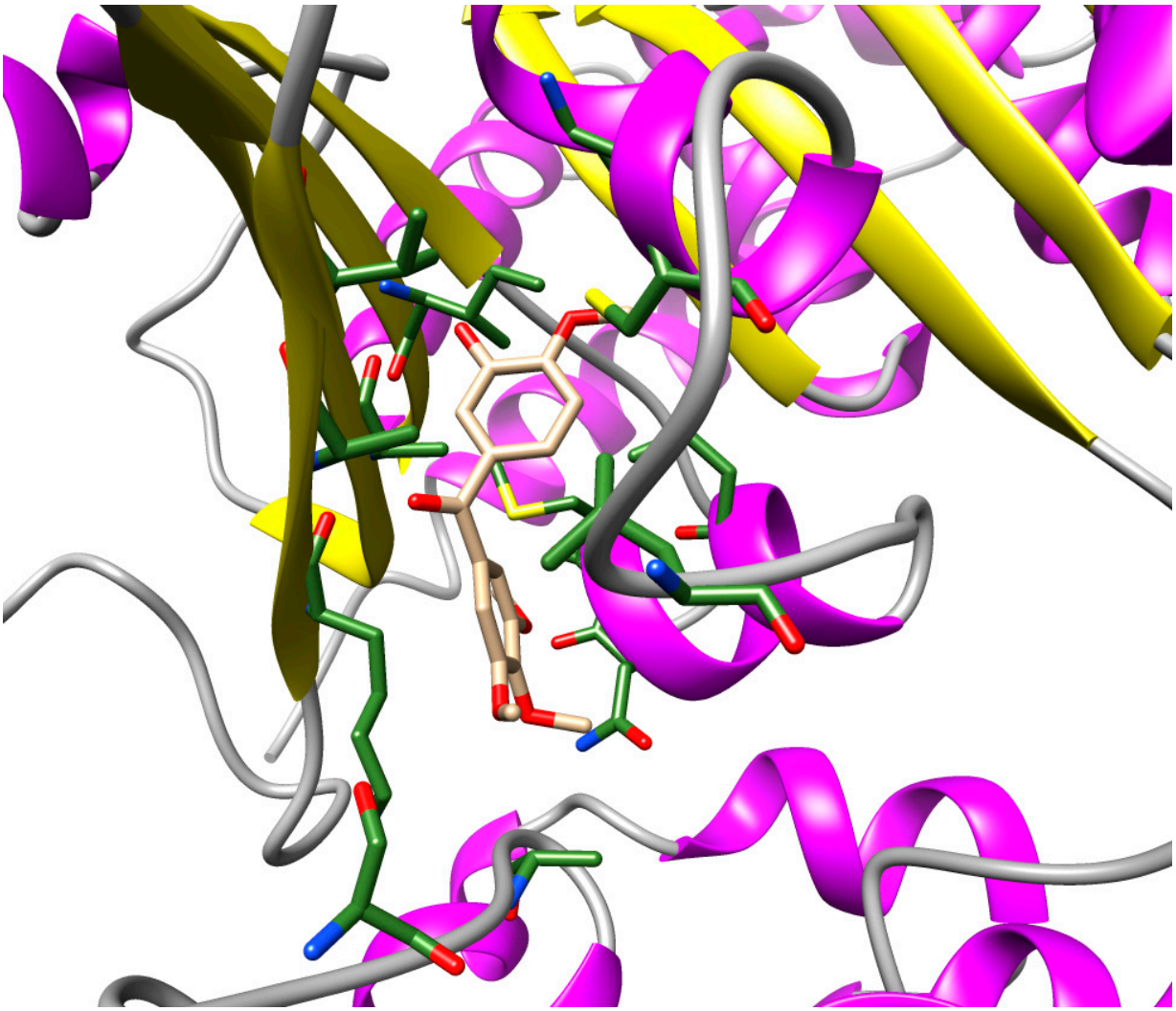
Compound 3i



Compound 3j



Compound 3l



Phenstatin