Supplementary Materials for

1,3,4-Thiadiazoline−coumarin hybrid compounds containing D-glucose/D-galactose moieties: Synthesis and evaluation of their antiproliferative activity

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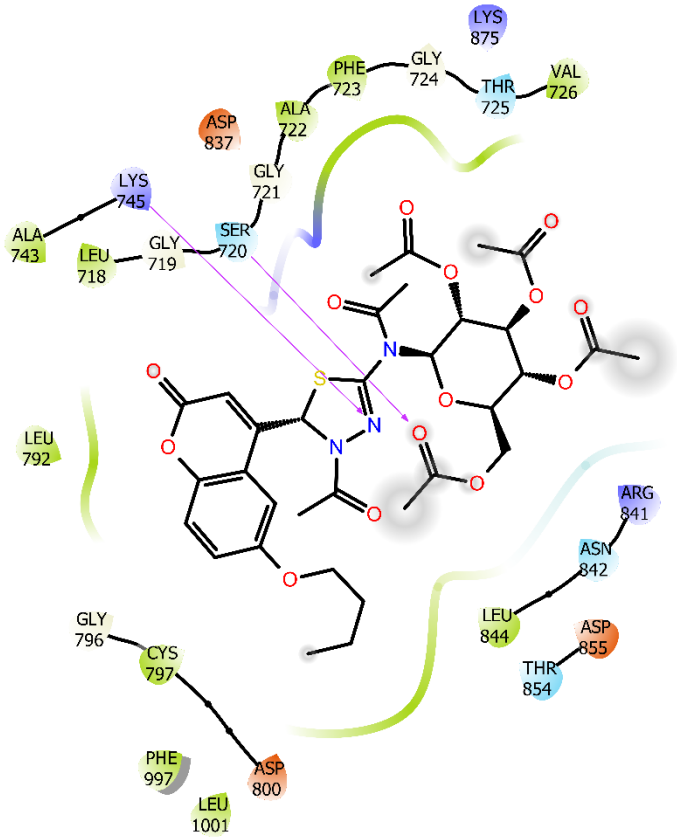
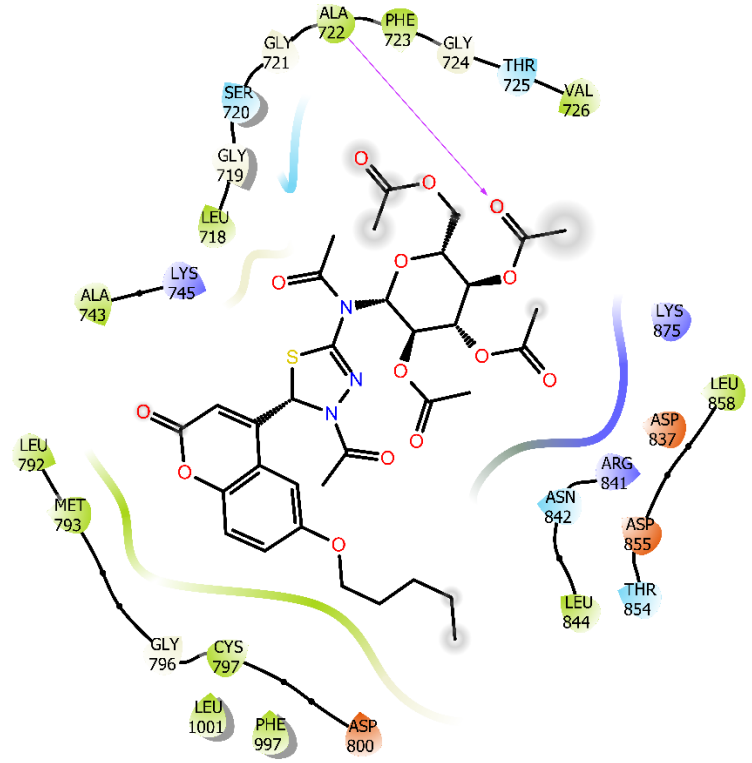
1. Results of molecular docking study

1.1. 2D interactions with EGFR (enzyme 3POZ) of selected compounds 9a,9c.9d,9f, and 9g (A−E) and of Sorafenib (F)

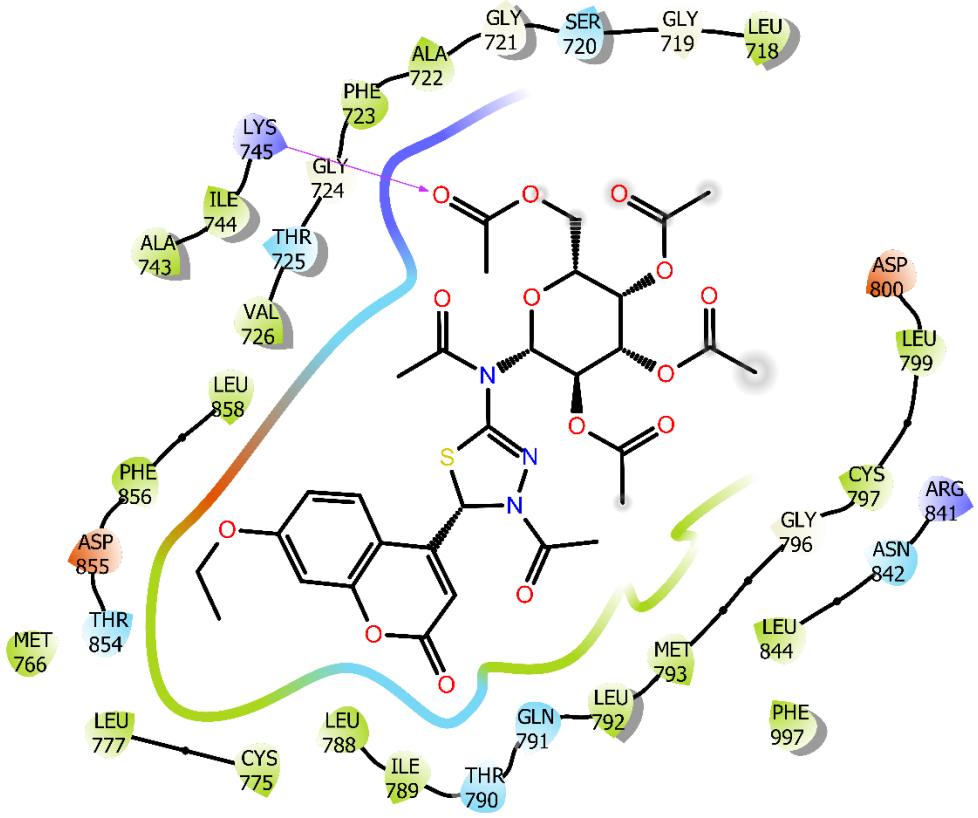
(A) Compound **9b** (R = 6-O^{n}C$_4$H$_9$)



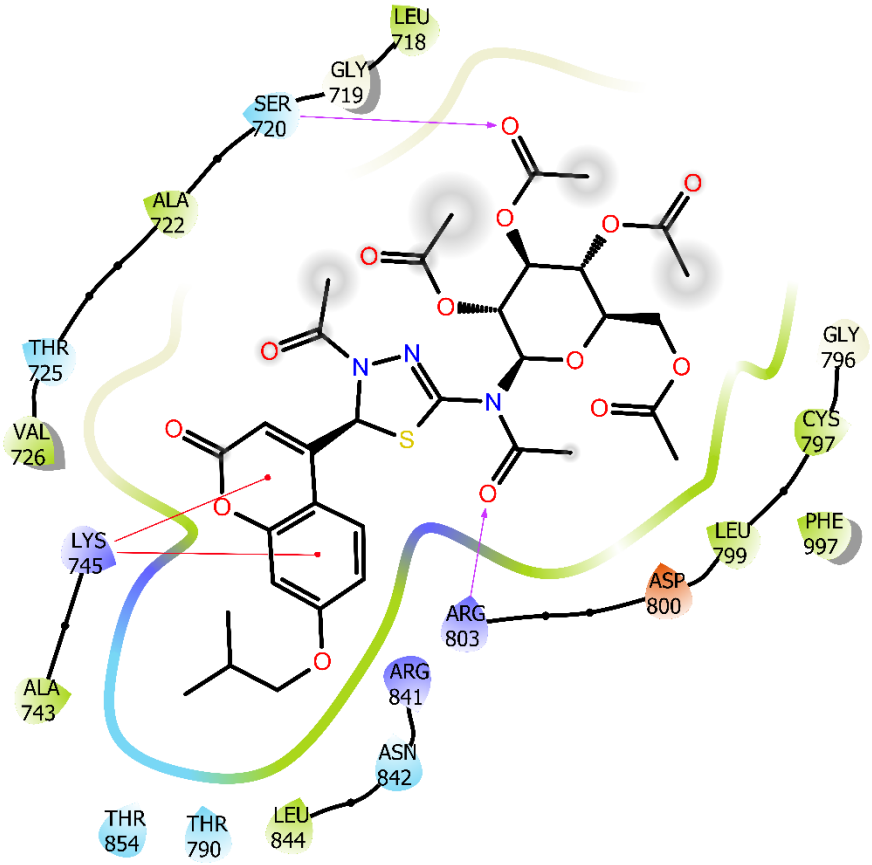
(B) Compound **9c** (R = 6-O^{n}C$_5$H$_{11}$)



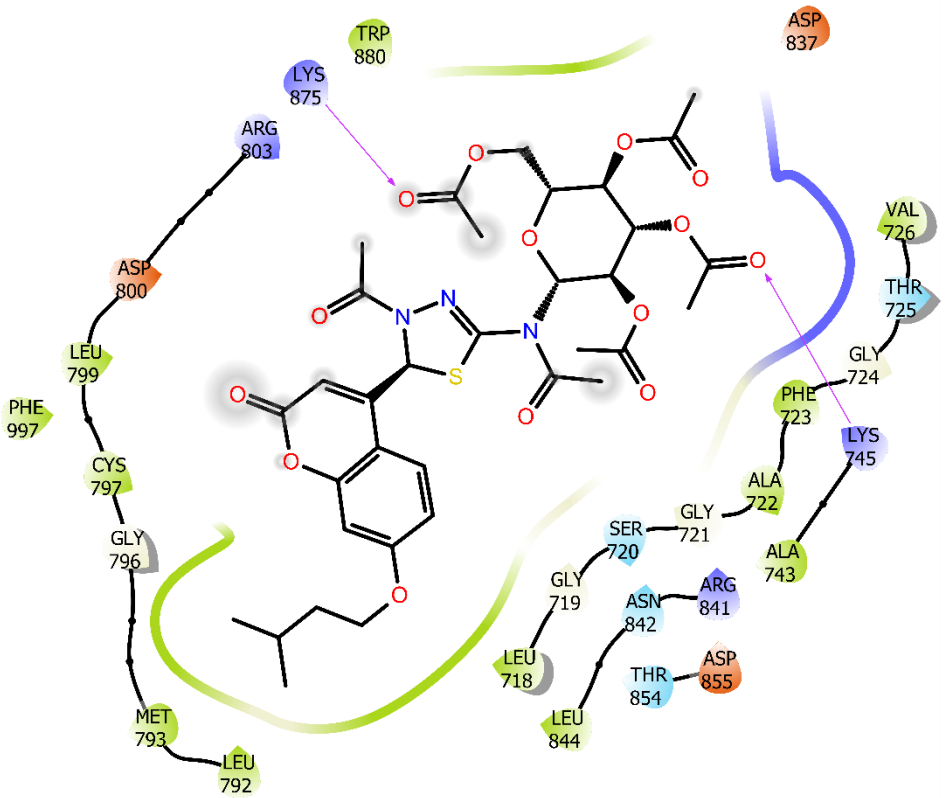
(C) Compound **9e** (R = 7-OC_2H_5)



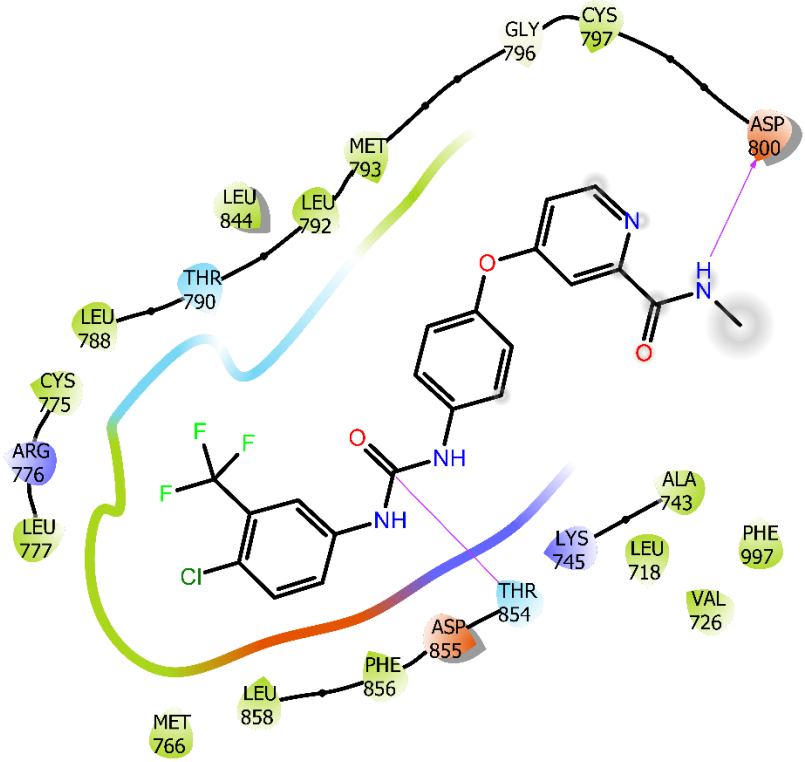
(D) Compound **9f** (R = 7-$O^iC_4H_9$)



(E) Compound **9g** (R = 7-O^{i}C$_5$H$_{11}$)

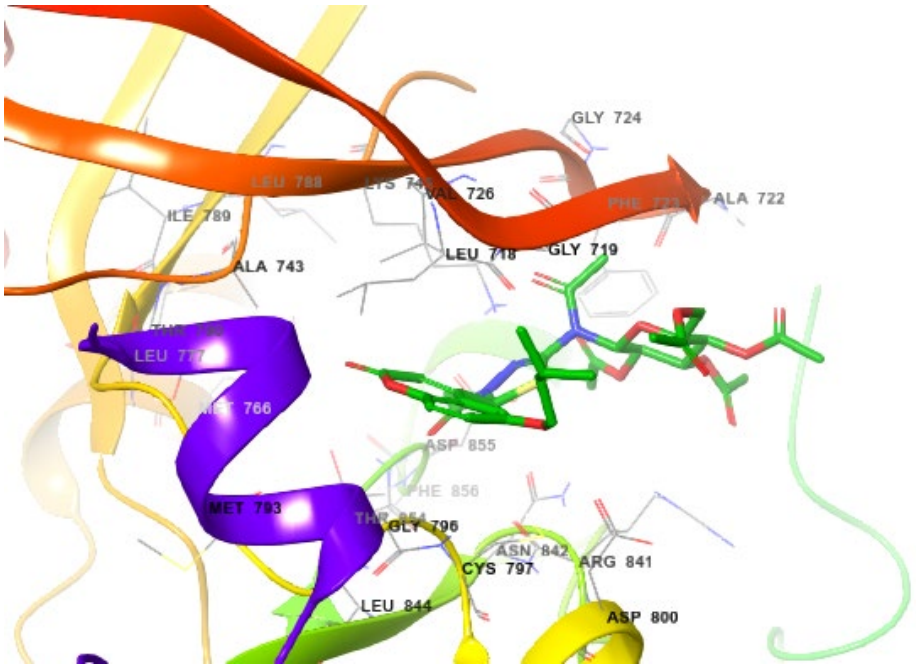


(F) Sorafenib



1.2. 3D interactions with EGFR of selected compounds 9a,9c.9d,9f, and 9g (A−E) and of Sorafenib (F)

(A) Compound **9b** (R = 6-O^{n}C$_4$H$_9$)



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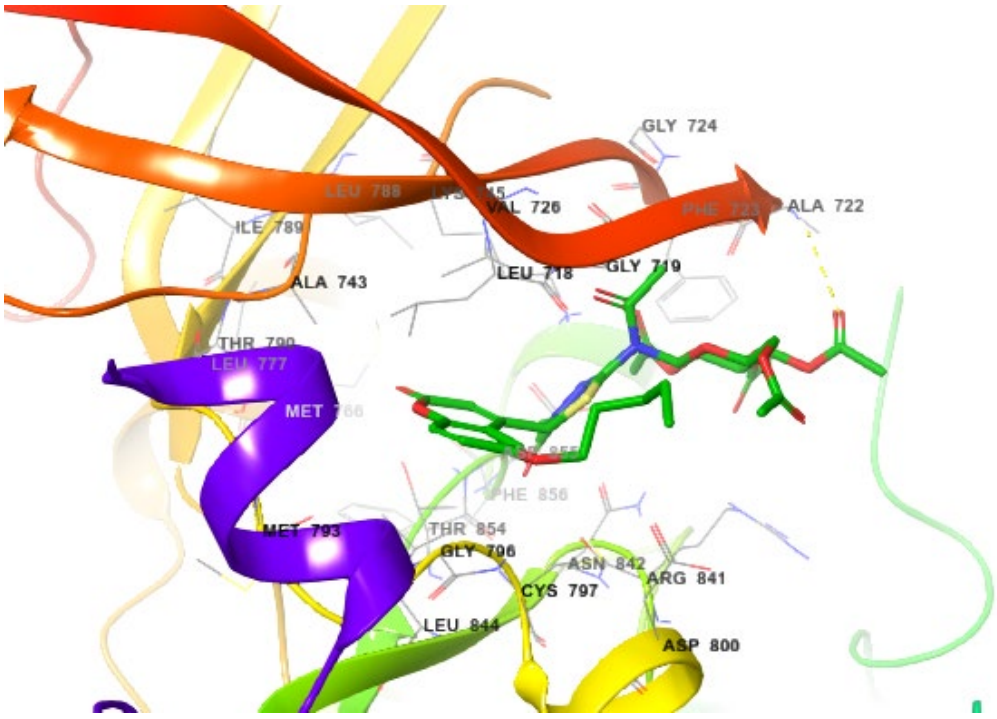

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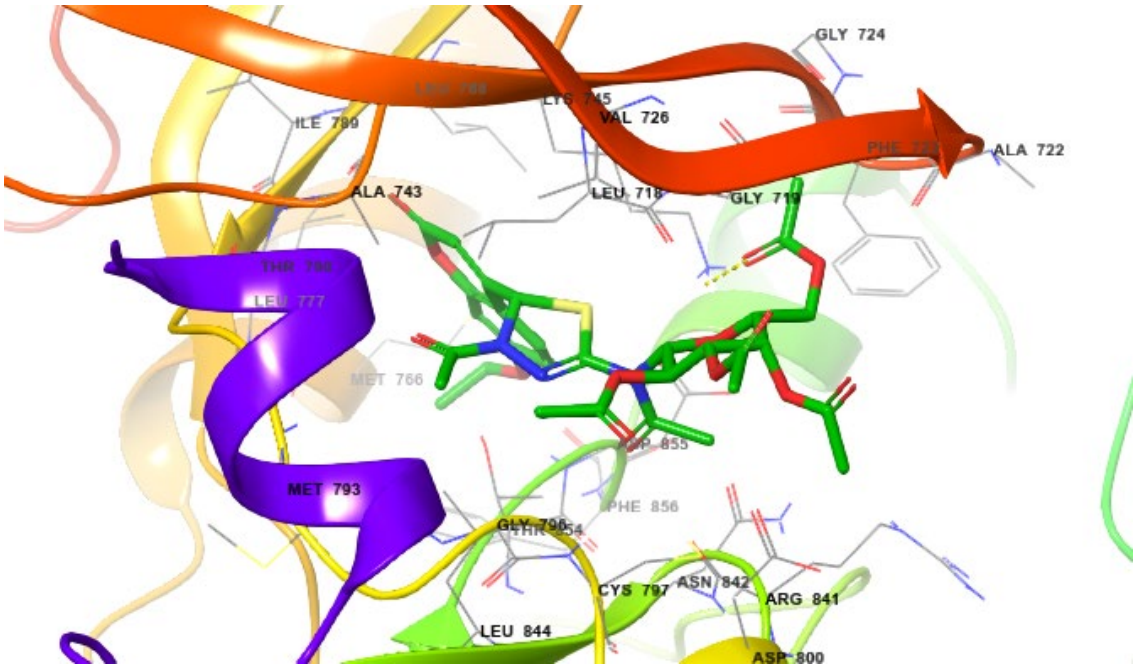
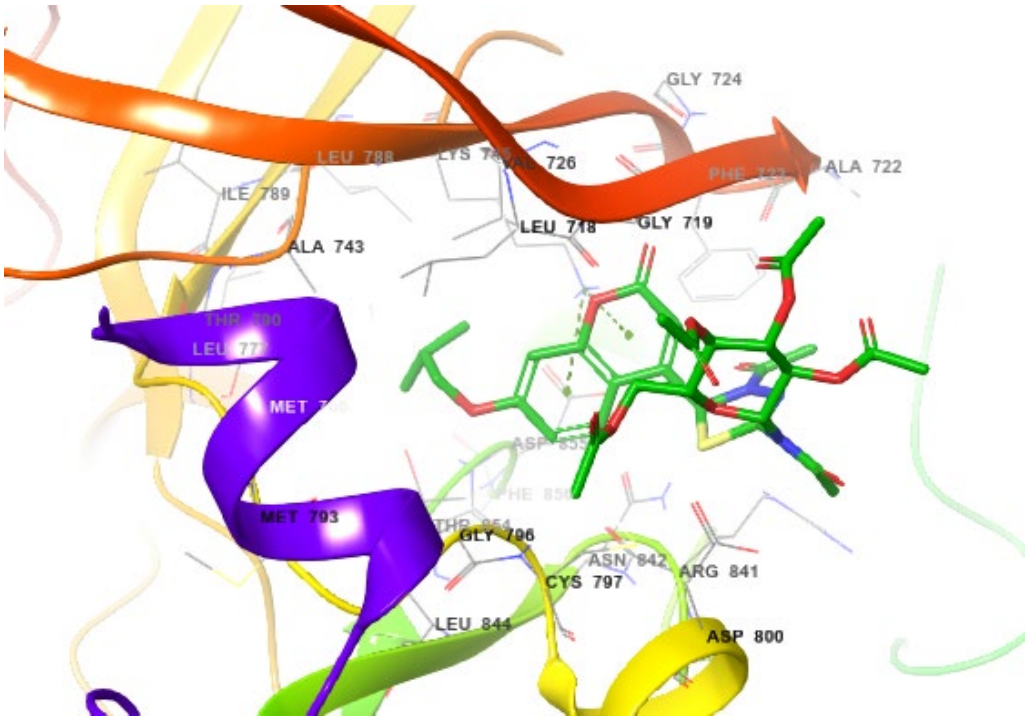


(D) Compound **9f** (R = 7-$O^iC_4H_9$)



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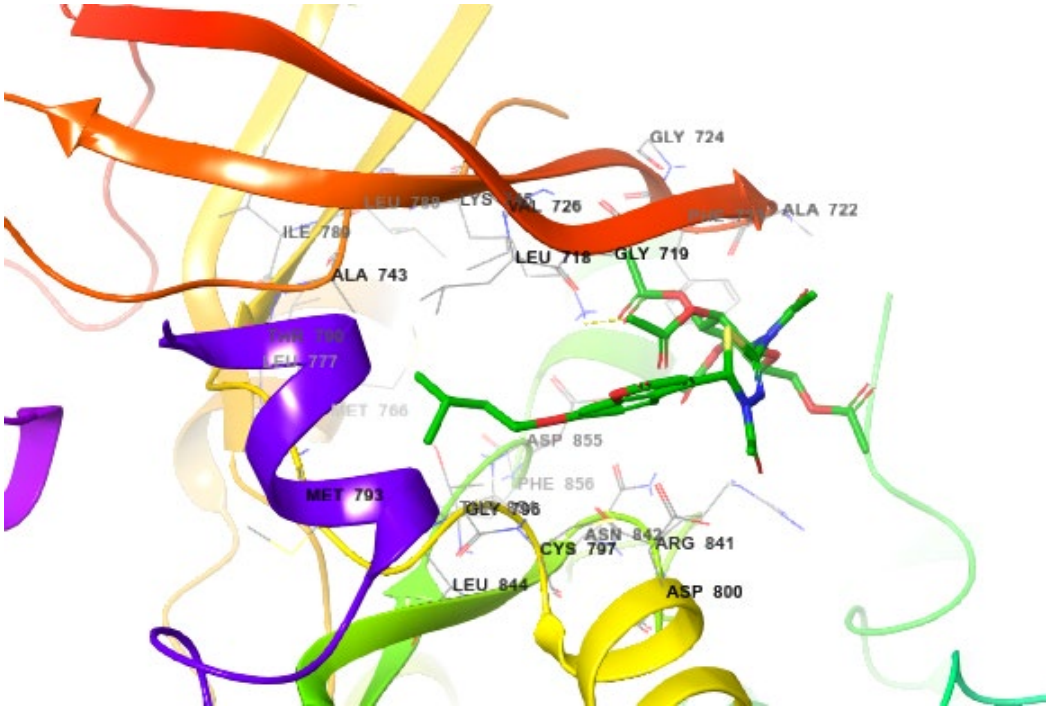

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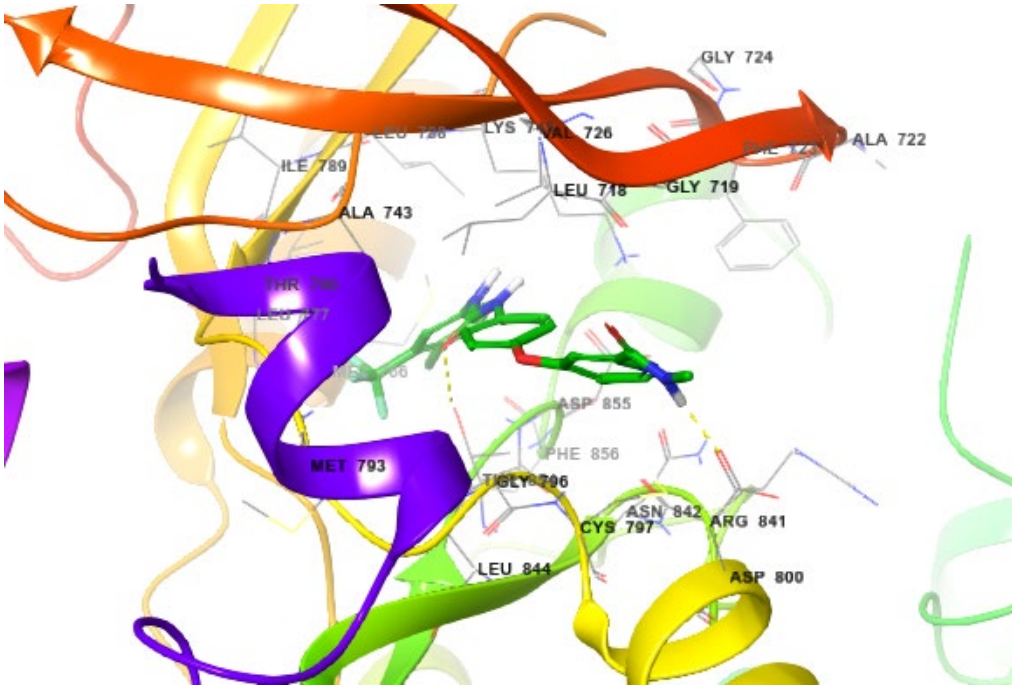

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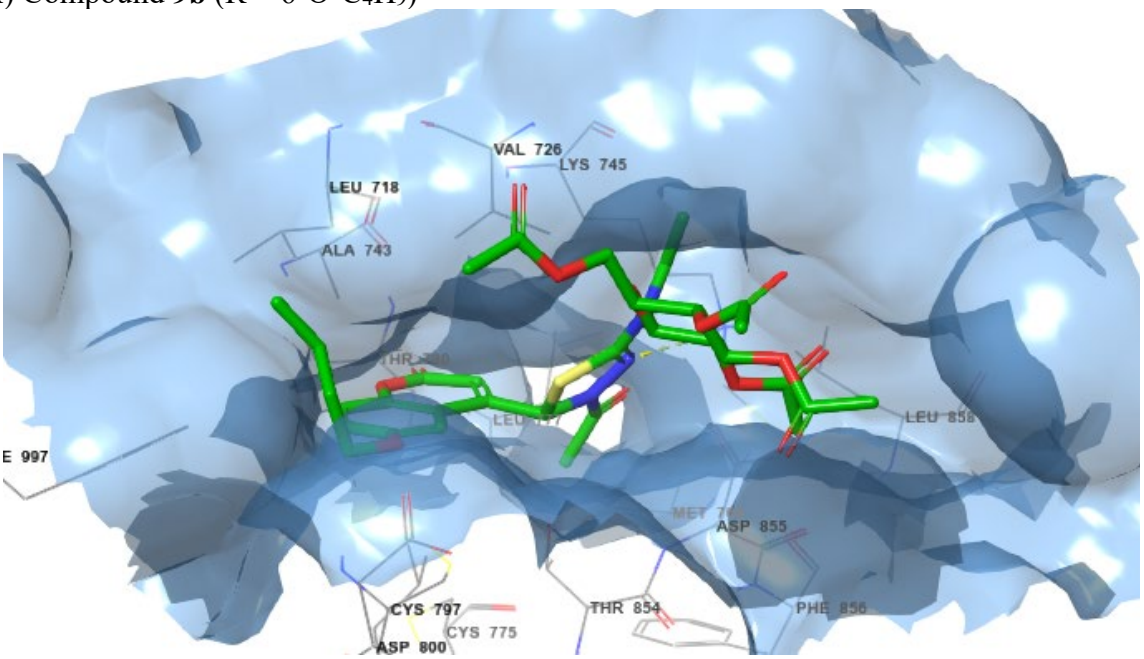

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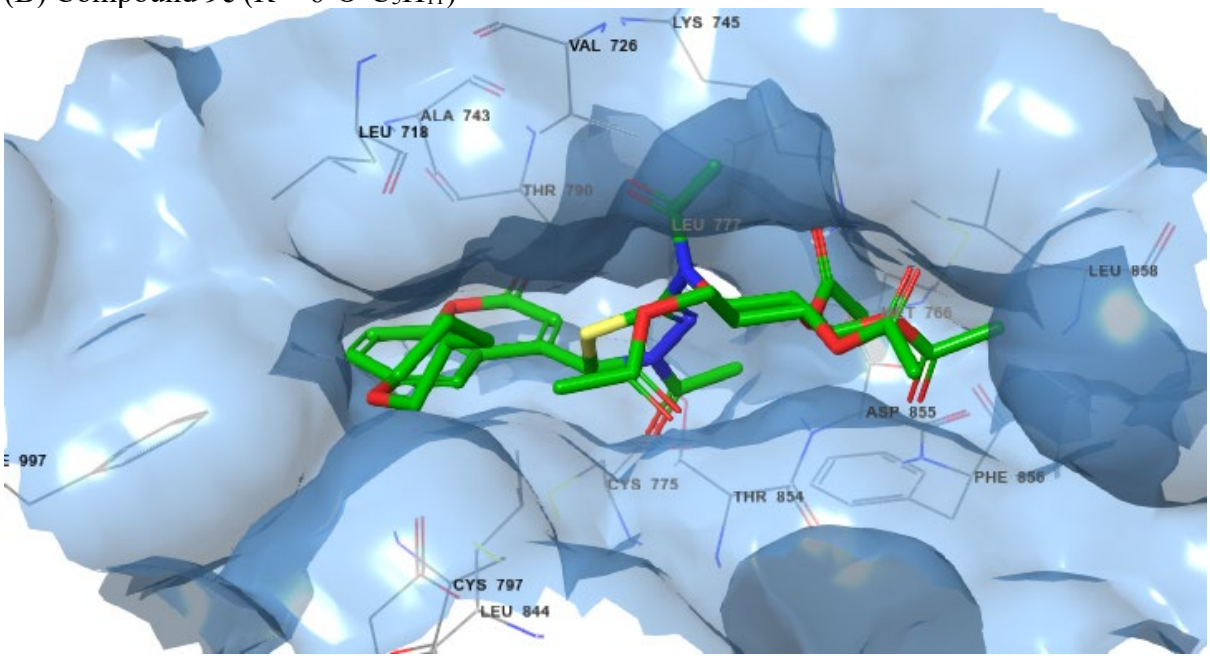

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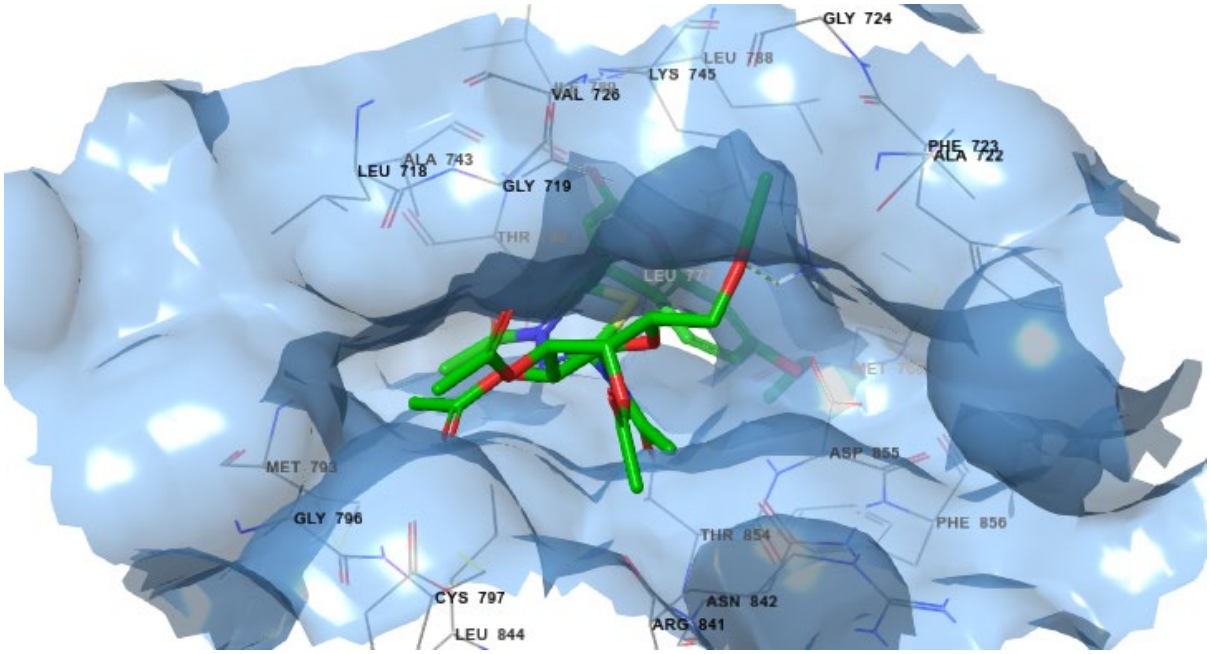

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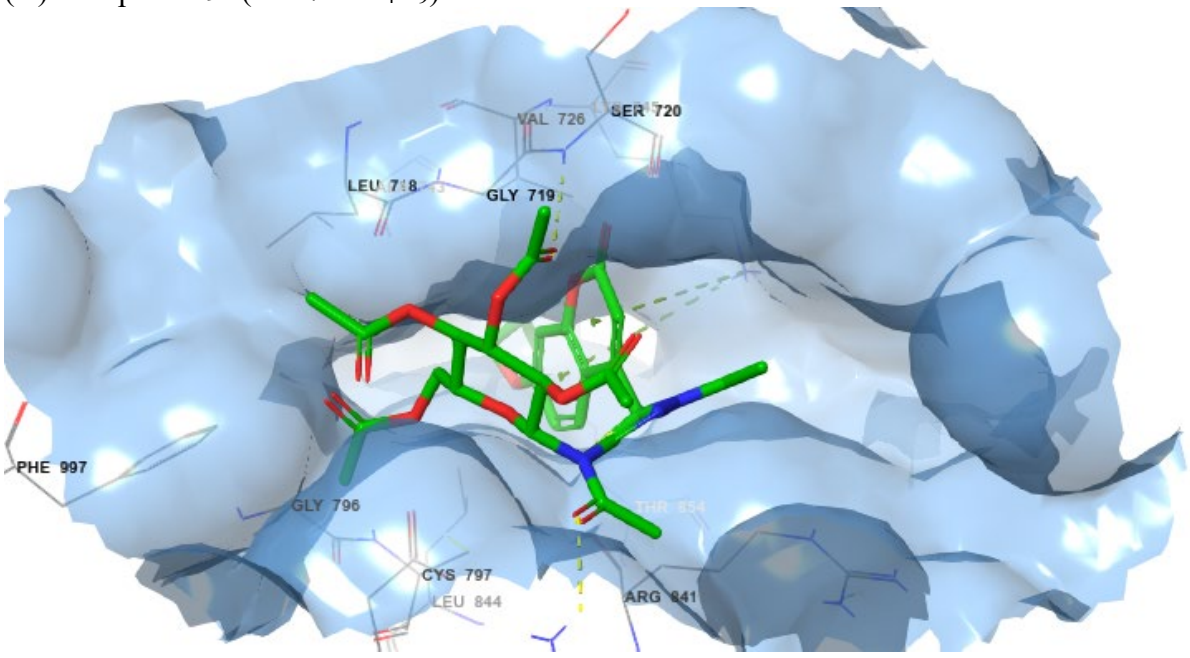

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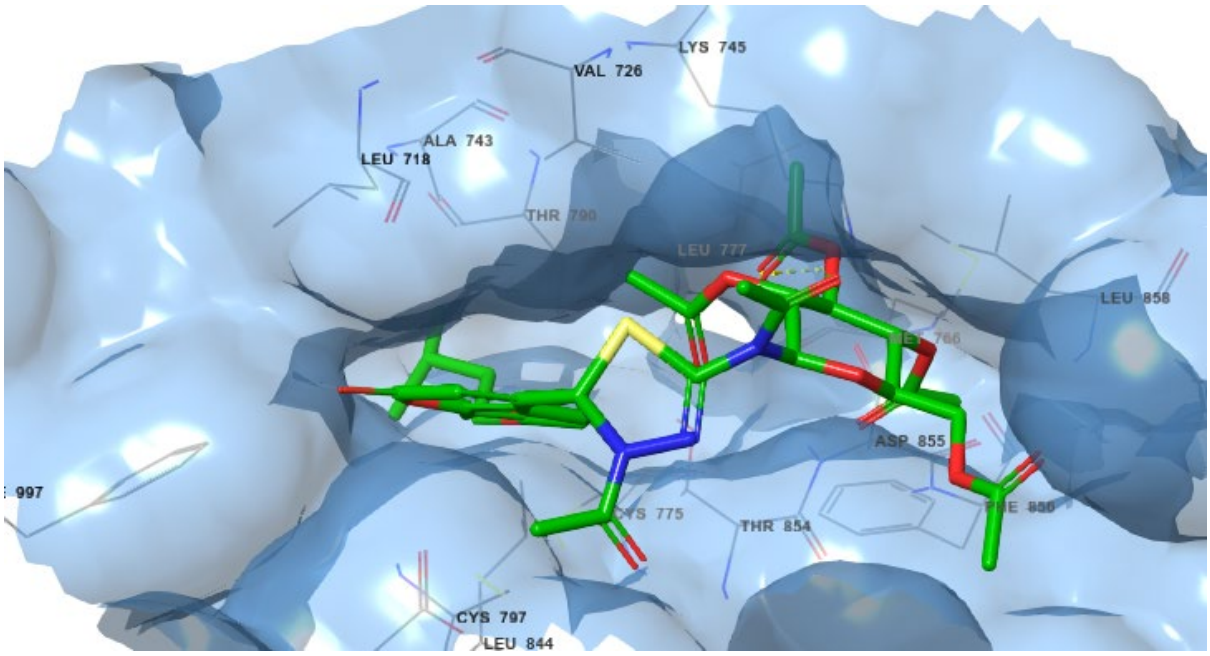

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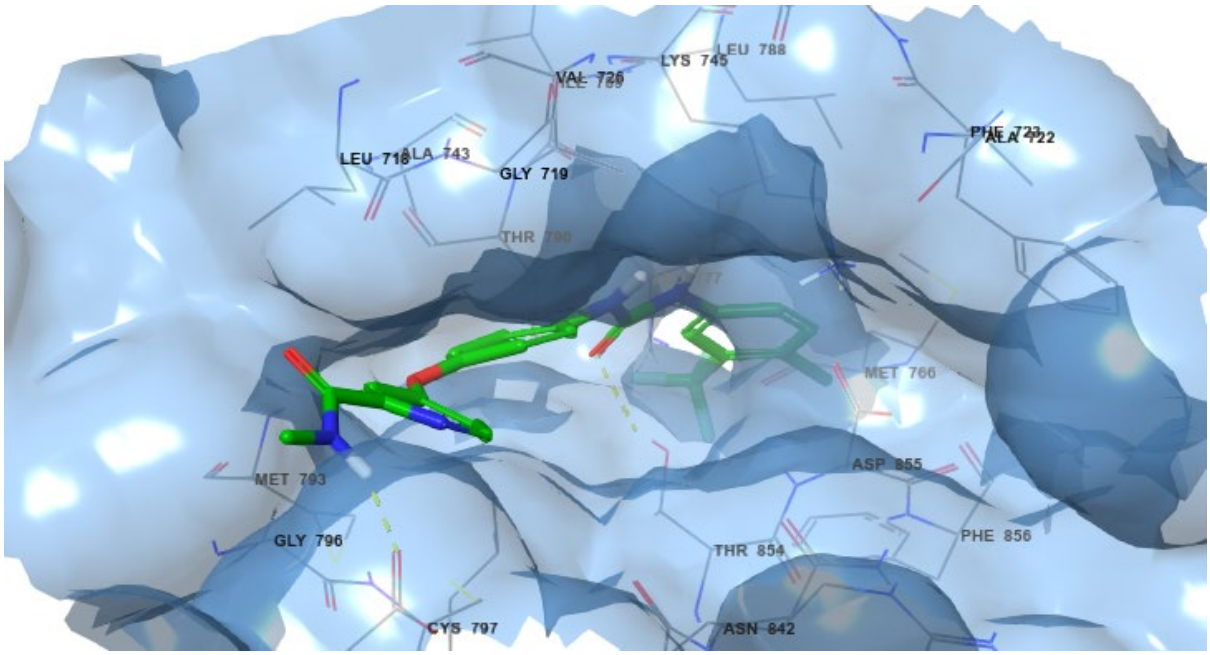

1.4. 2D interactions with HER2 (enzyme 3CRD) of selected compounds 9a,9c,9d,9f, and 9g (A−E) and of Sorafenib (F)

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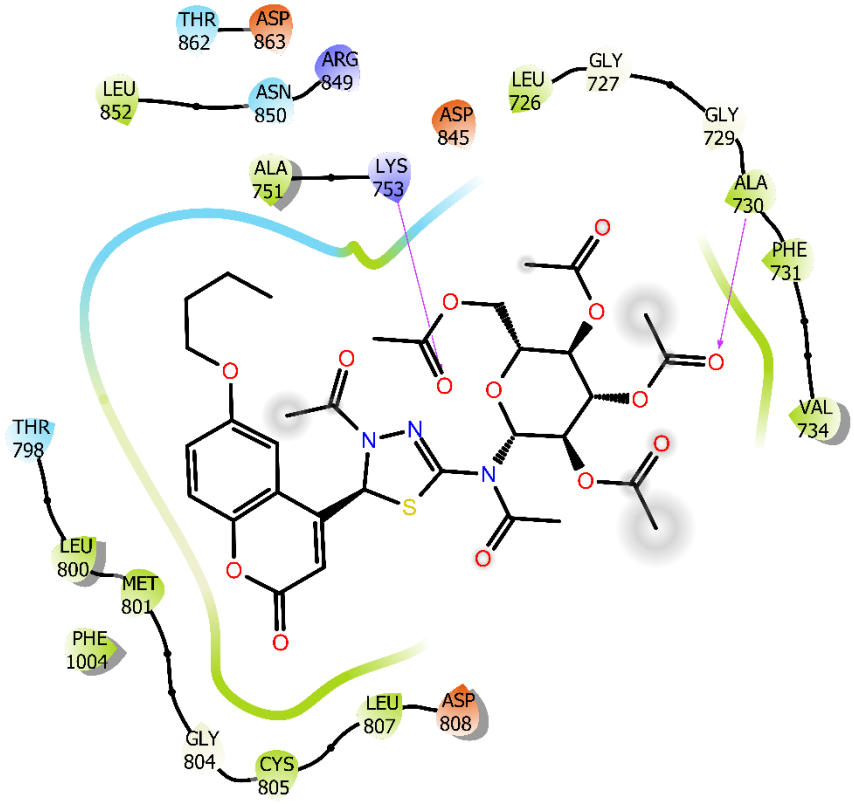

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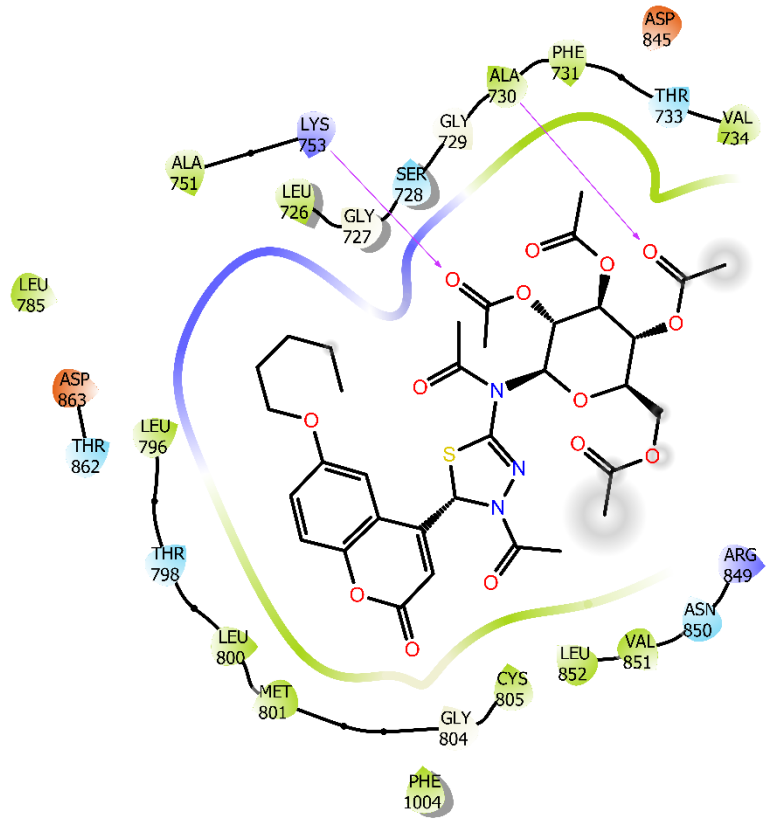

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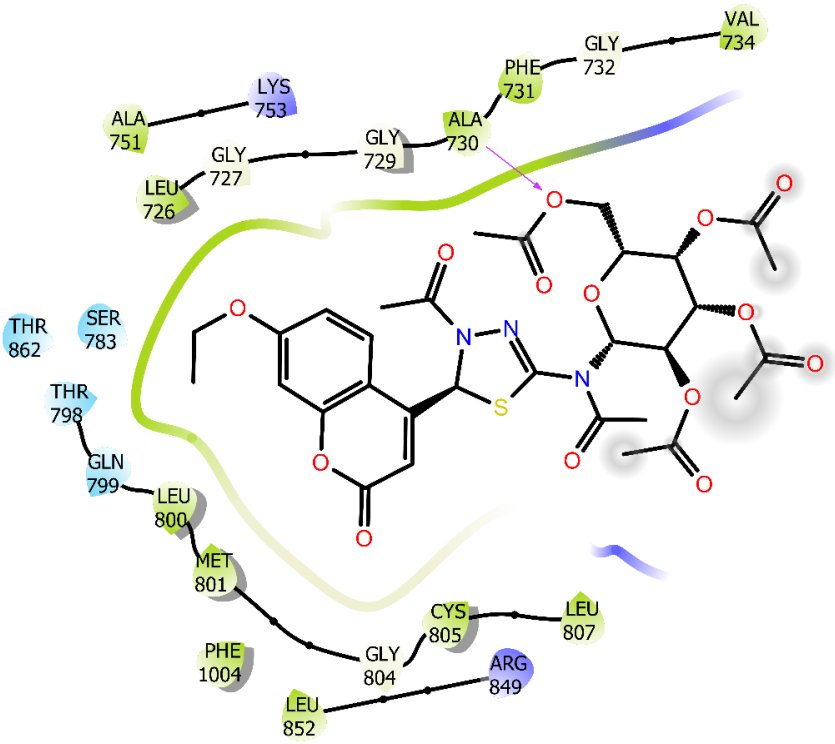

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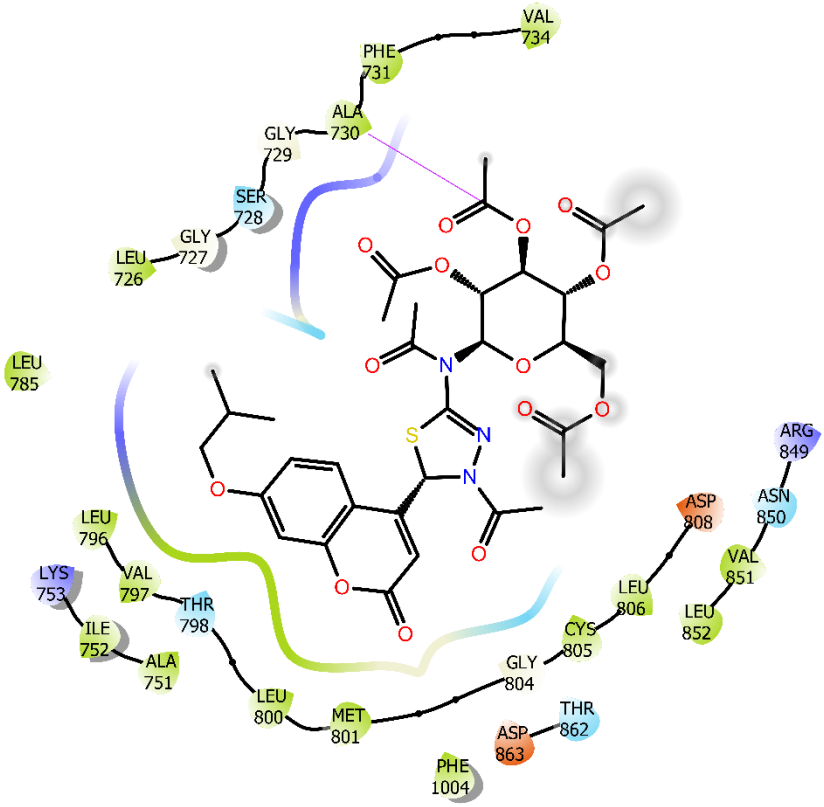

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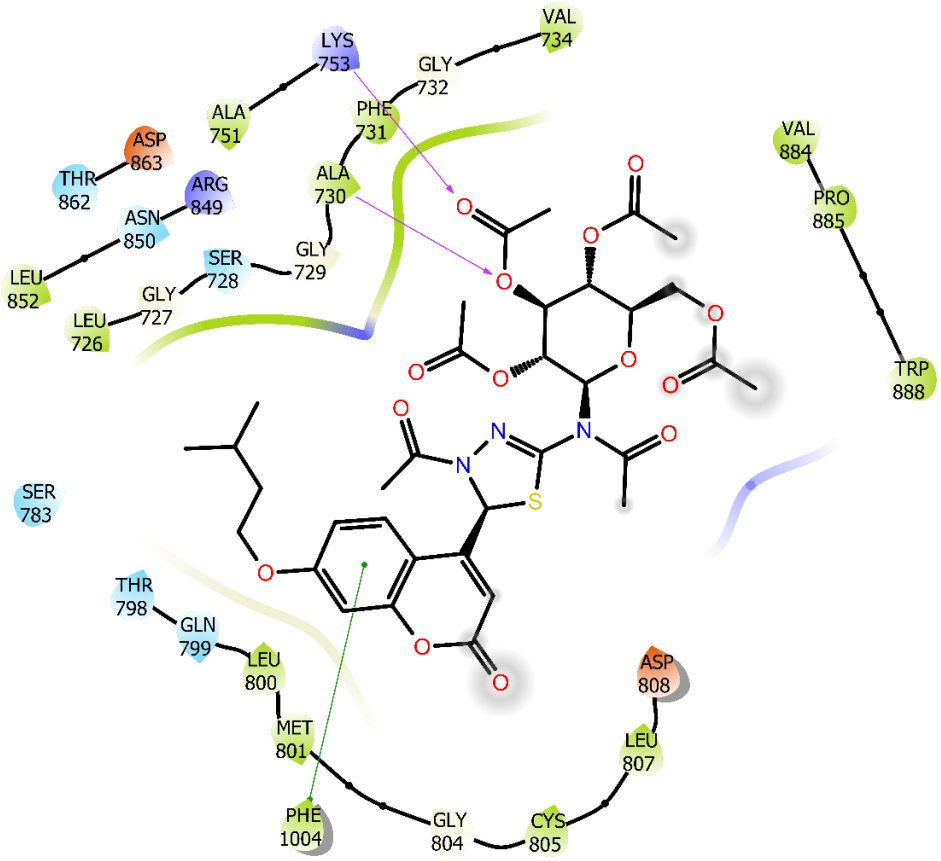

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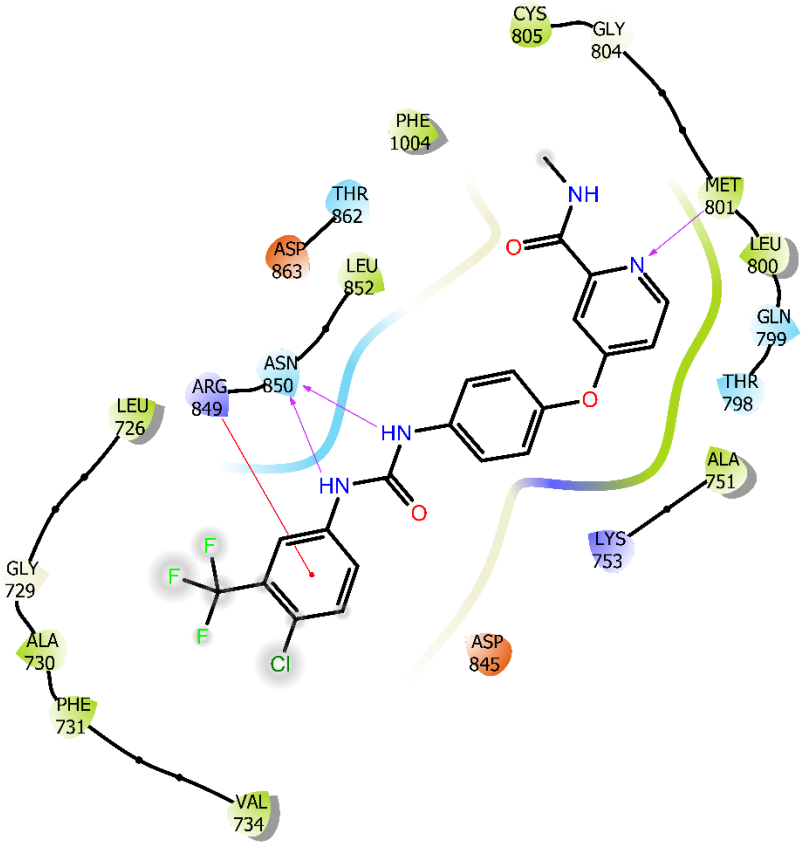

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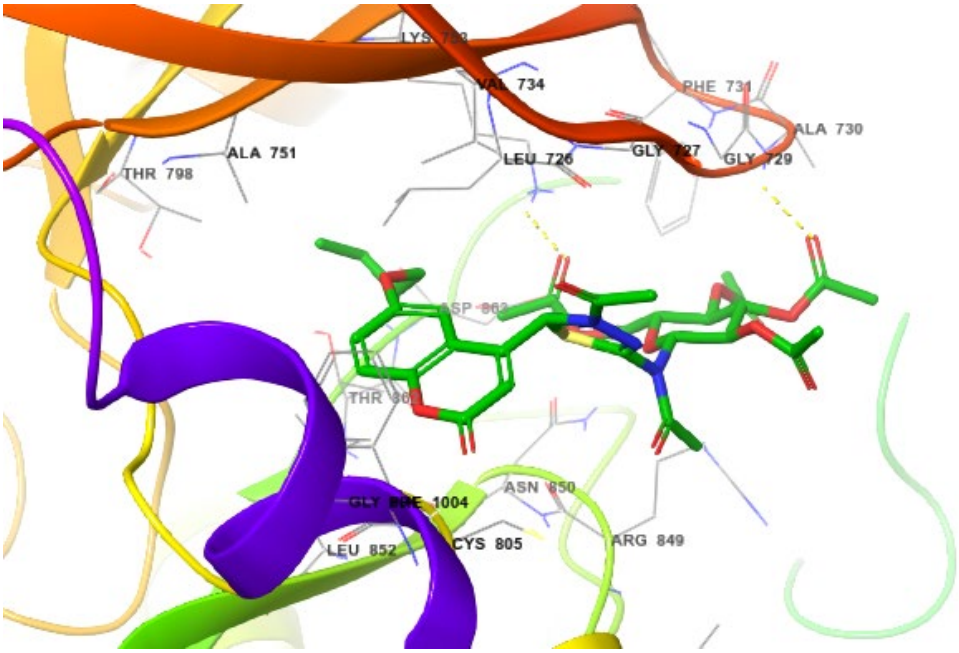

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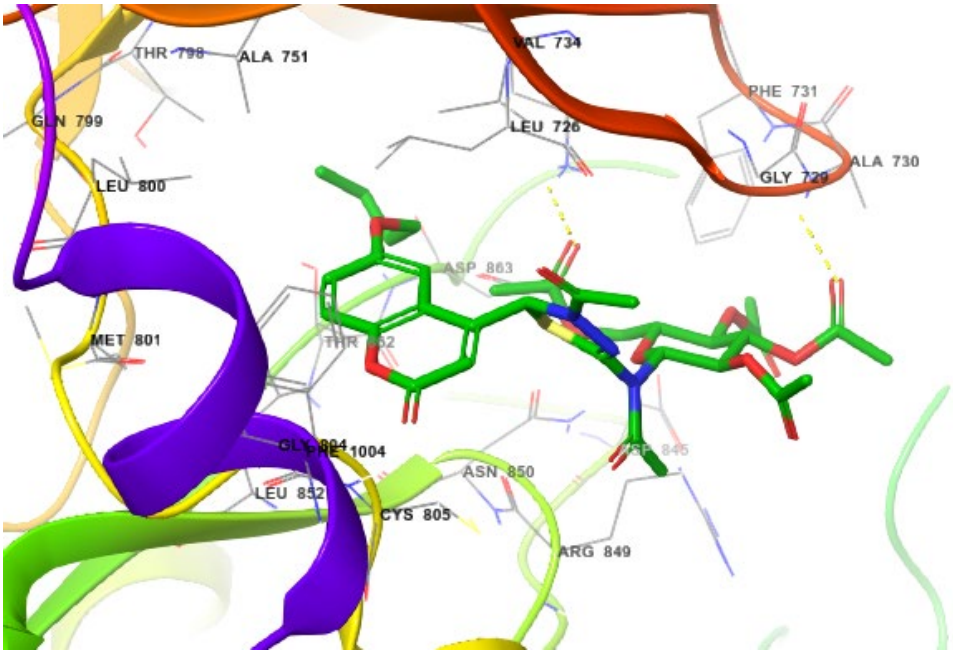

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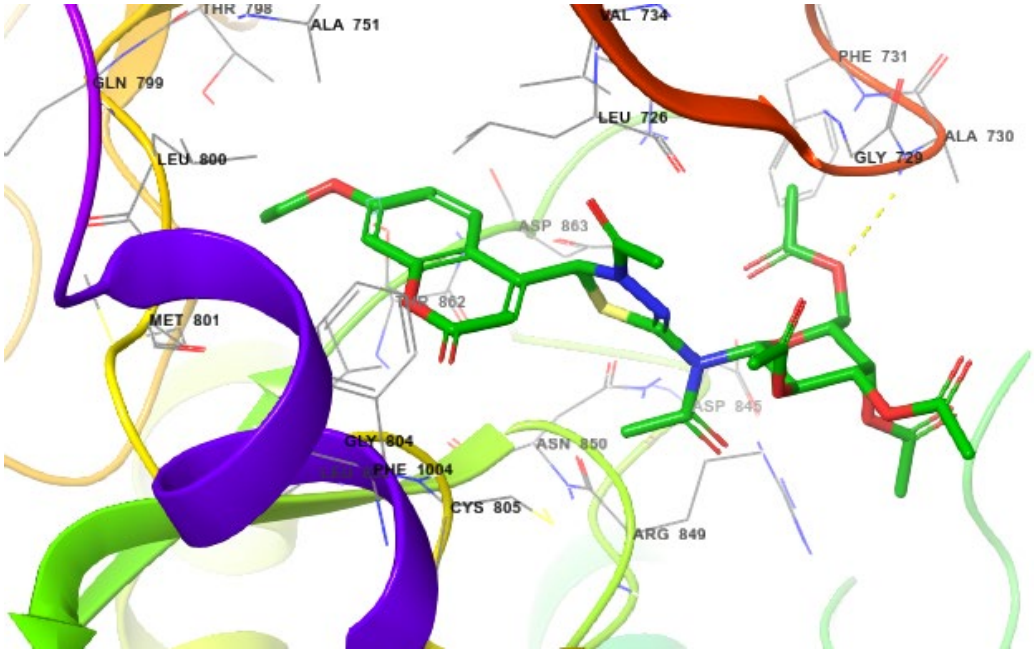

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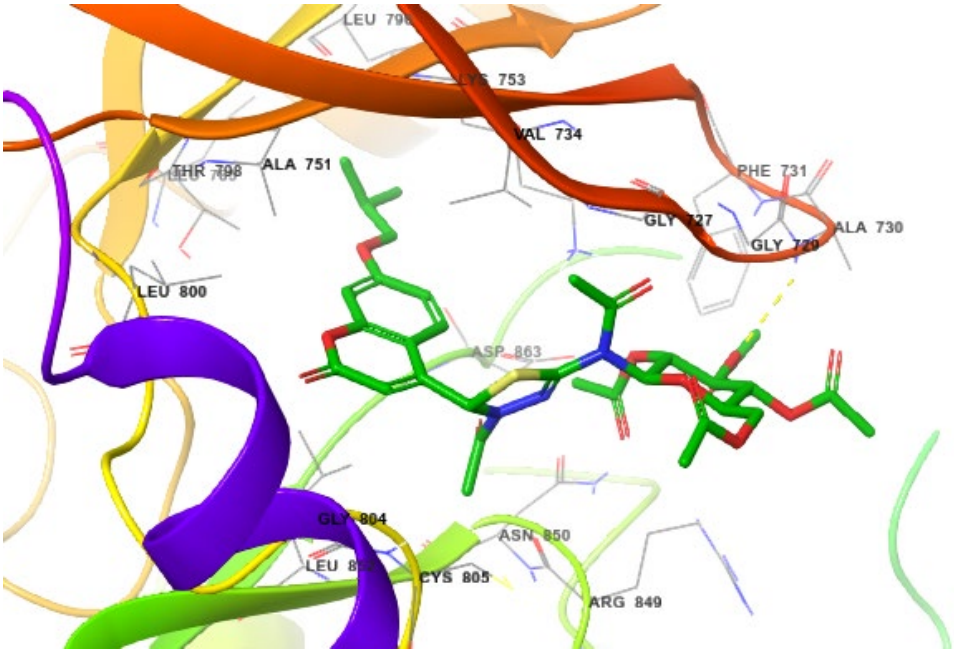

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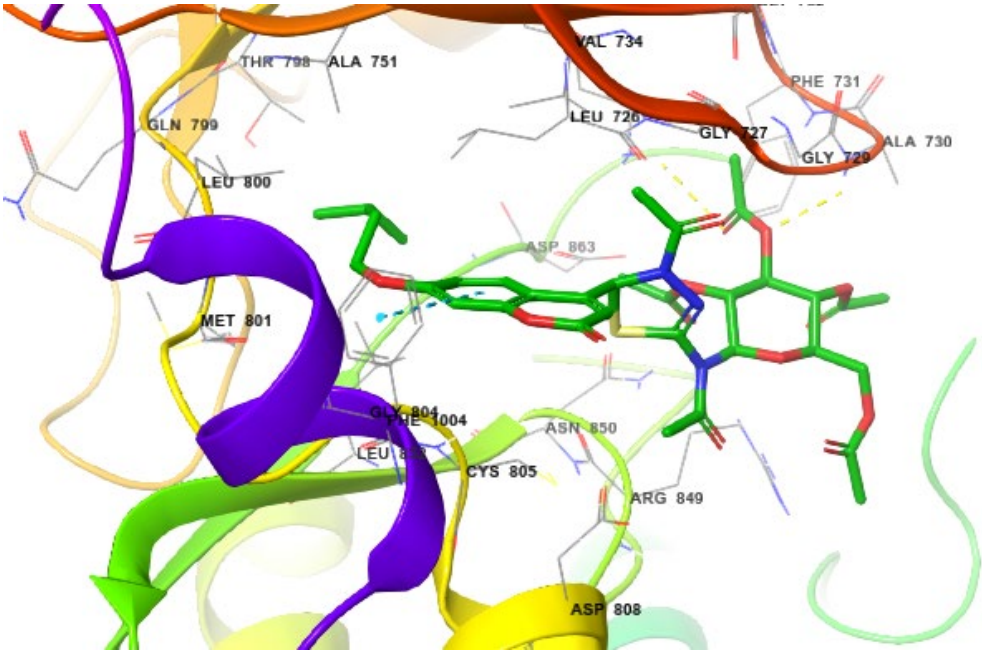

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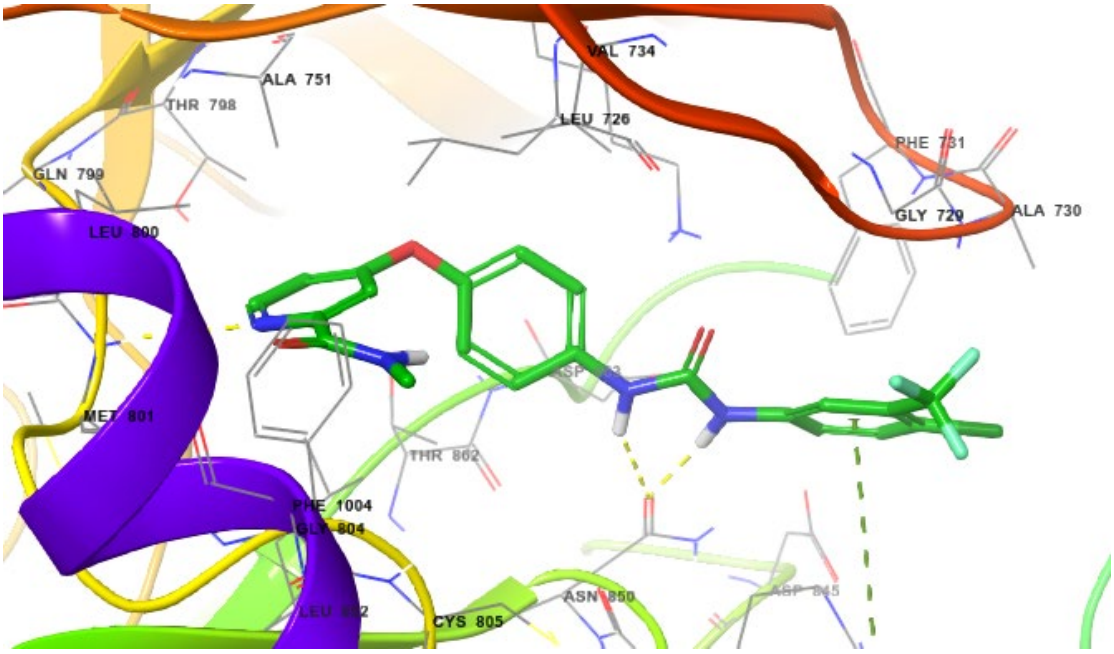

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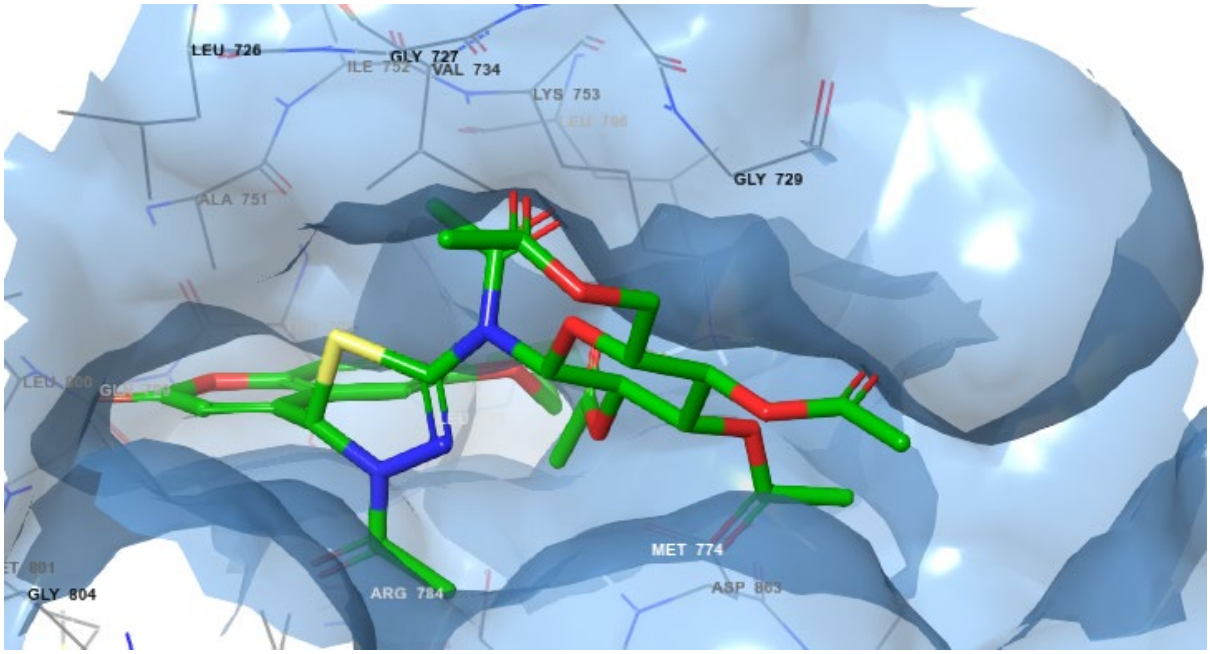

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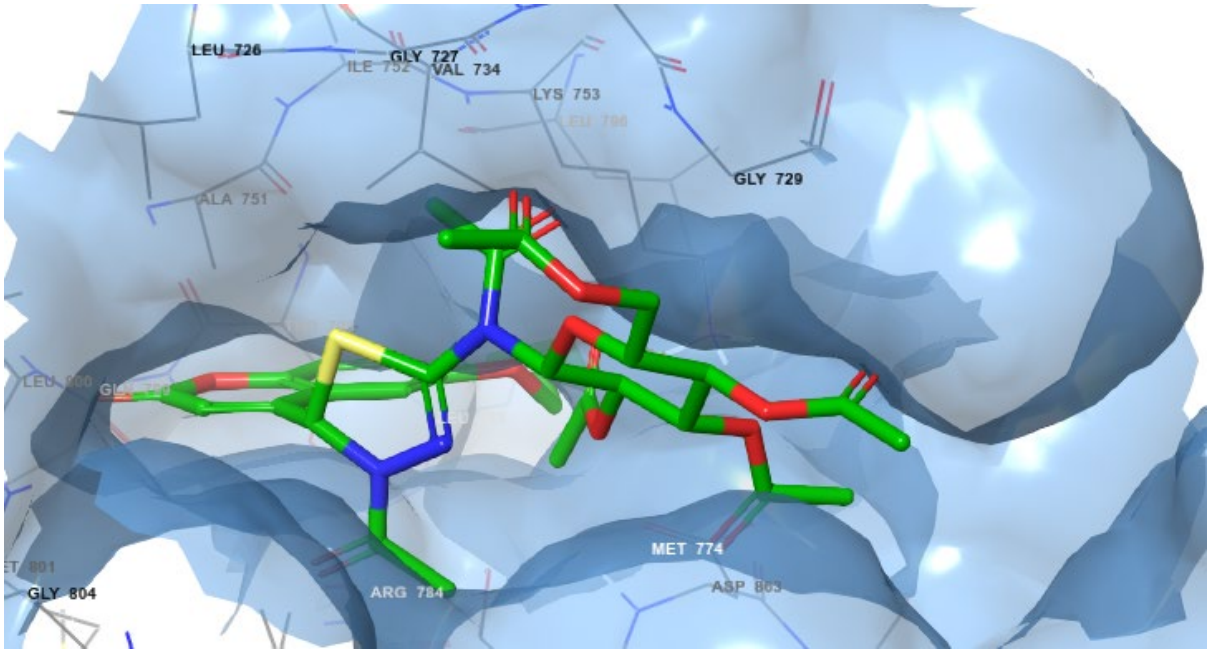

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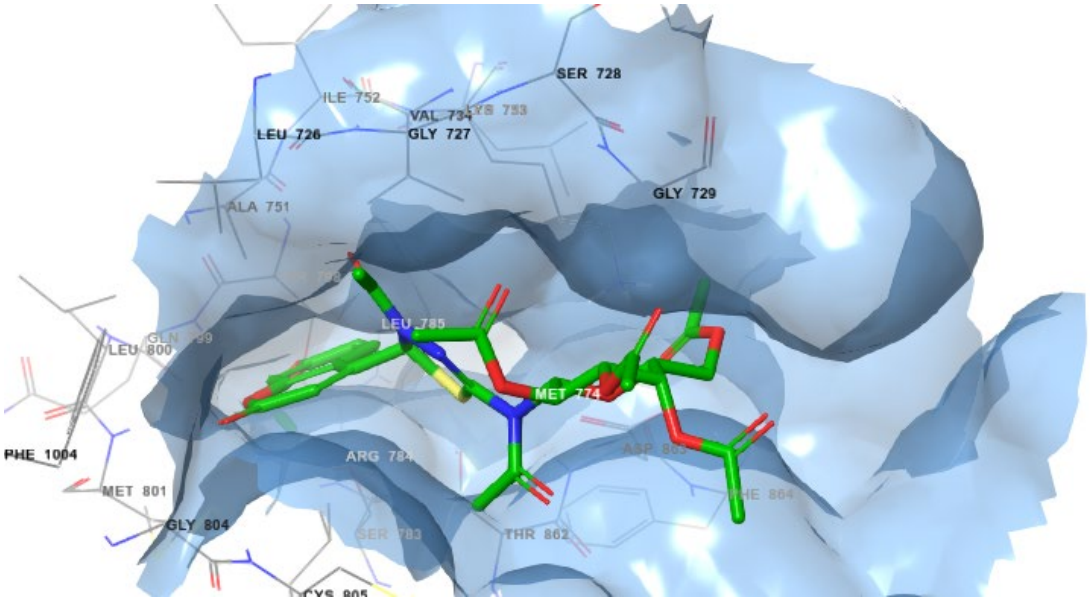

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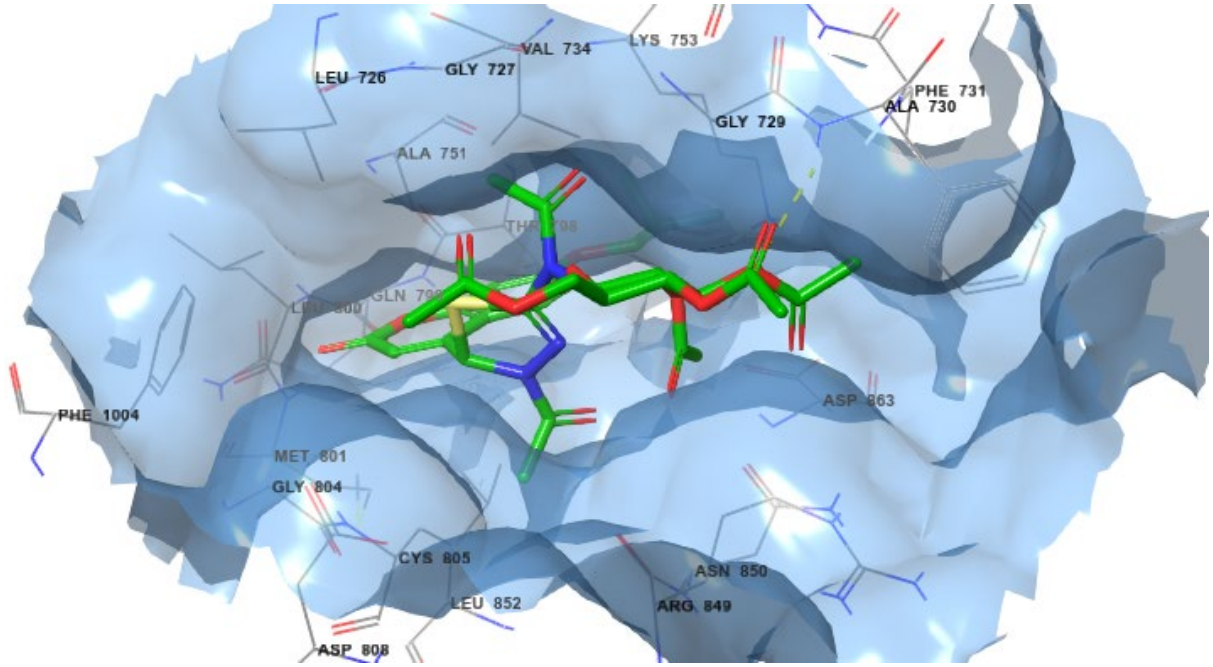

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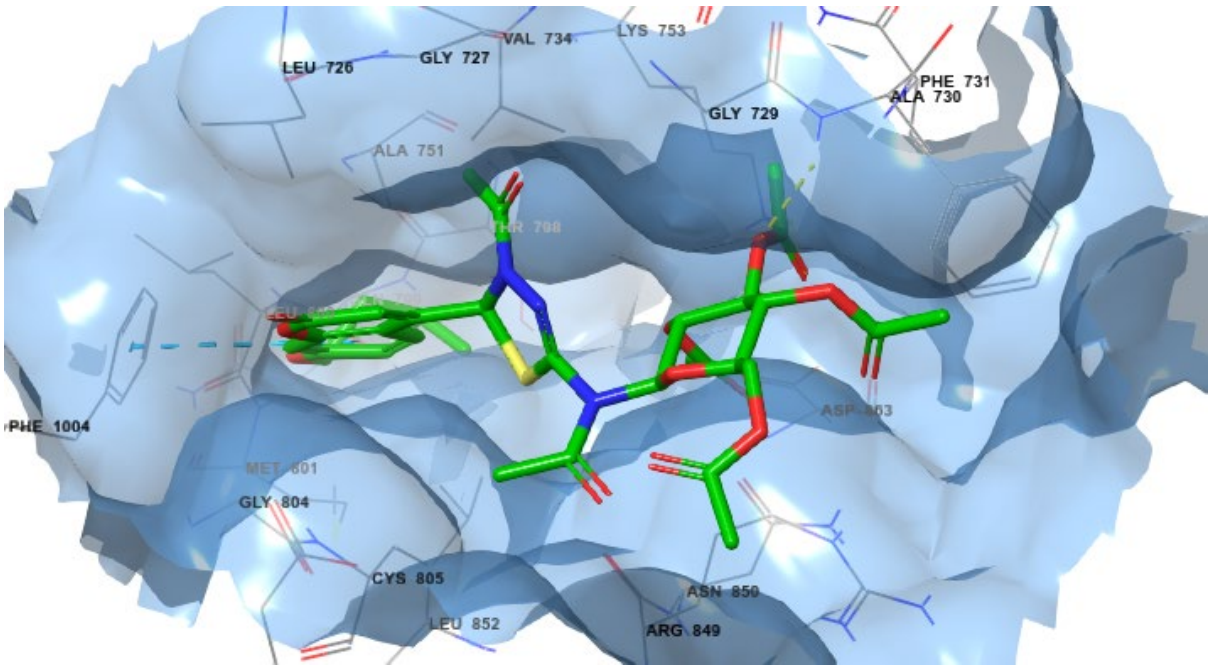
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LEU 852
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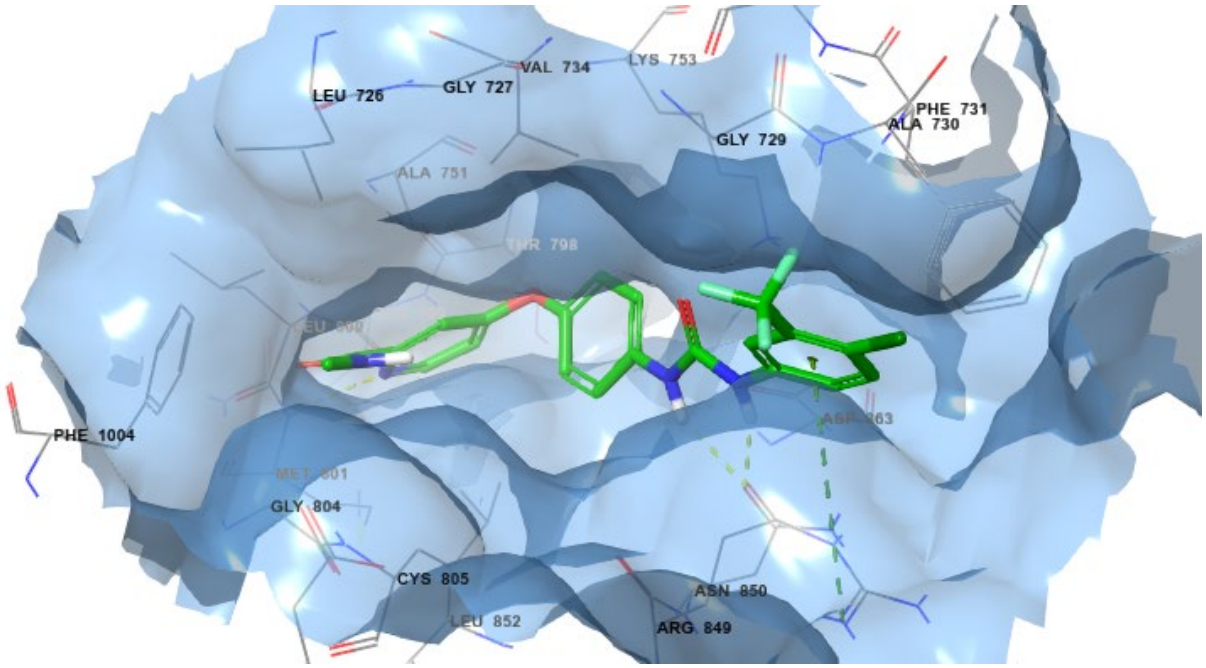
(F) Sorafenib


VAL 734
LYS 753
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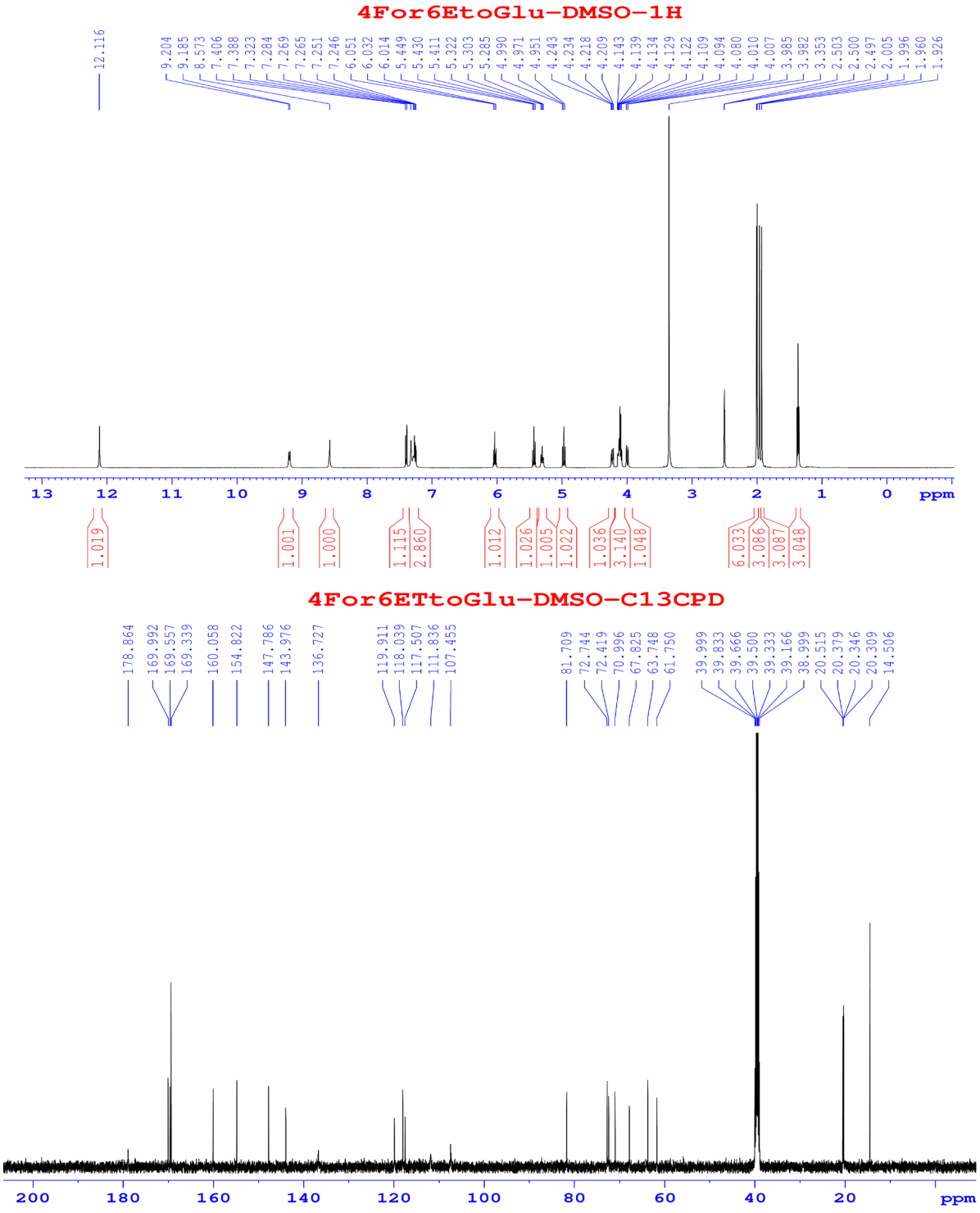
GLY 727
PHE 731
ALA 730
GLY 729
ALA 751
THR 798
PHE 1004
ASP 803
MET 801
GLY 804
CYS 805
ASN 850
LEU 852
ARG 849

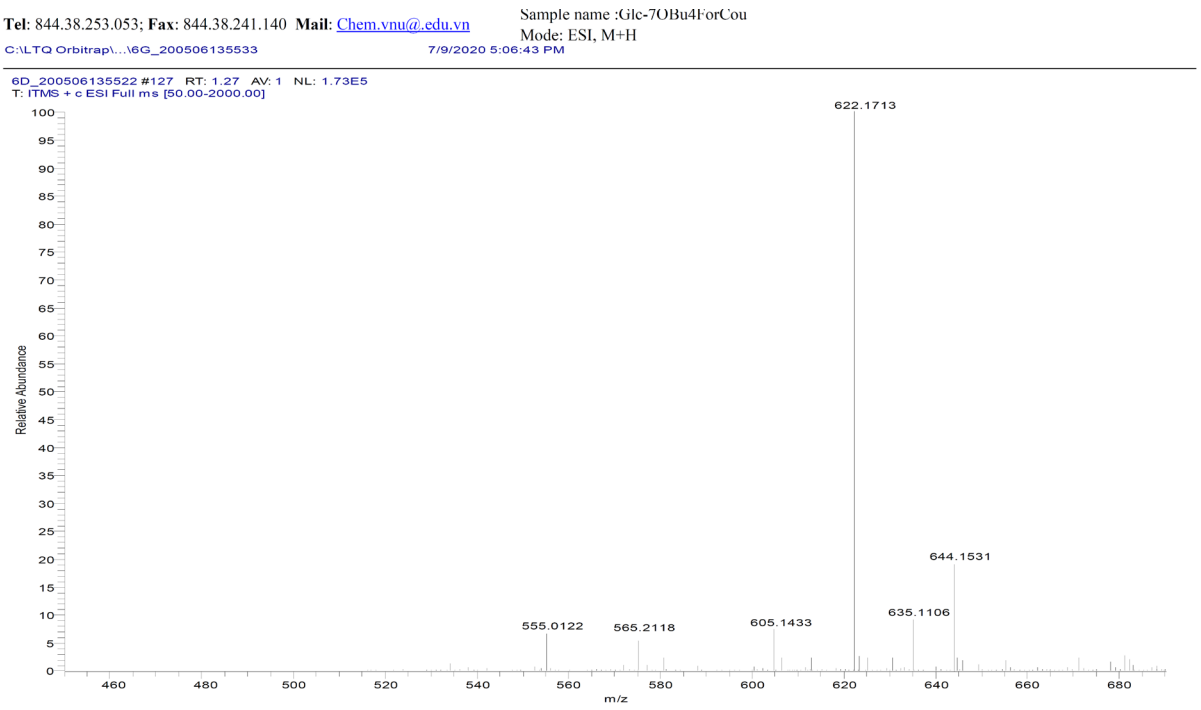
2. Spectra of synthesized compounds

2.1. Spectra of 6- and 7- alkoxy-2-oxo-2*H*-chromene-4-carbaldehyde *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucocopyranosyl)thiosemicarbazones (8a-g)

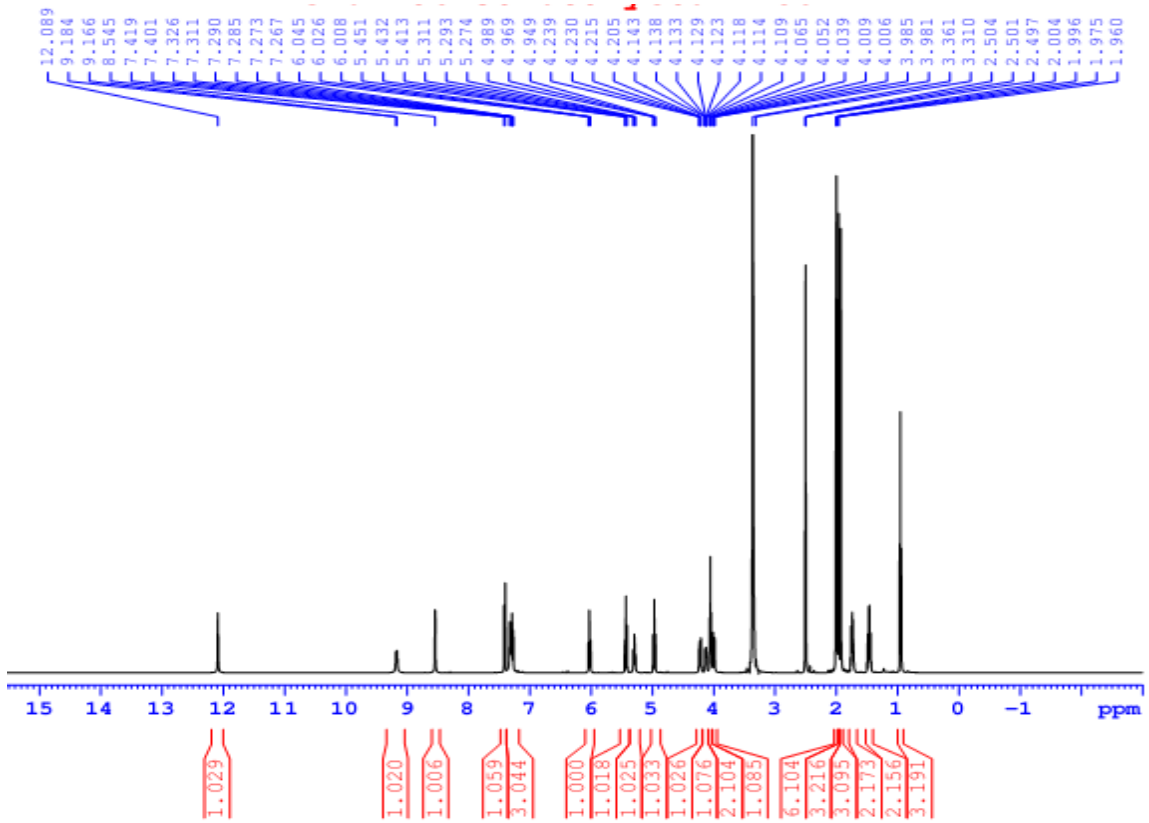
*(1) 6-Ethoxy-2-oxo-2H-chromene-4-carbaldehyde N-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)thiosemicarbazone (**8a**)*

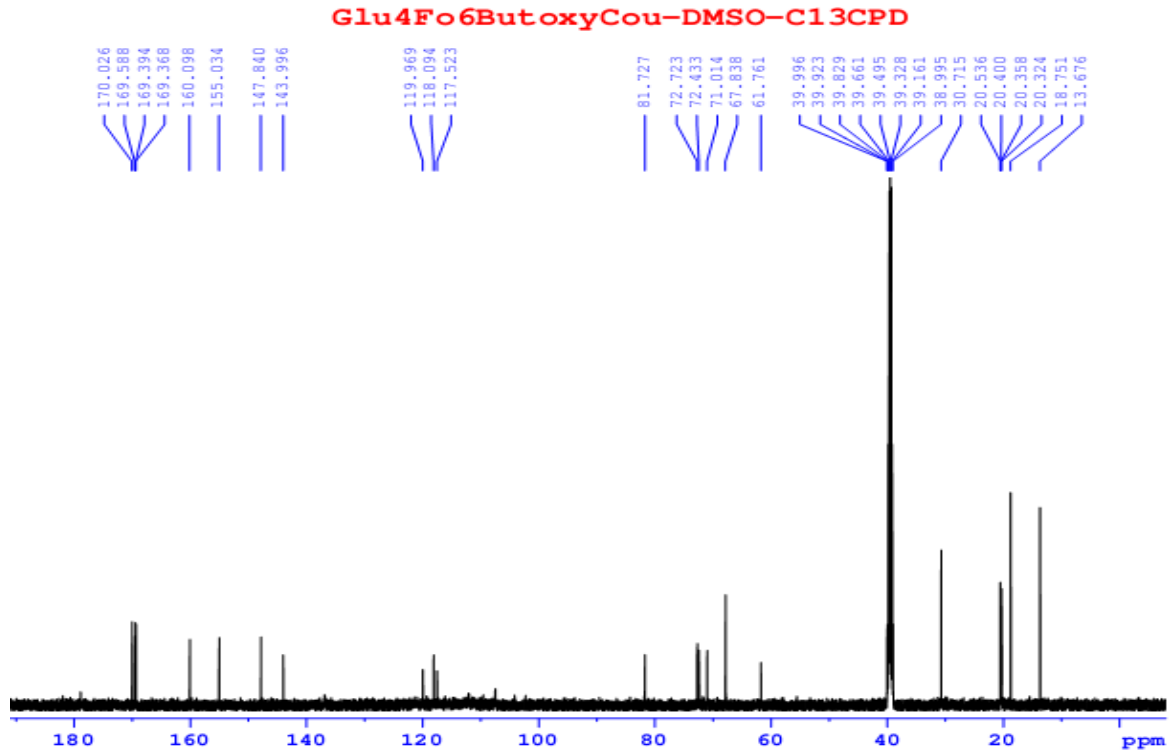


Tel: 844.38.253.053; **Fax**: 844.38.241.140 **Mail**: Chem.vnu@.edu.vn



*(2) 6-Butoxy-2-oxo-2H-chromene-4-carbaldehyde N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (**8b**)*





Tel: 844.38.253.053; **Fax**: 844.38.241.140 **Mail**: Chem.vnu@.edu.vn

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Mode: ESI, M+H

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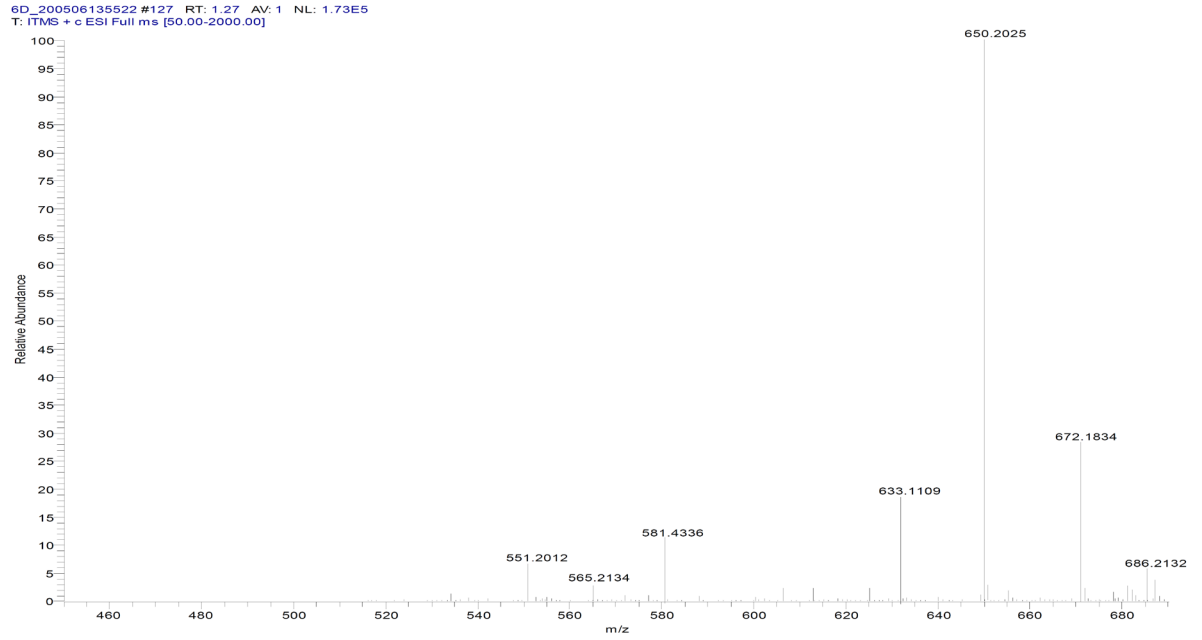
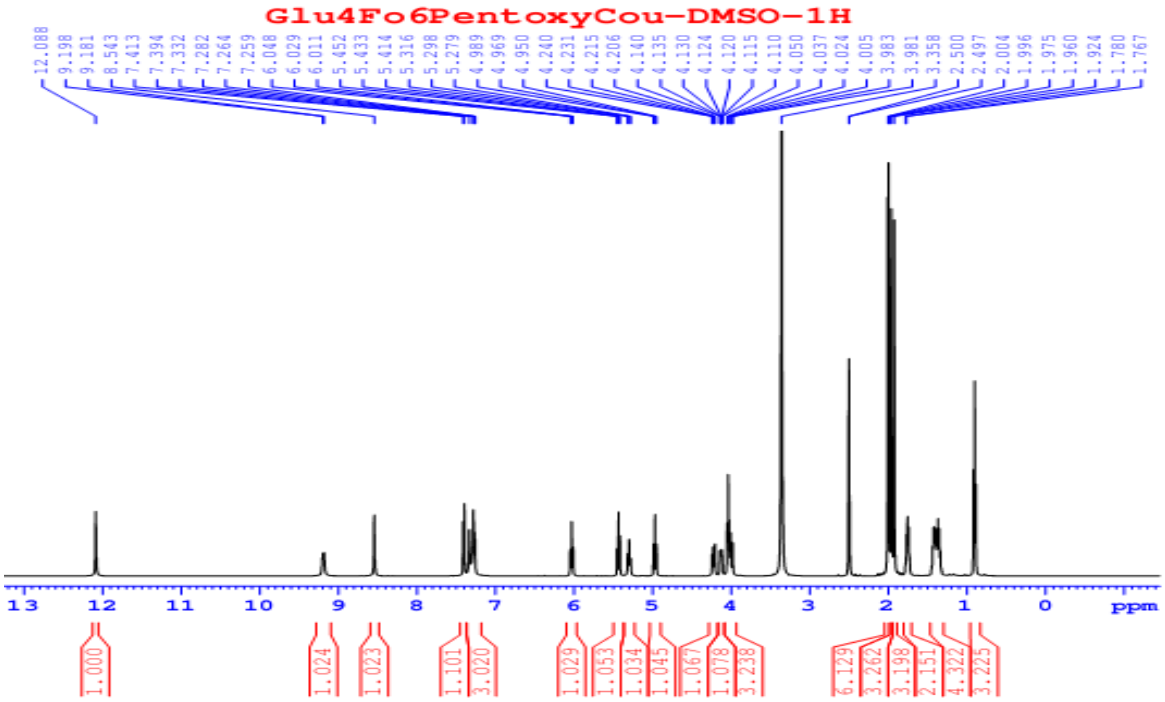
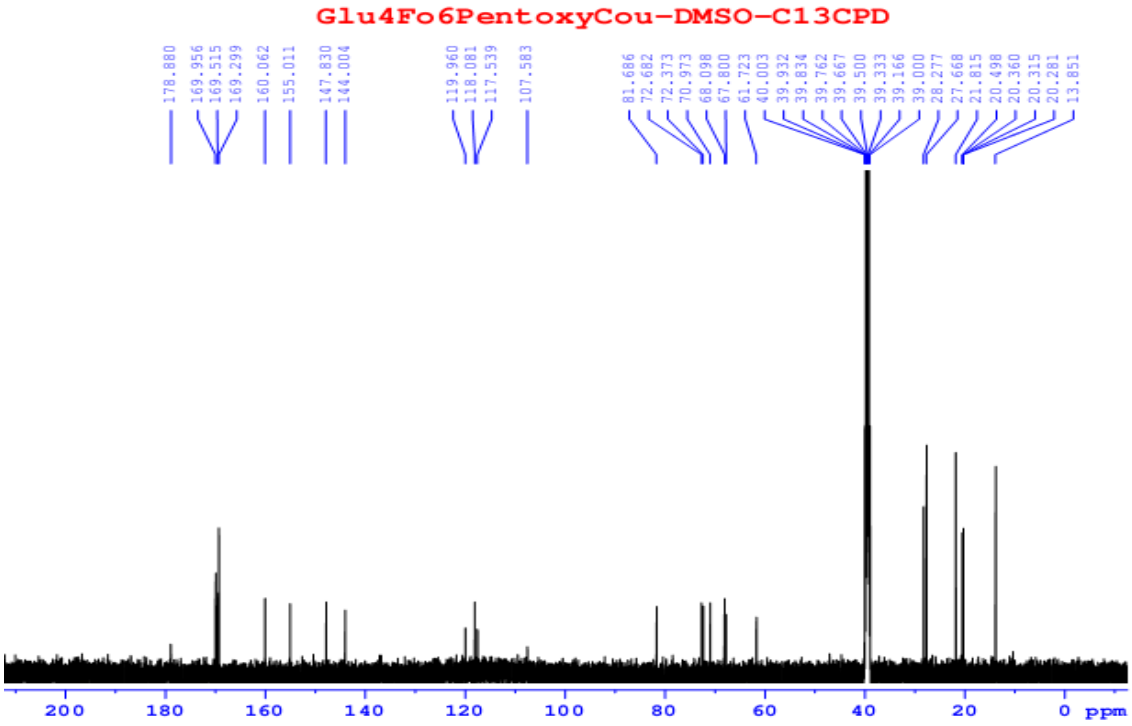


*(3) 6-Pentoxy-2-oxo-2H-chromene-4-carbaldehyde N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (**8c**)*





Tel: 844.38.253.053; **Fax**: 844.38.241.140 **Mail**: Chem.vnu@.edu.vn

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Mode: ESI, M+H

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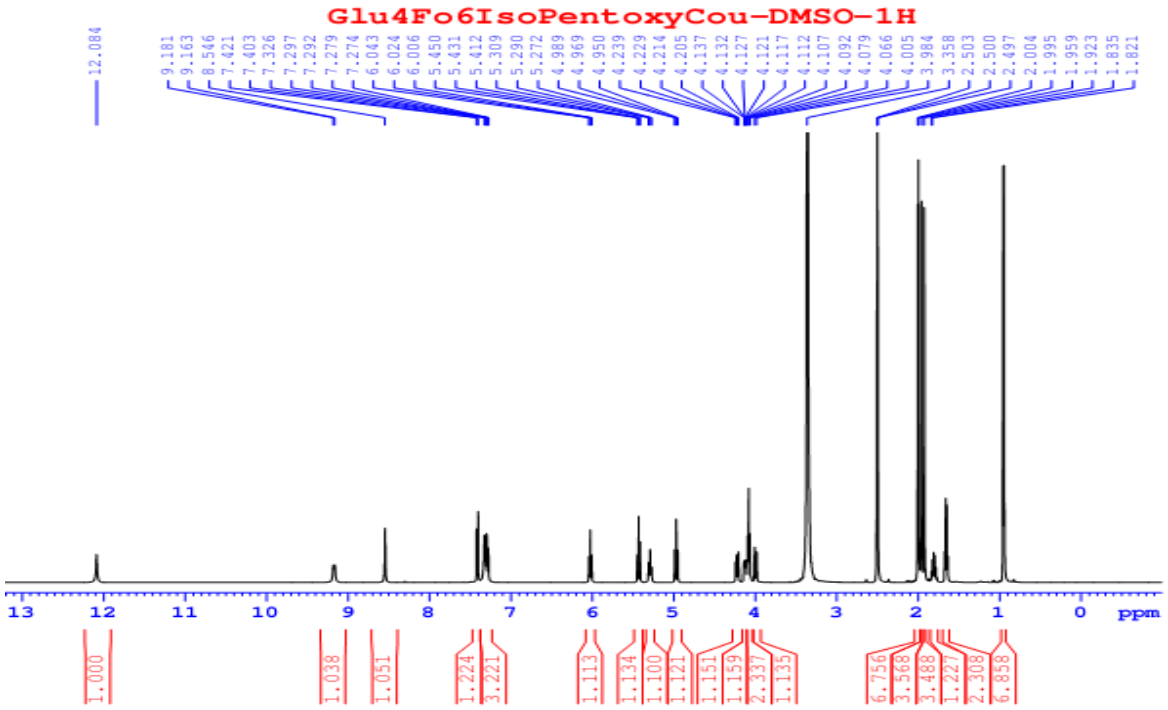
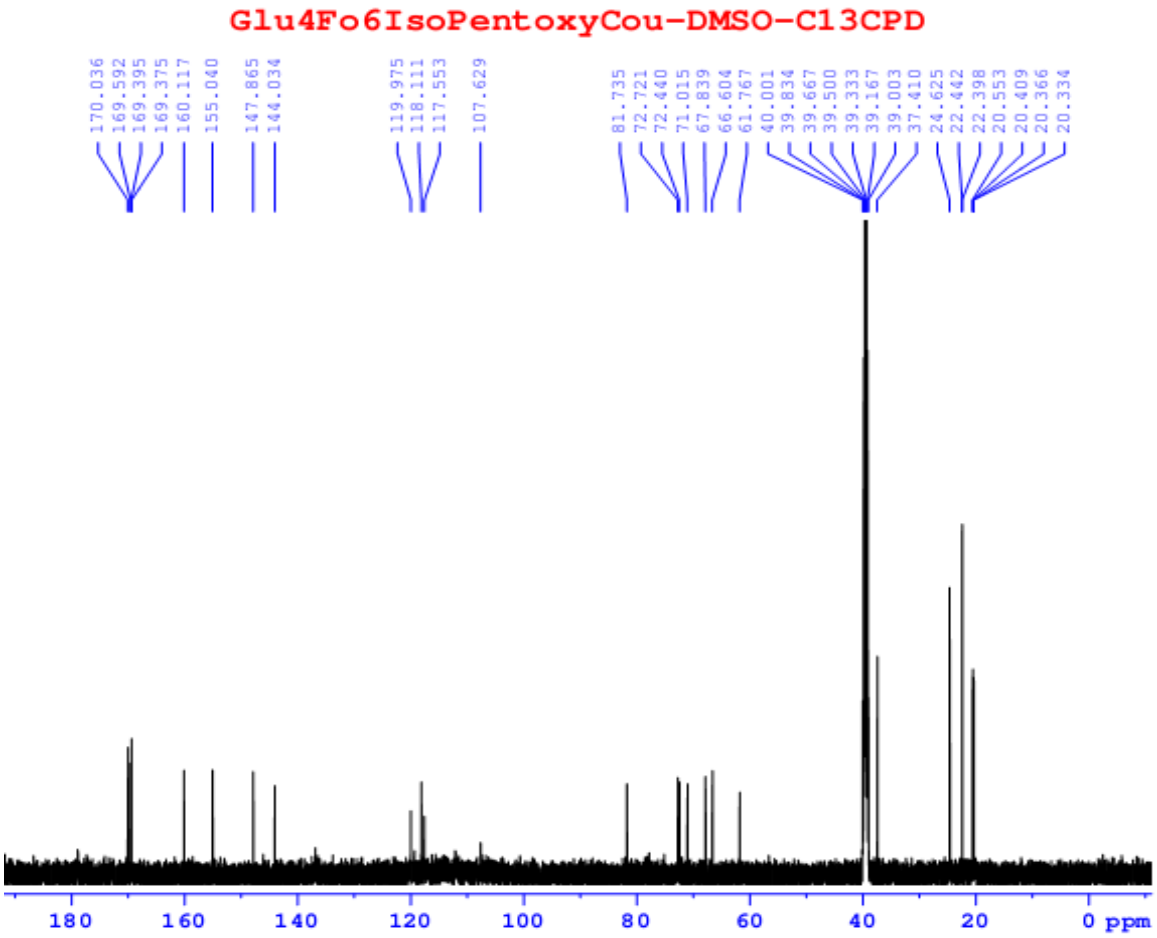
*(4) 6-Isopentoxy-2-oxo-2H-chromene-4-carbaldehyde N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (**8d**)*





Tel: 844.38.253.053; **Fax**: 844.38.241.140 **Mail**: Chem.vnu@.edu.vn

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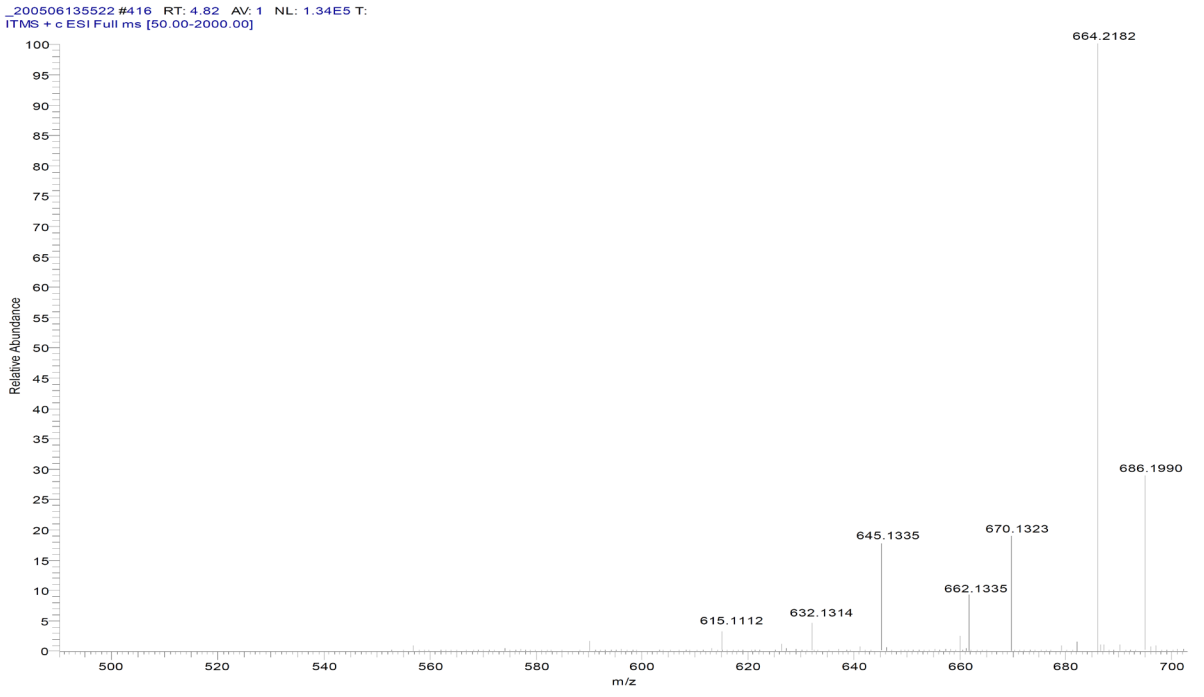
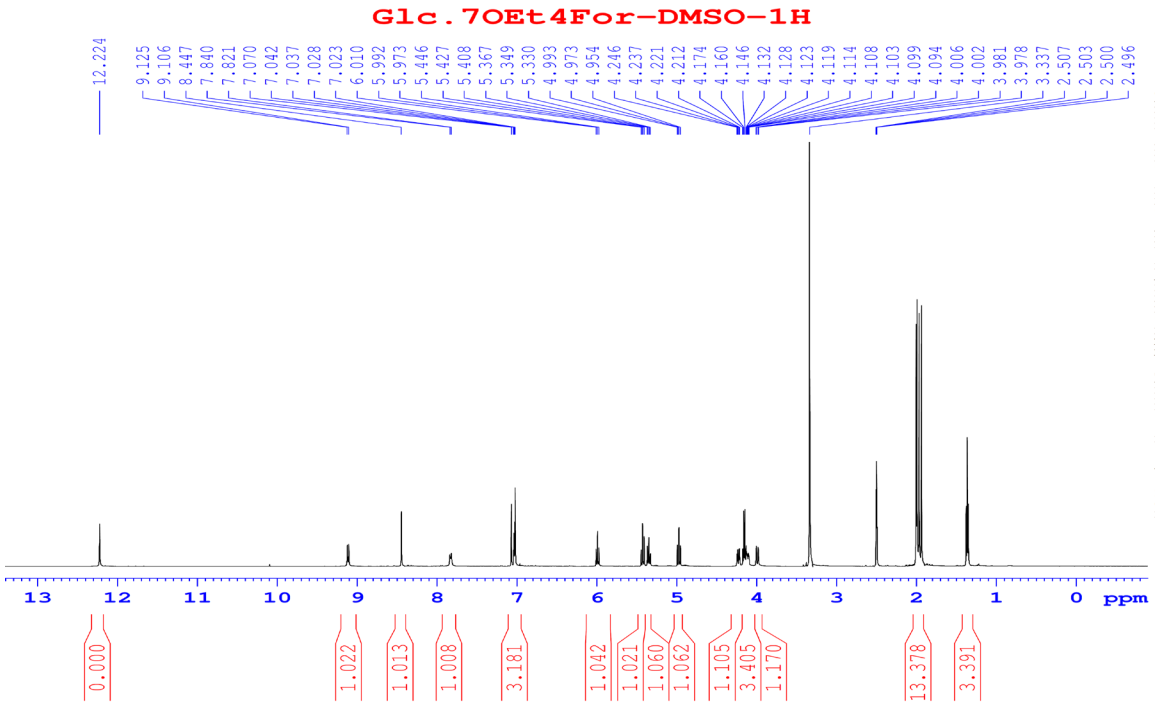
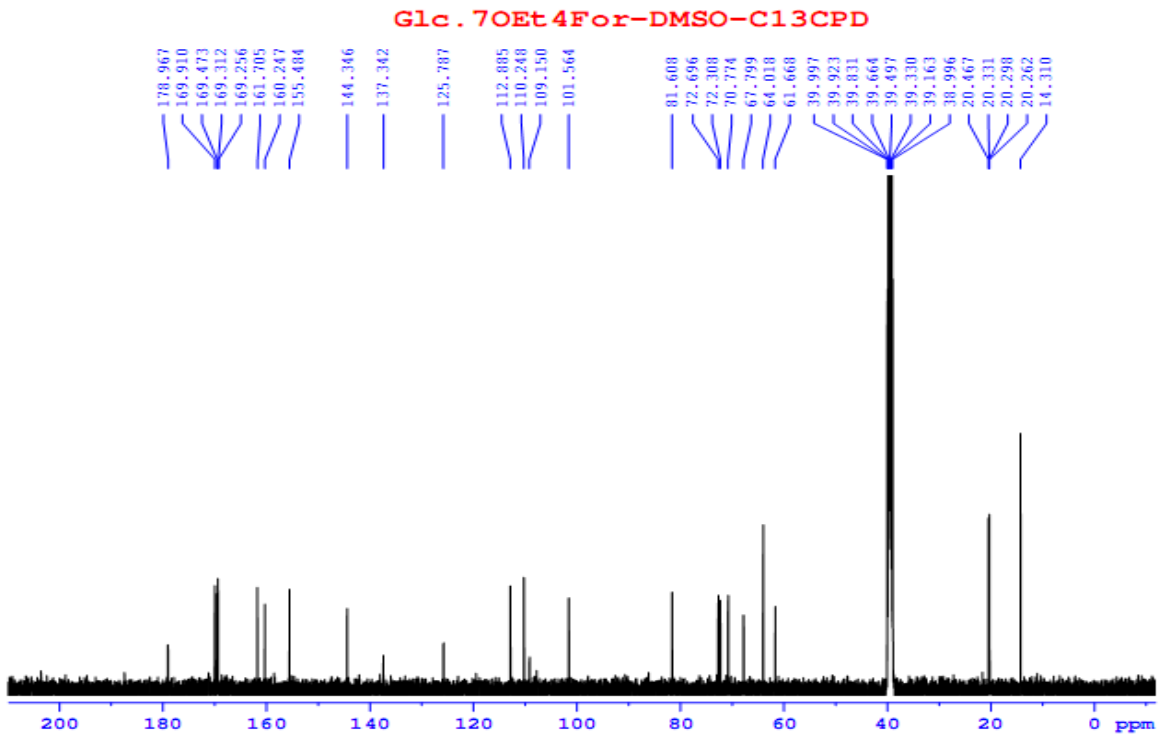
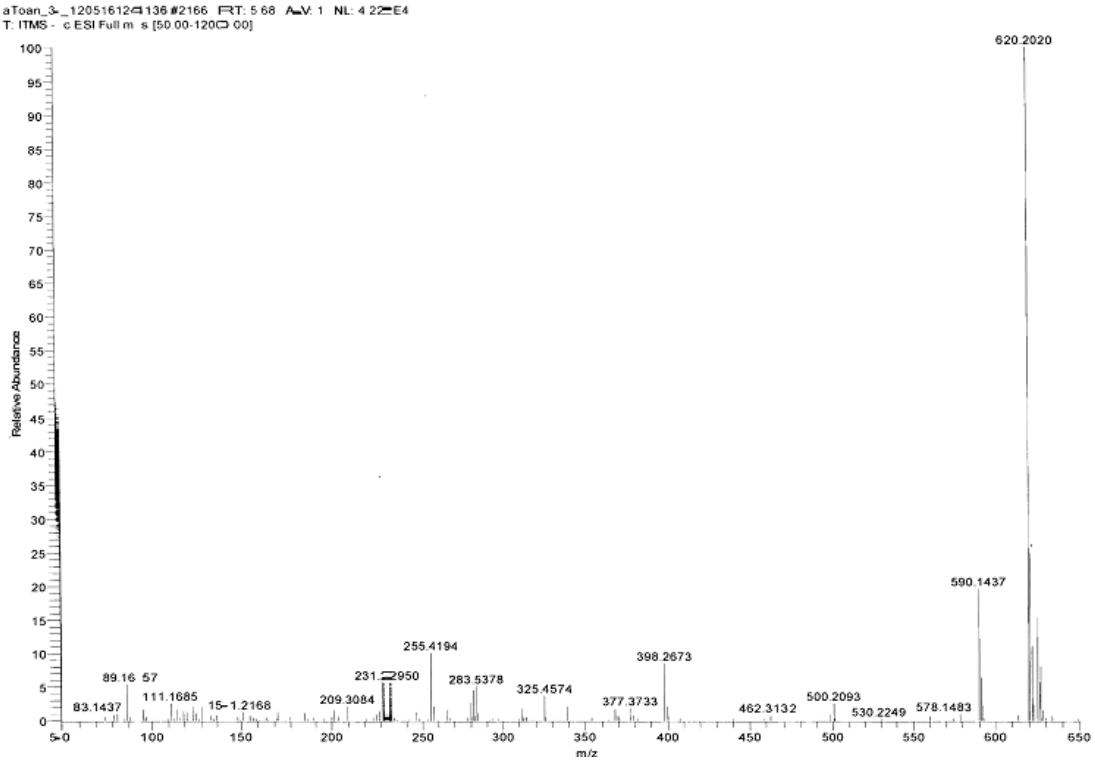


*(5) 7-Ethoxy-2-oxo-2H-chromene-4-carbaldehyde N-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)thiosemicarbazone (**8e**)*







Tel: 844.38.253.053; **Fax**: 844.38.241.140 **Mail**: Chem.vnu@.edu.vn

Sample name : 7OEt4ForCouGlc

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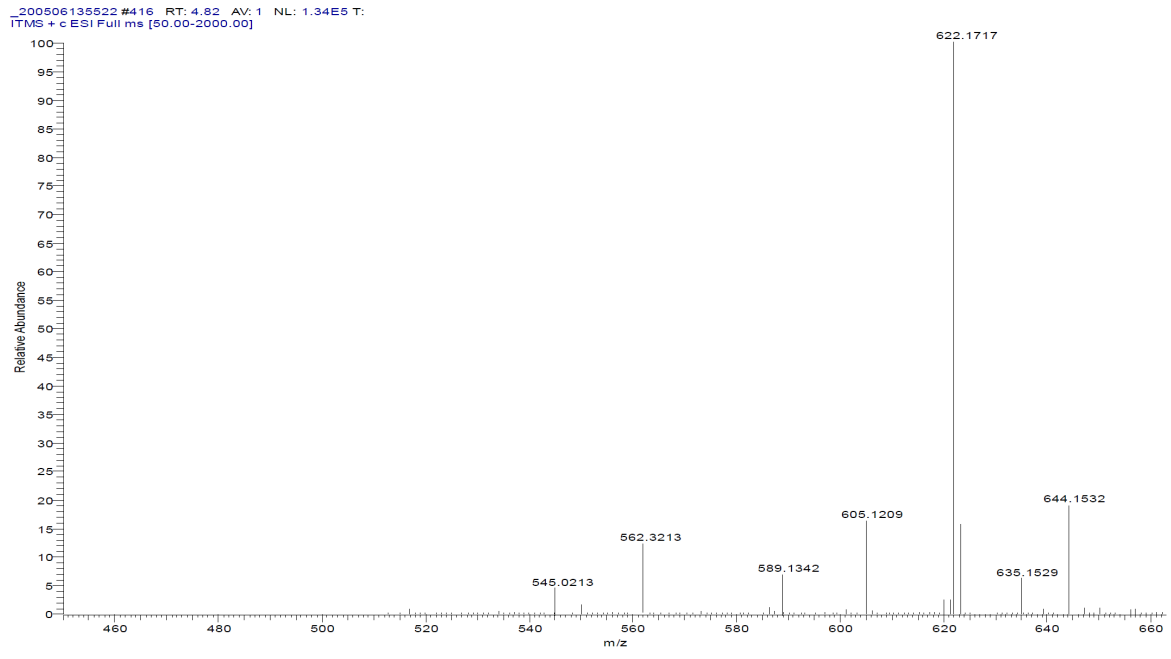
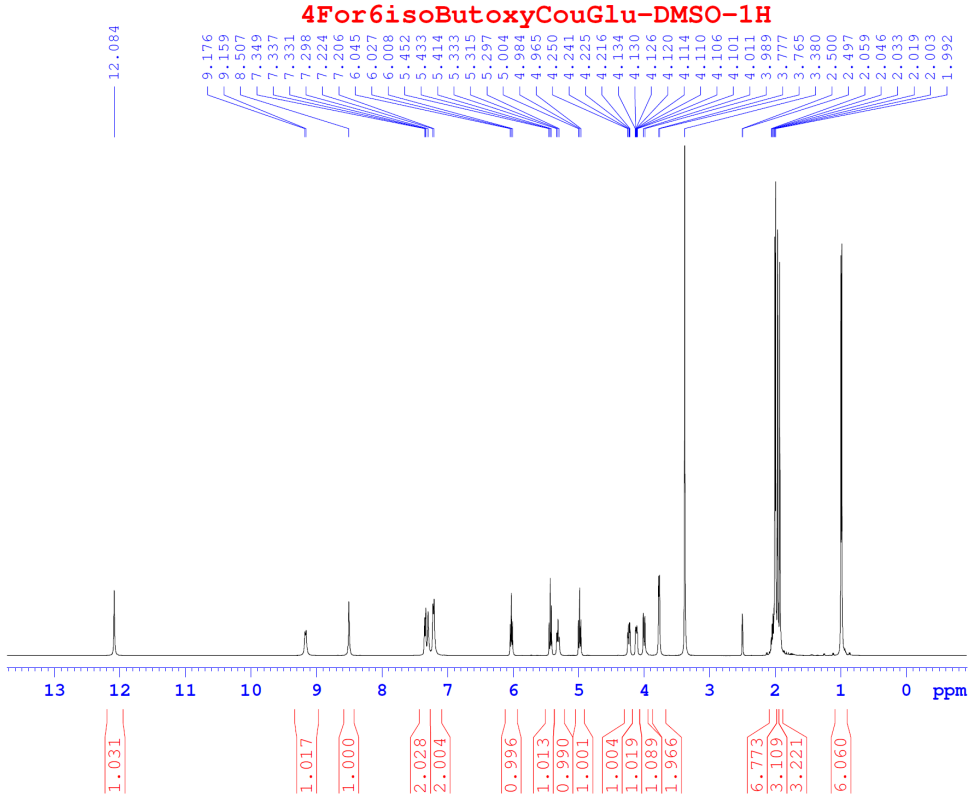
Mode: ESI, M+H



(6) 7-Isobutoxy-2-oxo-2H-chromene-4-carbaldehyde N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone ***(8f)***

4For6isoButoxyCouGlu-DMSO-1H

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PROCNO                    1

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TD               65536
SOLVENT           DMSO
NS                  16
DS                   0
SWH          10000.000 Hz
FIDRES           0.152588 Hz
AQ            3.2769001 se
RG                 10.1
DW              50.000 us
DE               6.00 us
TE                0.0 K
D1          1.00000000 se
MCREST      0.00000000 se
MCWRK       0.01500000 se

======== CHANNEL f1 ======
NUC1                 1H
P1                8.50 us
PL1               3.00 dB
SFO1        500.1335009 MH

F2 - Processing parameters
SI                32768
SF          500.1300048 MH
WDW                  EM
SSB                   0
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GB                    0
PC                1.00
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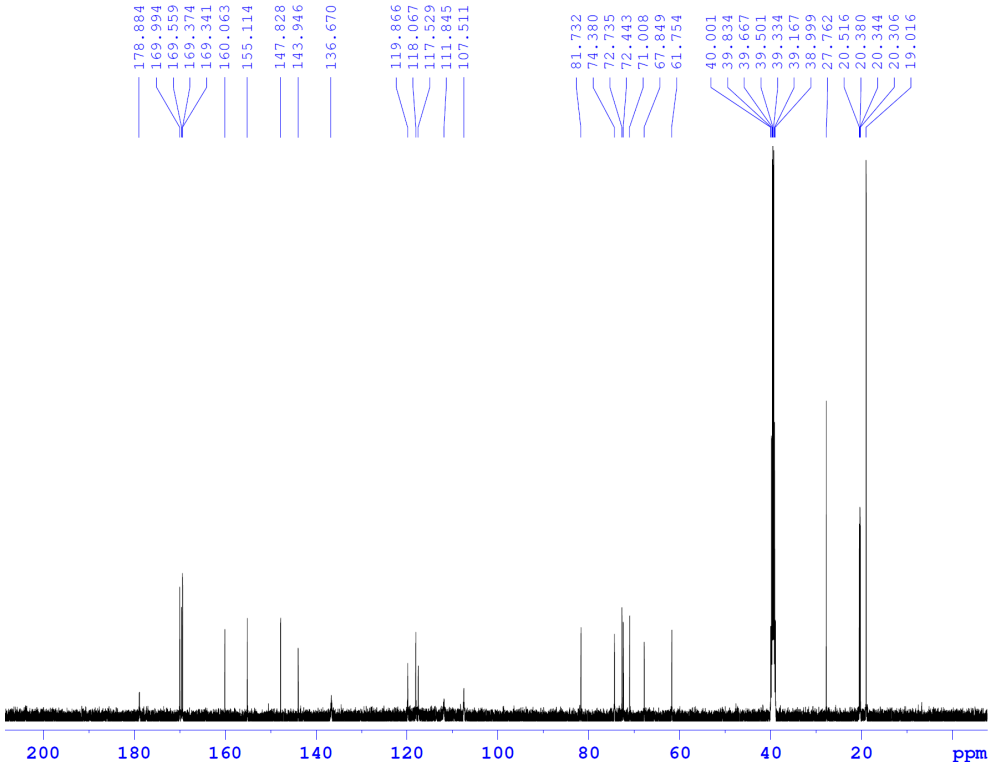
4For6isoButoxyCouGlu-DMSO-C13CPD

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PROCNO                    1

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NS                  256
DS                    2
SWH          31446.541
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AQ            1.0420883
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DE                6.00
TE                 0.0
D1          2.00000000
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DELTA       1.89999998
MCREST      0.00000000
MCWRK       0.01500000

======== CHANNEL f1 ====
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P1               11.50
PL1              -3.00
SFO1        125.7716224

======== CHANNEL f2 ====
CPDPRG2          waltz16
NUC2                1H
PCPD2            80.00
PL2               3.00
PL12             22.47
PL13             22.00
SFO2        500.1320005

F2 - Processing paramete
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SF          125.7578456
WDW                 EM
SSB                  0
LB                0.60
GB                   0
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Tel: 844.38.253.053; **Fax**: 844.38.241.140 **Mail**: Chem.vnu@.edu.vn

Sample name : /6OBu4ForCouGlc
Mode: ESI, M+H

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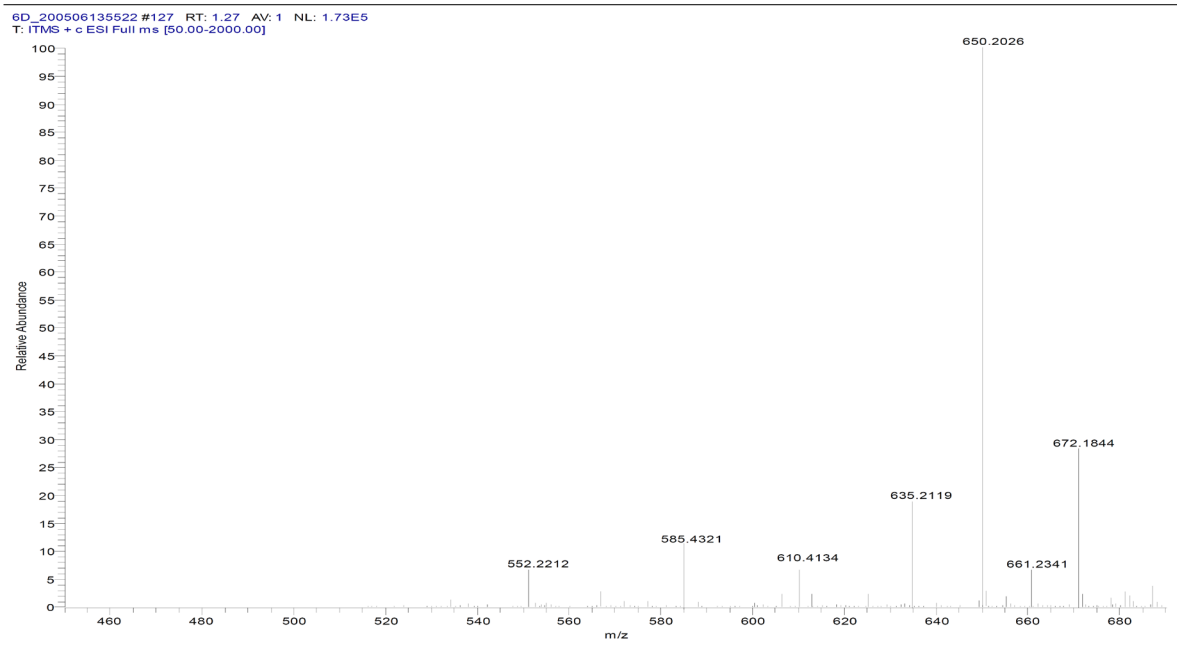
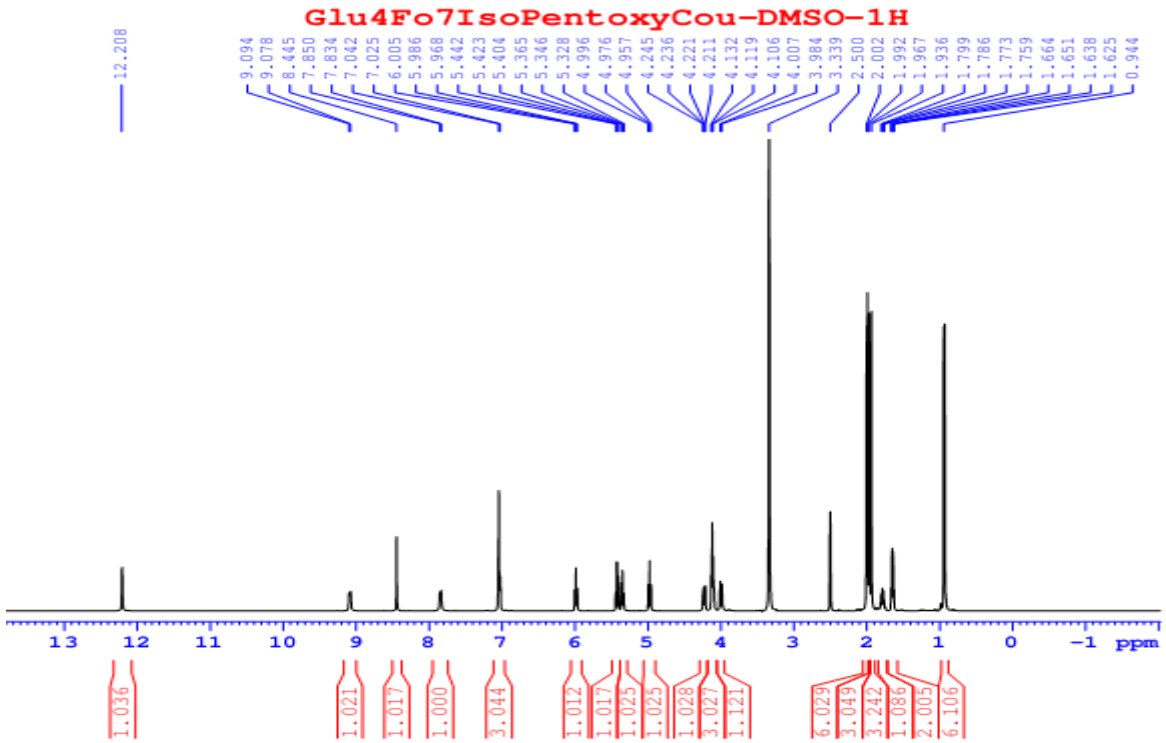
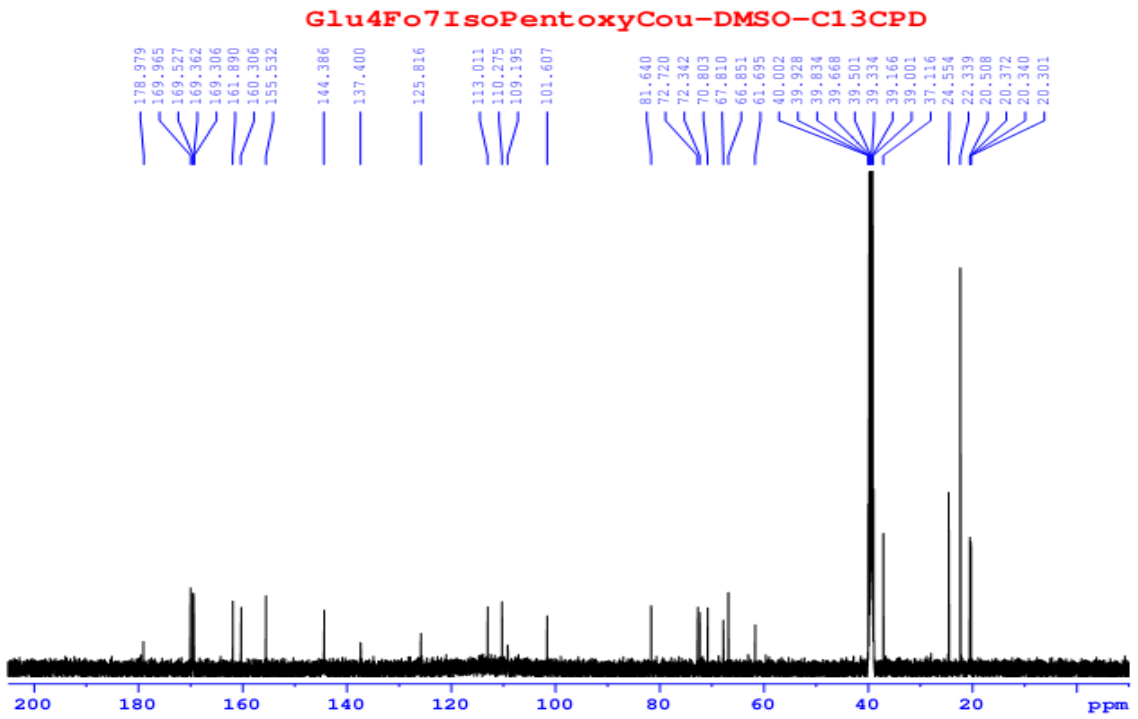


*(7) 7-Isopentoxy-2-oxo-2H-chromene-4-carbaldehyde N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemicarbazone (**8g**)*





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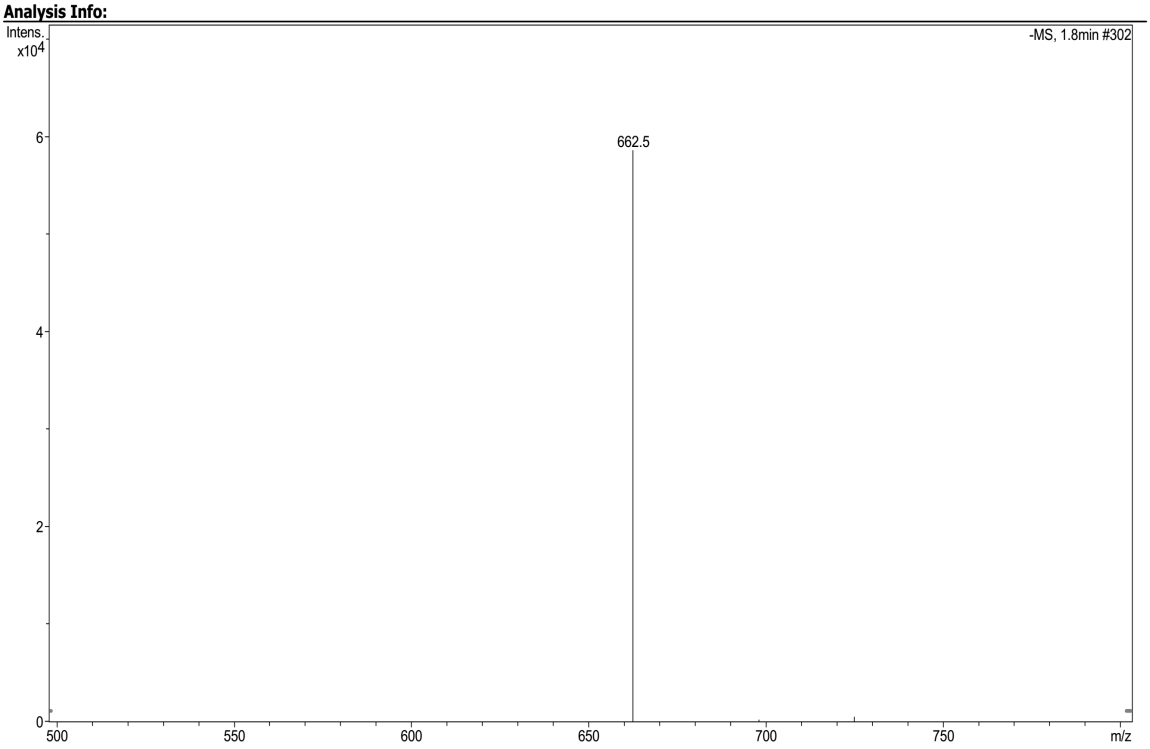

Tel: 844.38.253.053; **Fax**: 844.38.241.140 **Mail**: Chem.vnu@.edu.vn

Sample name : 6b-Glc6OPn4For6Et

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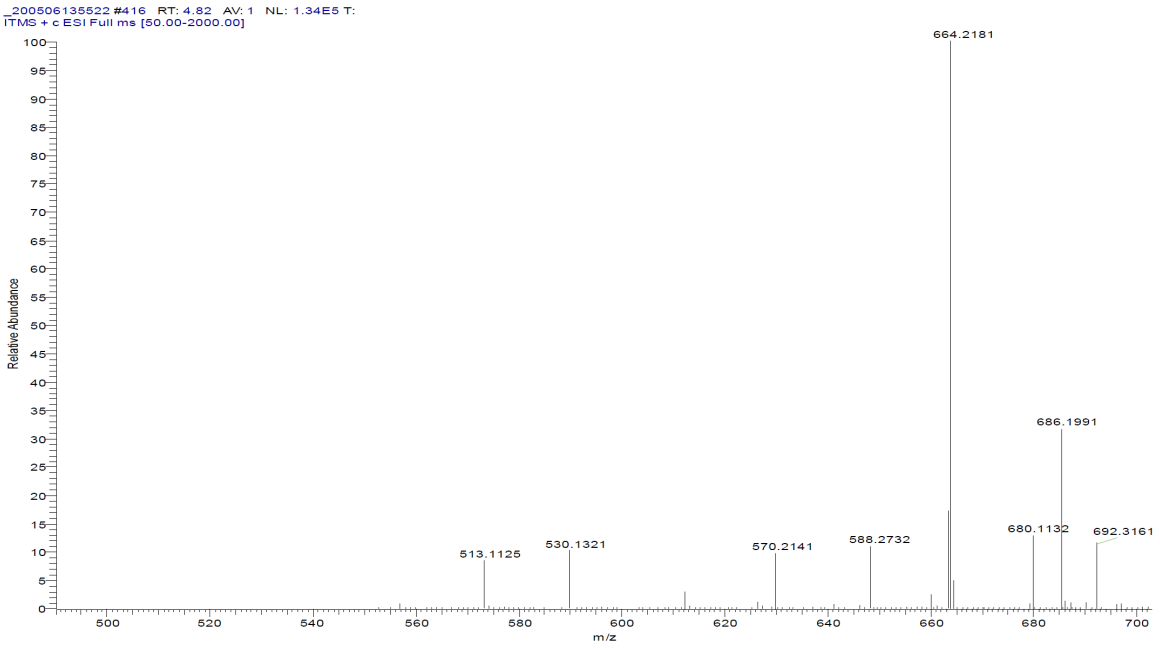
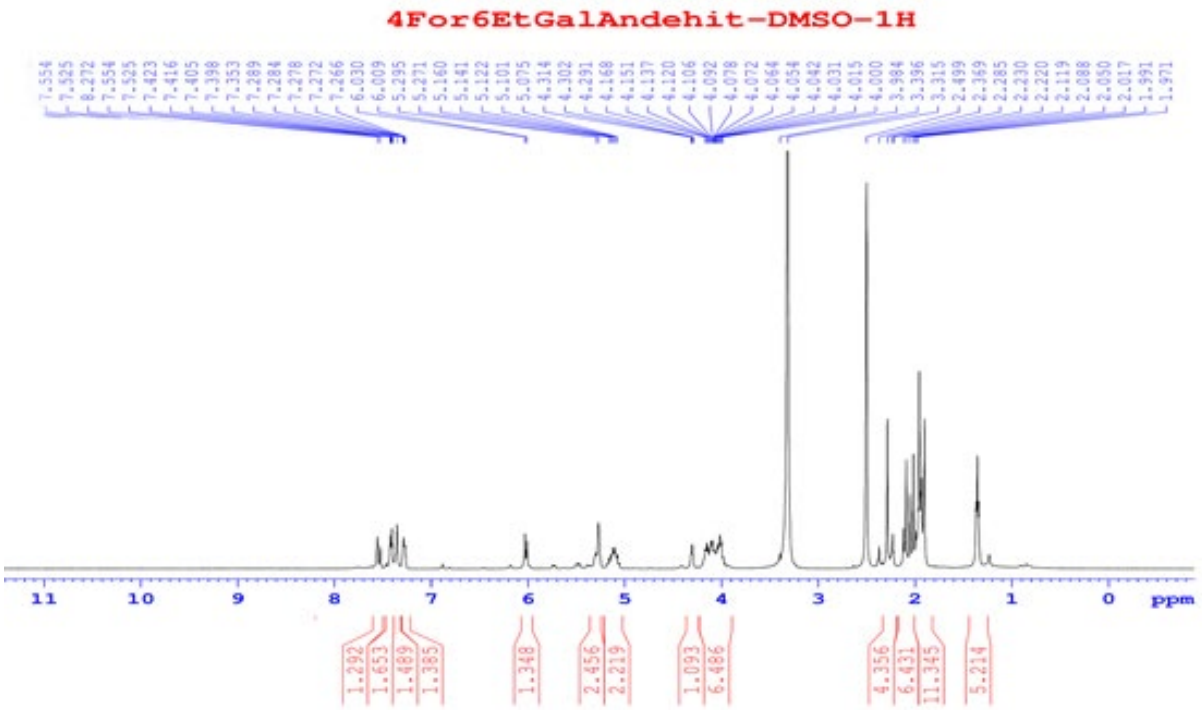
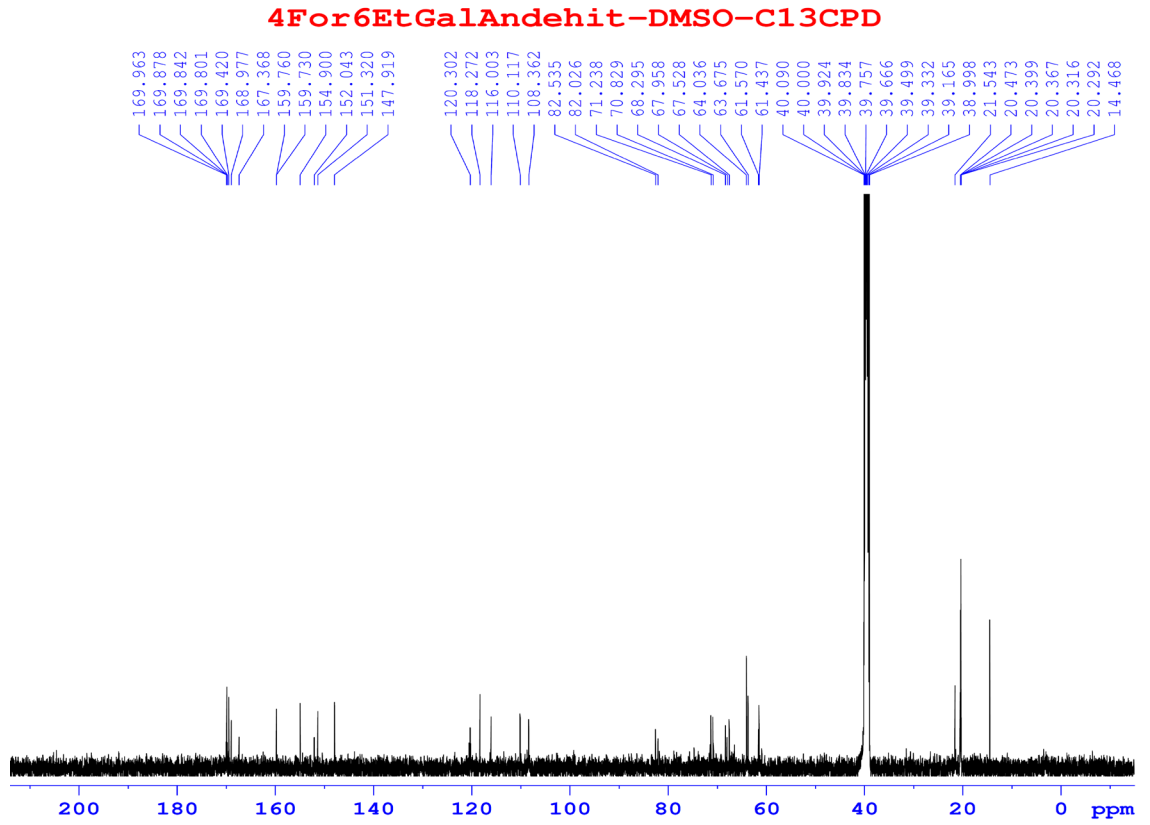


2.2. Spectra of synthesized 1,3,4-thiadiazoline−coumarin hybrid compounds (9a-g)

*(1) 4-(3'-Acetyl-5'-(N-(2'',3'',4'',6''-tetra-O-acetyl-β-D-galactopyranosyl)acetamido-2'-methyl-2',3'-dihydro-1',3',4'-thiadiazol-2'-yl)-6-ethoxycoumarin (**9a**)*





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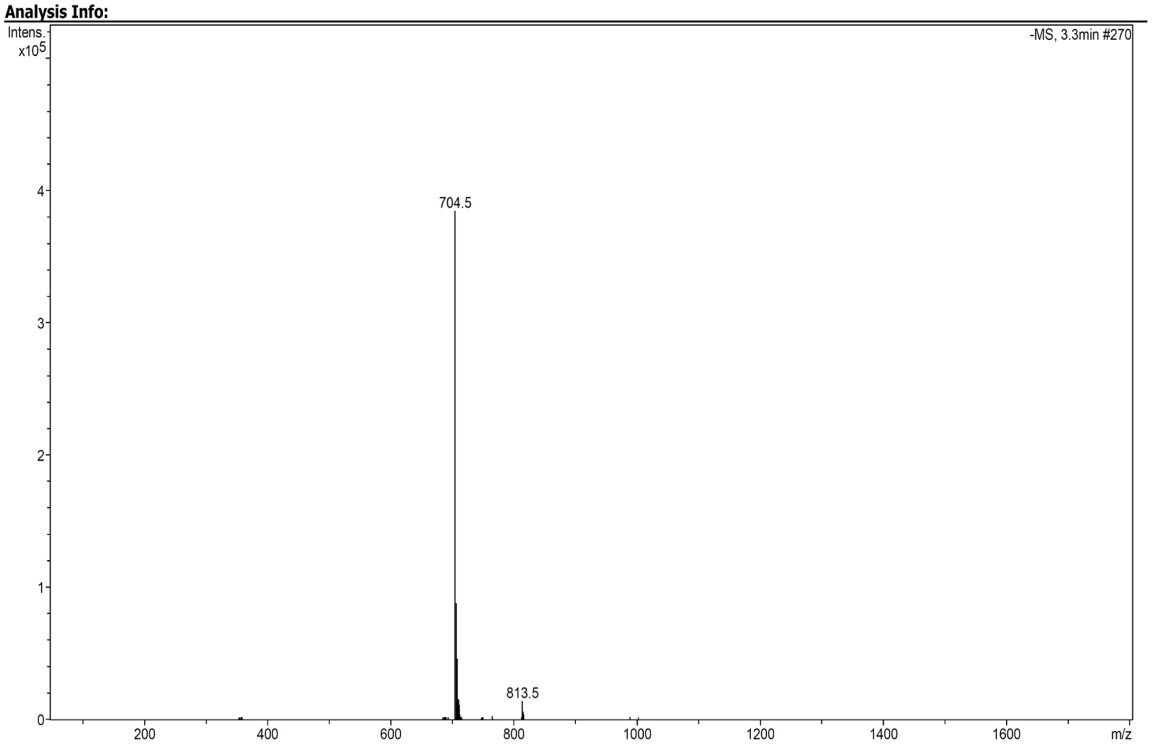
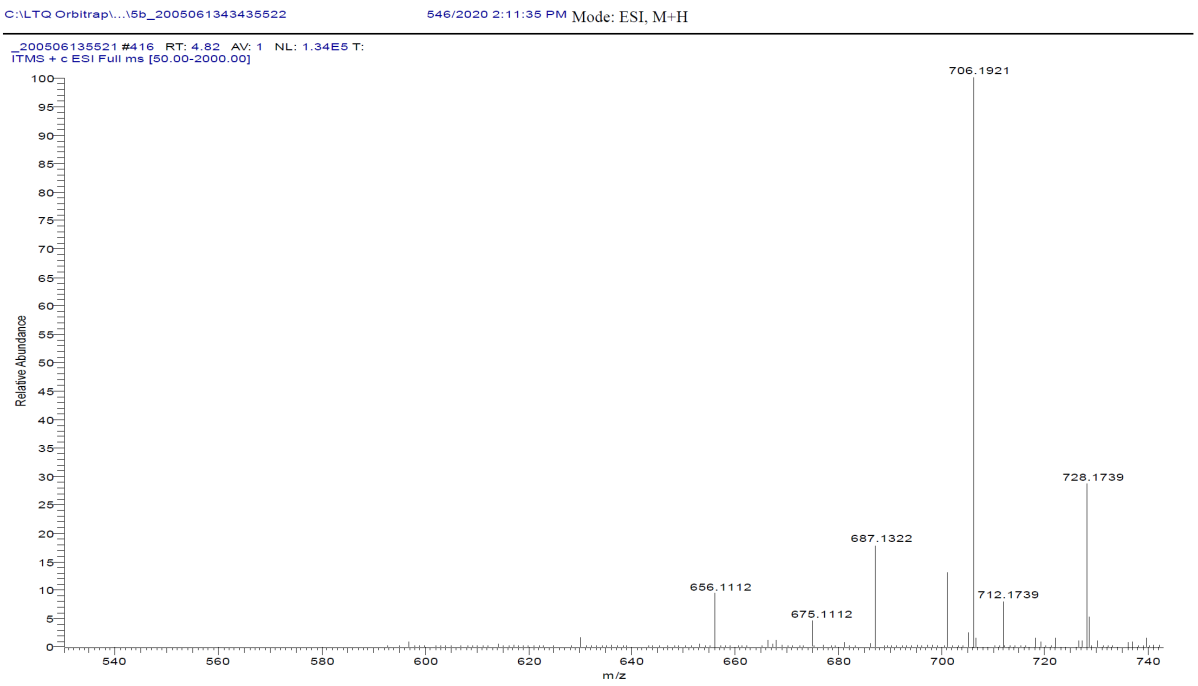
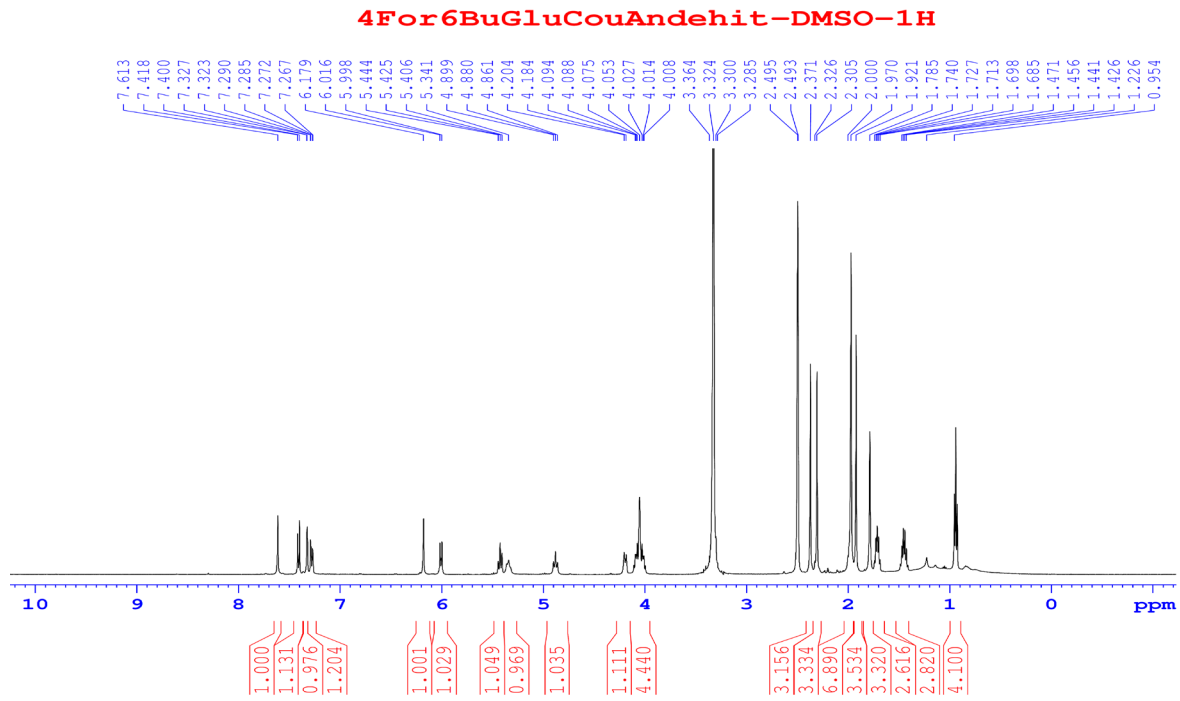
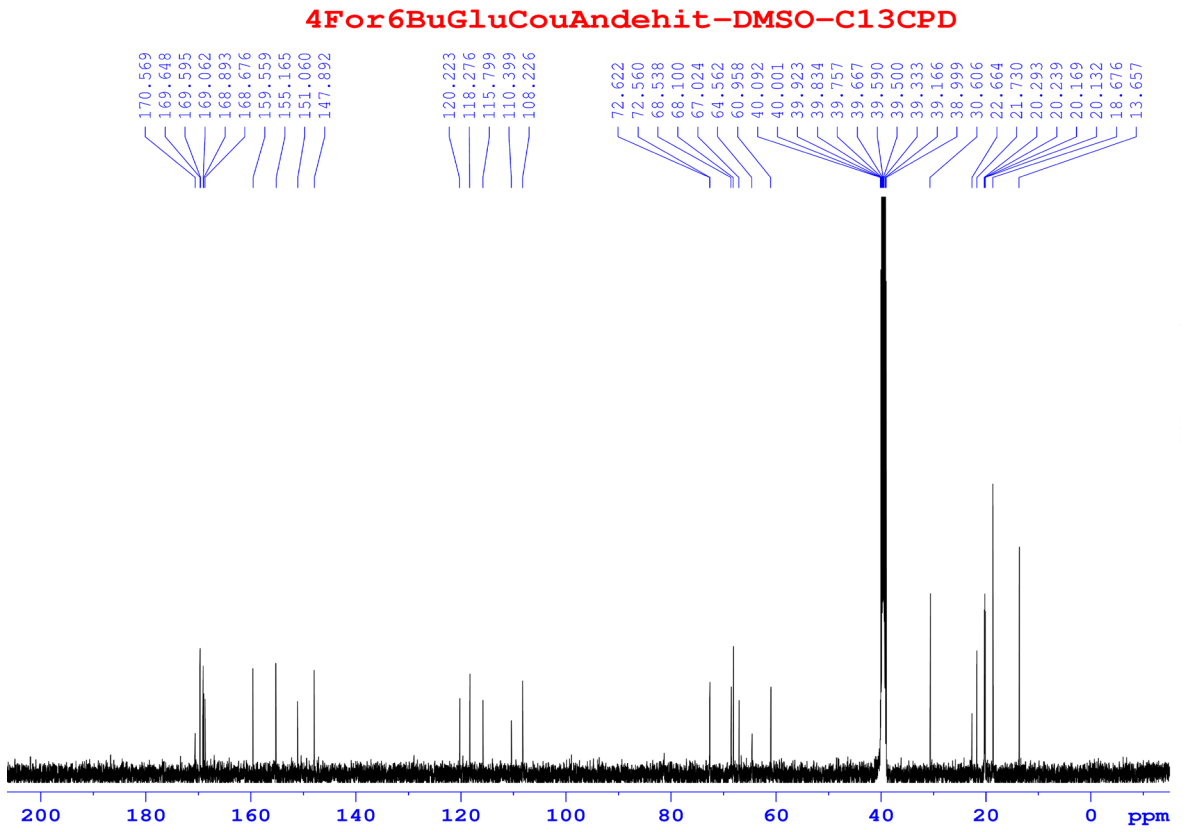




*(2) 4-(3'-Acetyl-5'-(N-(2'',3'',4'',6''-tetra-O-acetyl-β-D-glucopyranosyl)acetamido-2'-methyl-2',3'-dihydro-1',3',4'-thiadiazol-2'-yl)-6-butoxycoumarin (**9b**)*





Lab: Materials chemistry, Faculty of Chemistry, HUS-VNU
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Operator: Ms. Dao Thi Nhung
Mobile: 0948 119 043; Email: daothinhungtn@yahoo.com

Mass Spectrometter
LTQ Orbitrap XL™

Sample name : Glc6OPr4MeCouThiadiaz

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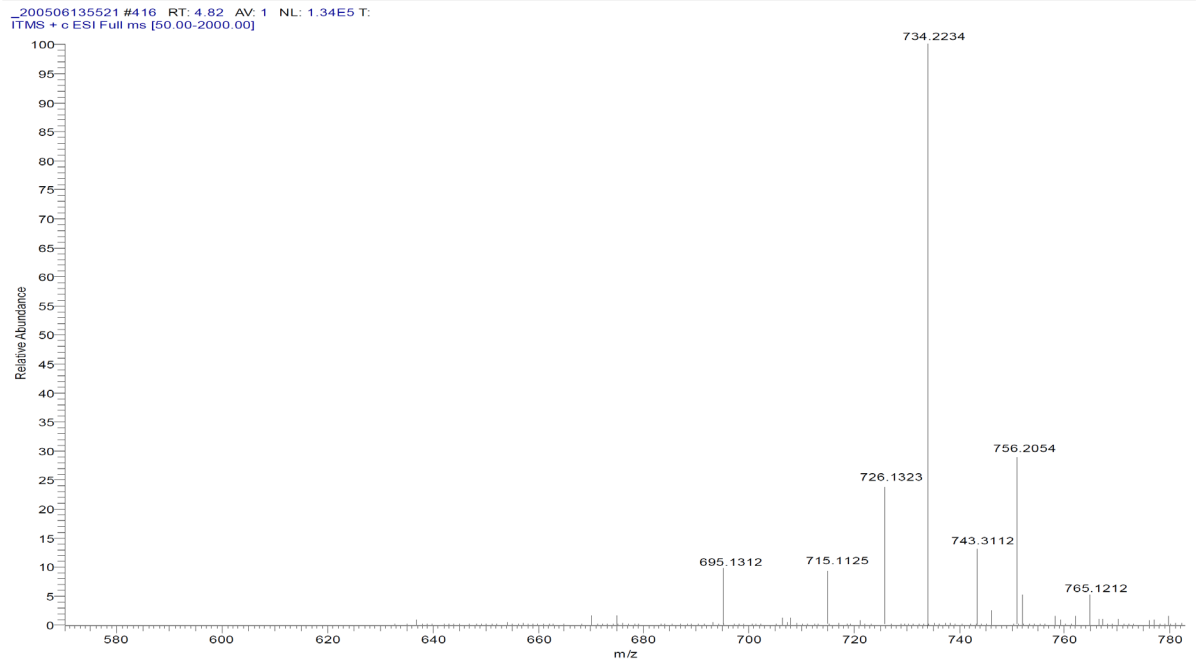
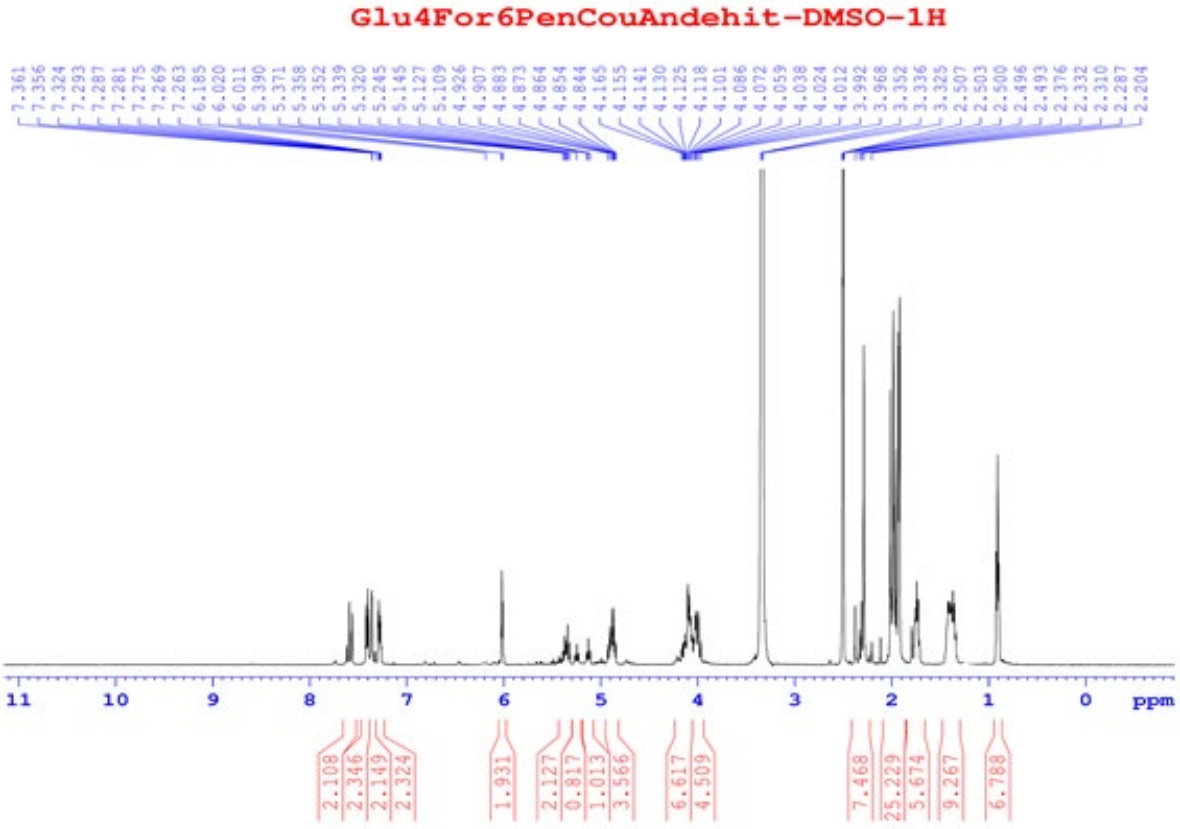
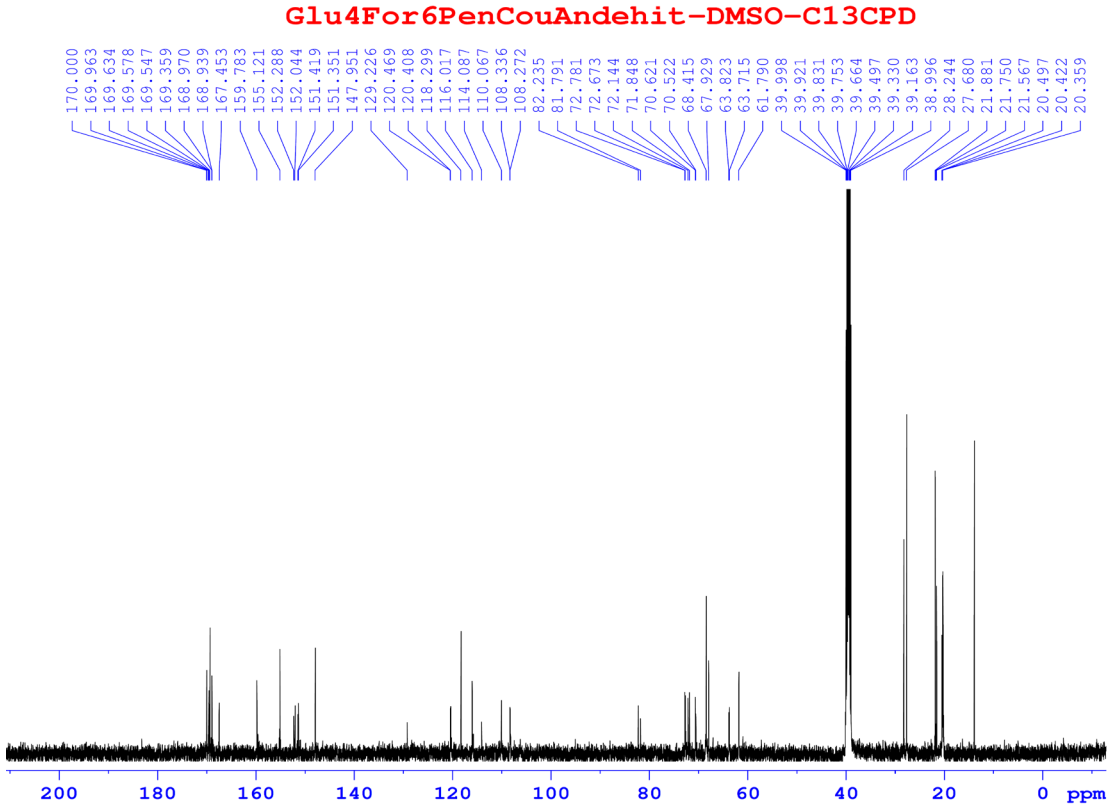


*(3) 4-(3'-Acetyl-5'-(N-(2'',3'',4'',6''-tetra-O-acetyl-β-D-glucopyranosyl)acetamido-2'-methyl-2',3'-dihydro-1',3',4'-thiadiazol-2'-yl)-6-pentoxycoumarin (**9c**)*





Lab: Materials chemistry, Faculty of Chemistry, HUS-VNU
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Operator: Ms. Dao Thi Nhung
Mobile: 0948 119 043; Email: daothinhungtn@yahoo.com

Mass Spectrometer
LTQ Orbitrap XL™

Sample name : Glc6OPn4MForCouThiadiaz

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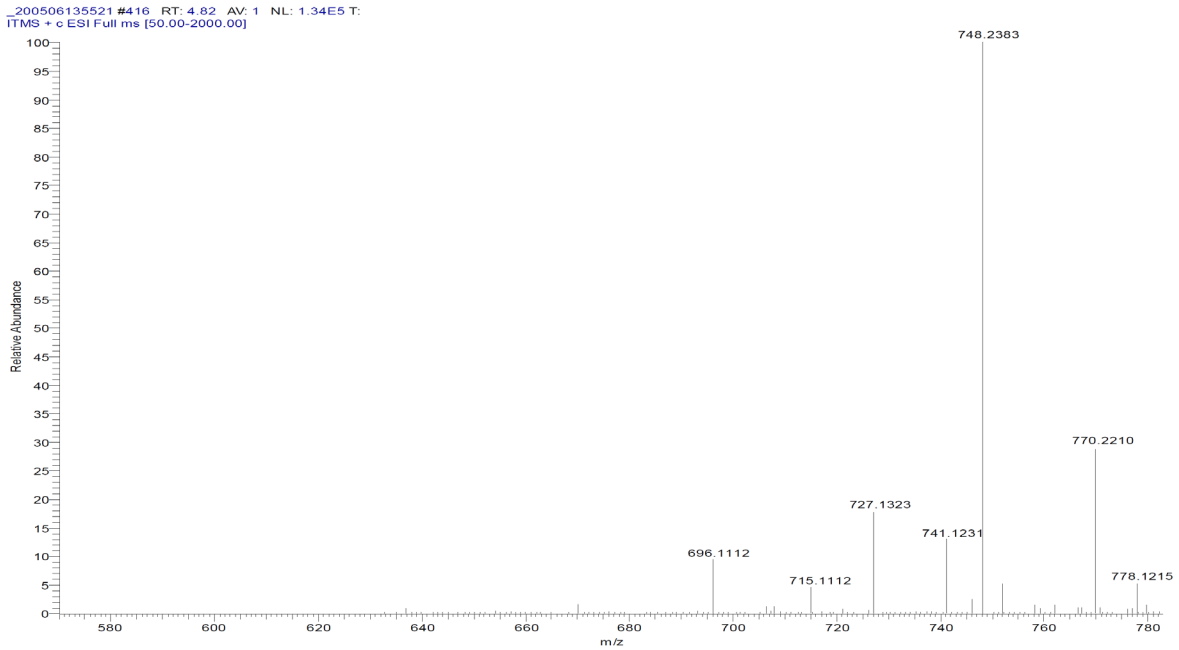
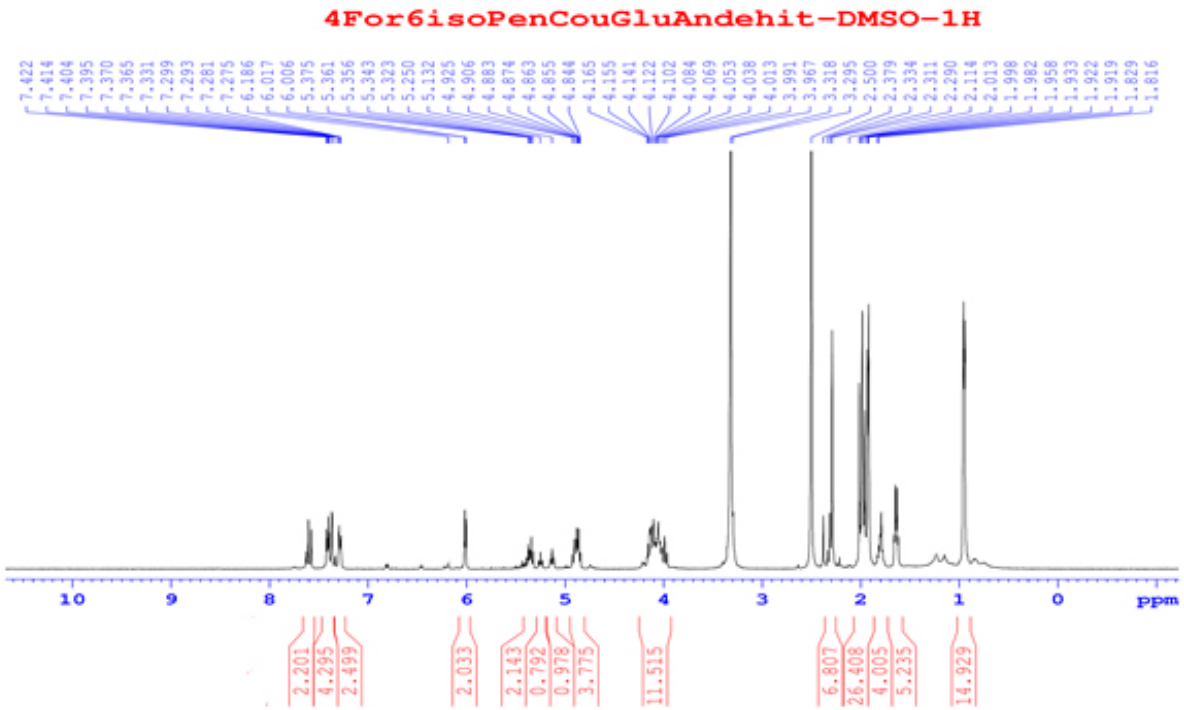
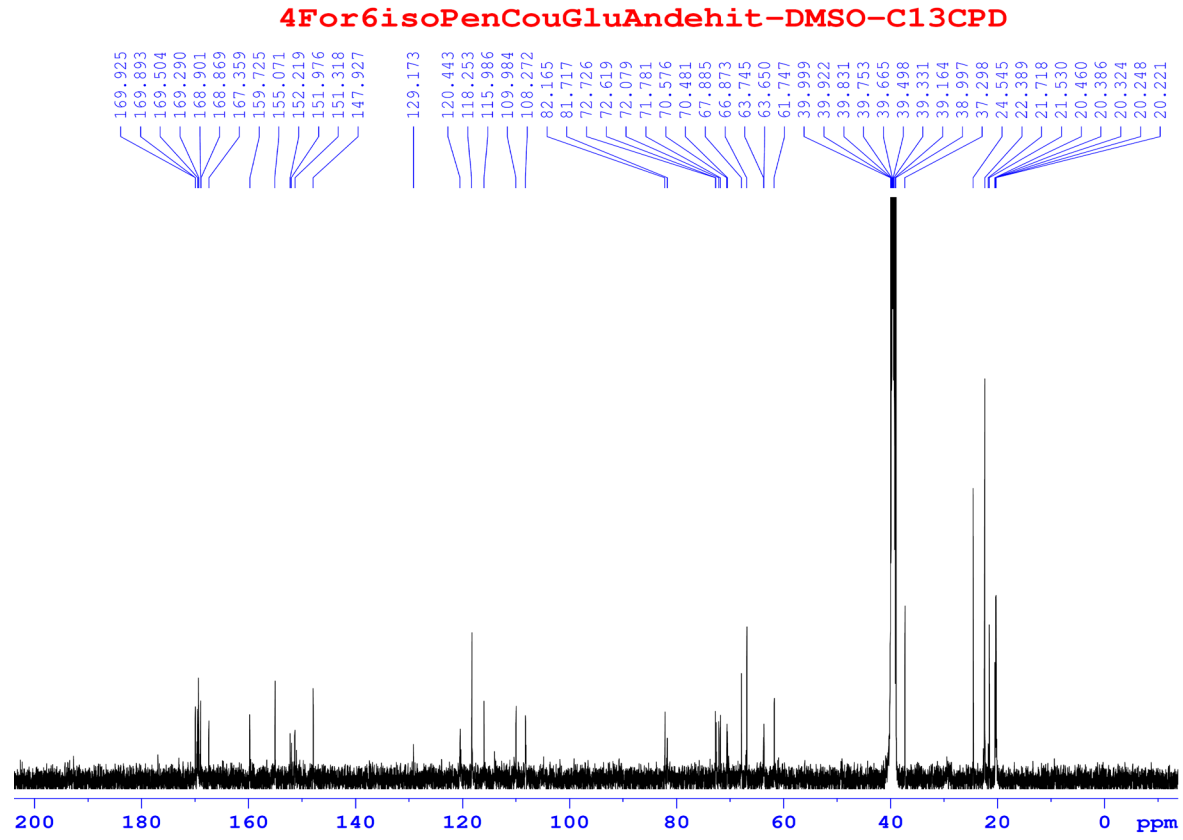


*(4) 4-(3'-Acetyl-5'-(N-(2'',3'',4'',6''-tetra-O-acetyl-β-D-galactopyranosyl)acetamido-2'-methyl-2',3'-dihydro-1',3',4'-thiadiazol-2'-yl)-6-ethoxycoumarin (**9a**)4) 4-(3'-Acetyl-5'-(N-(2'',3'',4'',6''-tetra-O-acetyl-β-D-glucopyranosyl)acetamido-2'-methyl-2',3'-dihydro-1',3',4'-thiadiazol-2'-yl)-6-isopentoxycoumarin (**9d**)*





Lab: Materials chemistry, Faculty of Chemistry, HUS-VNU
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Operator: Ms. Dao Thi Nhung
Mobile: 0948 119 043; Email: daothinhungtn@yahoo.com

Mass Spectrometter
LTQ Orbitrap XL™

Sample name : Glc6iOPn4ForCouThiadiaz

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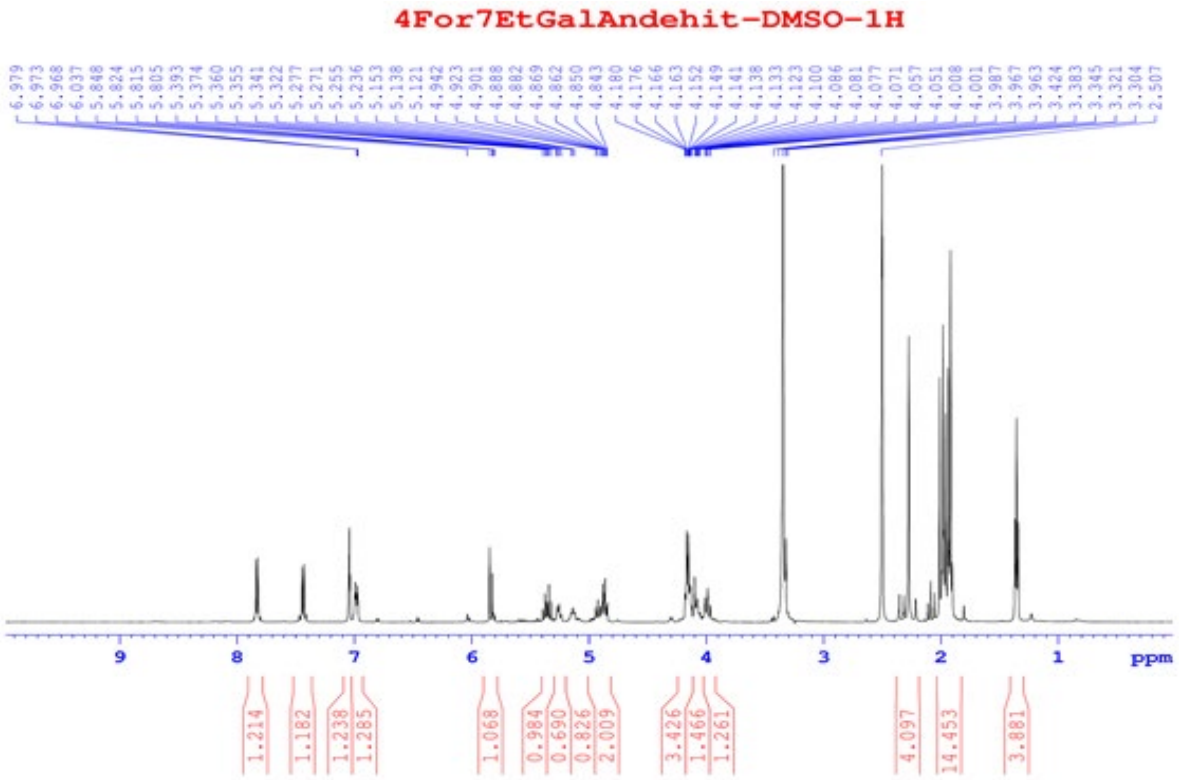
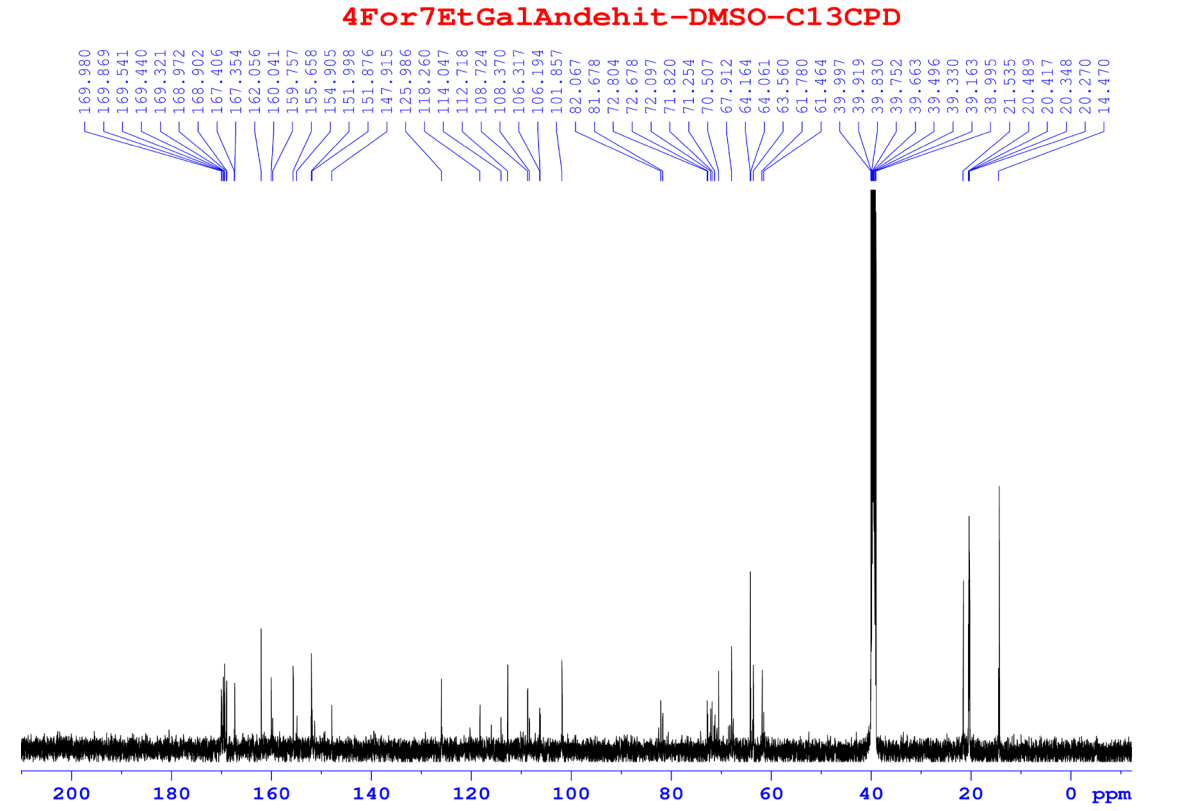
Mode: ESI, M+H

*(5) 4-(3'-Acetyl-5'-(N-(2'',3'',4'',6''-tetra-O-acetyl-β-D-galactopyranosyl)acetamido-2'-methyl-2',3'-dihydro-1',3',4'-thiadiazol-2'-yl)-7-ethoxycoumarin (**9e**)*





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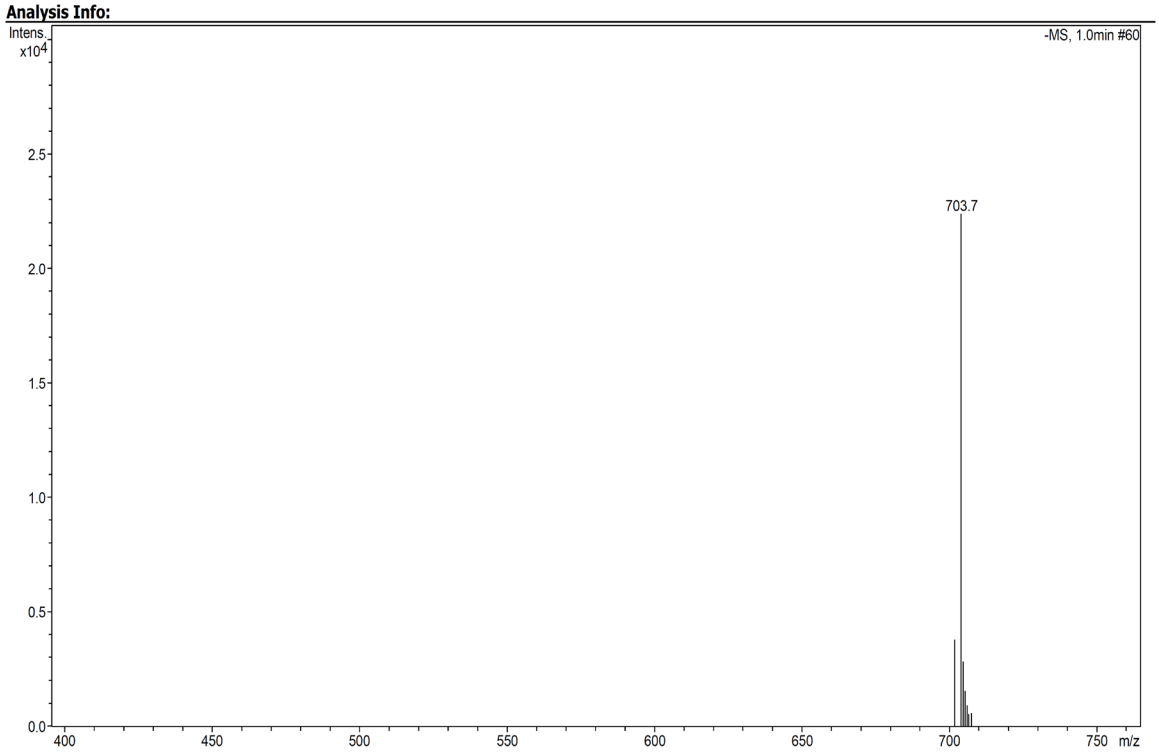

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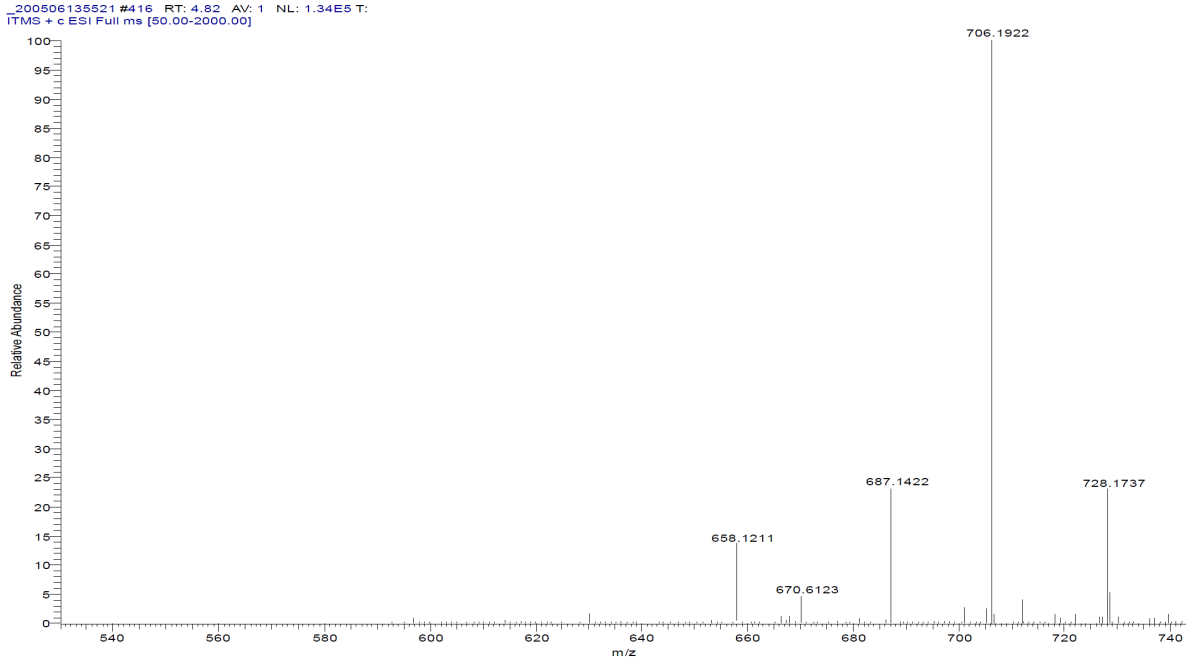
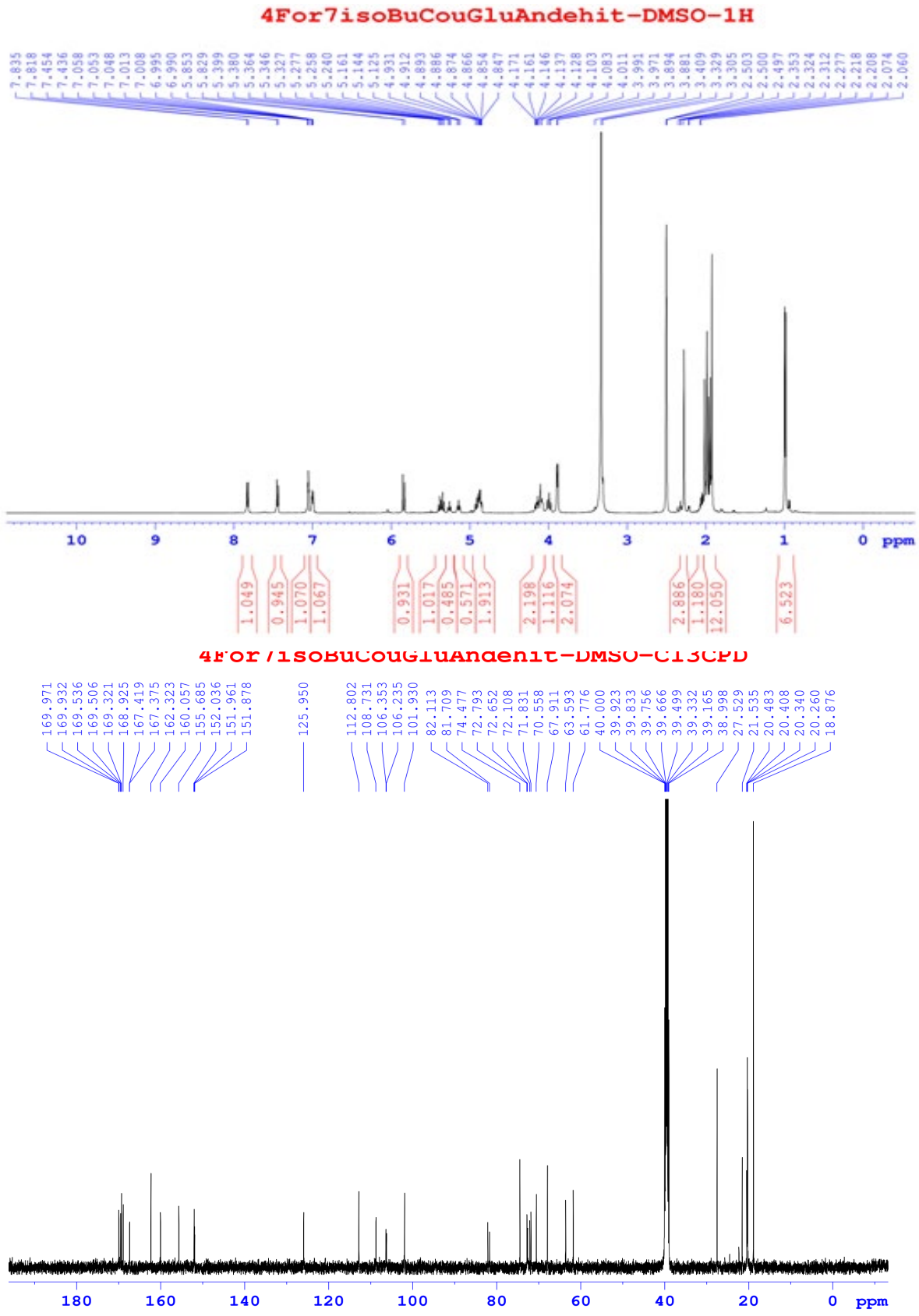


*(6) 4-(3'-Acetyl-5'-(N-(2'',3'',4'',6''-tetra-O-acetyl-β-D-glucopyranosyl)acetamido-2'-methyl-2',3'-dihydro-1',3',4'-thiadiazol-2'-yl)-7-isobutoxycoumarin (**9f**)*



Lab: Materials chemistry, Faculty of Chemistry, HUS-VNU
19 Le Thanh Tong, Hoan Kiem, Ha Noi

Tel: 844.38.253.053; **Fax**: 844.38.241.140 **Mail**: Chem.vnu@.edu.vn

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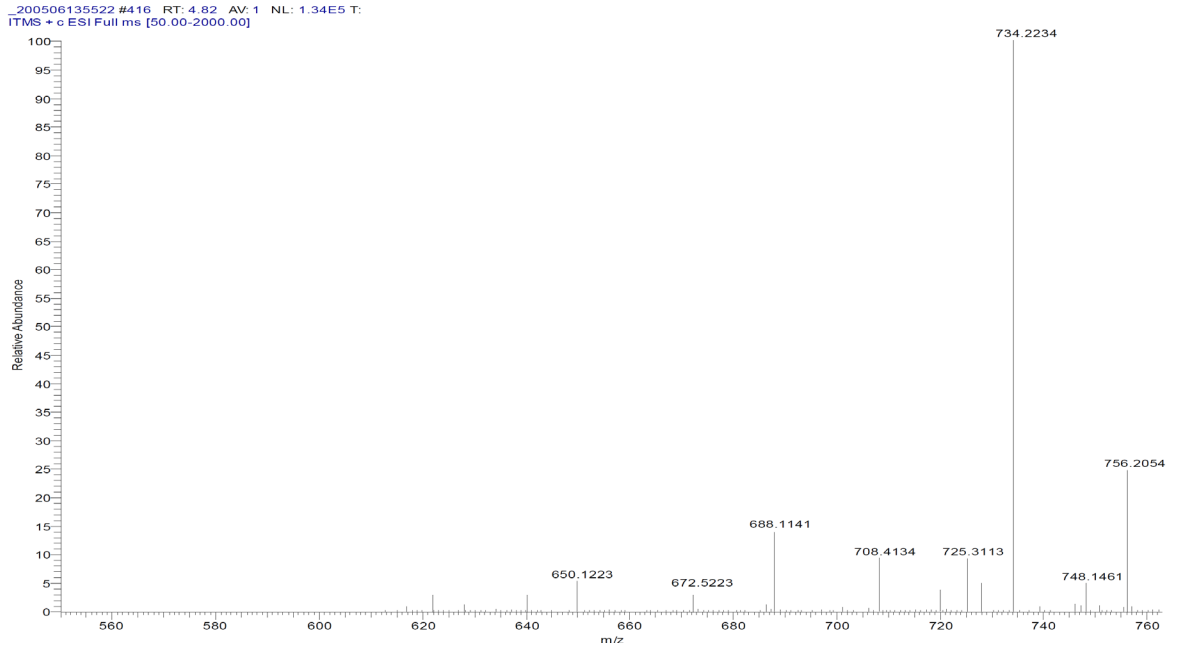
Operator: Ms. Dao Thi Nhung
Mobile: 0948 119 043; Email: daothinhungtn@yahoo.com

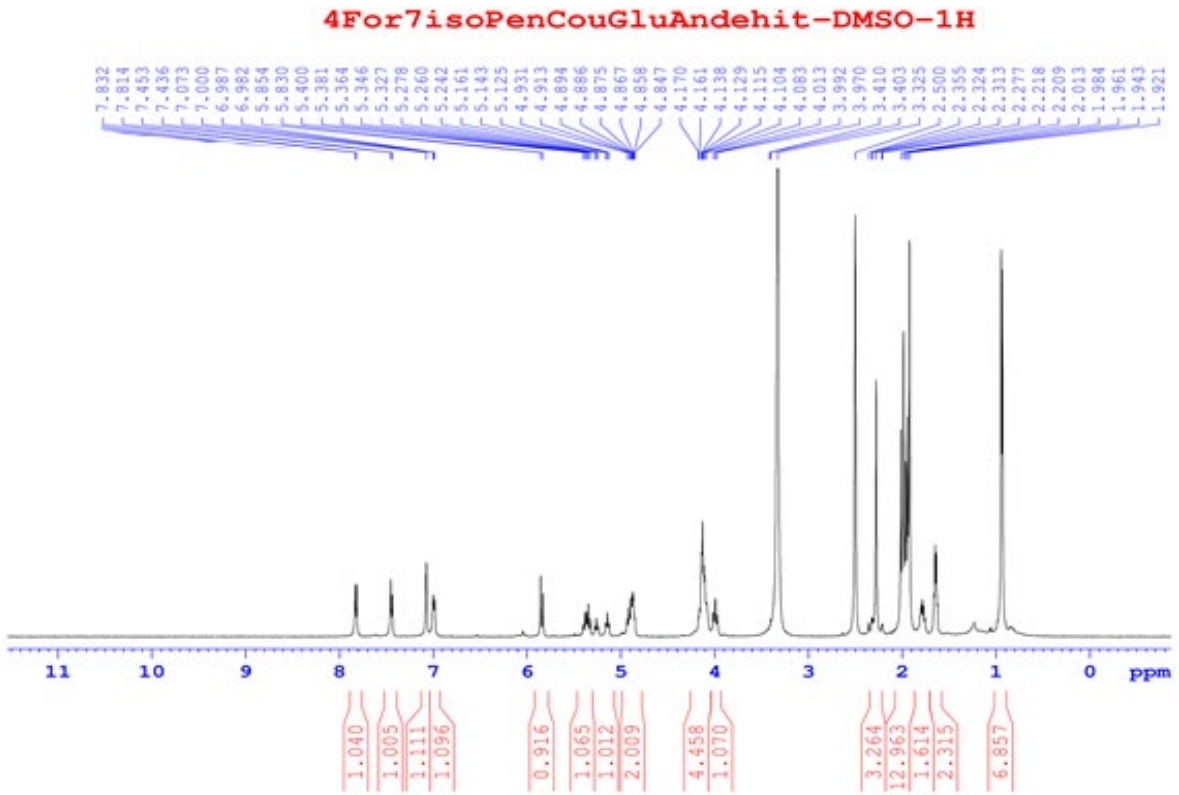
Sample name : Glc7OiBu4ForCou Thiadiaz

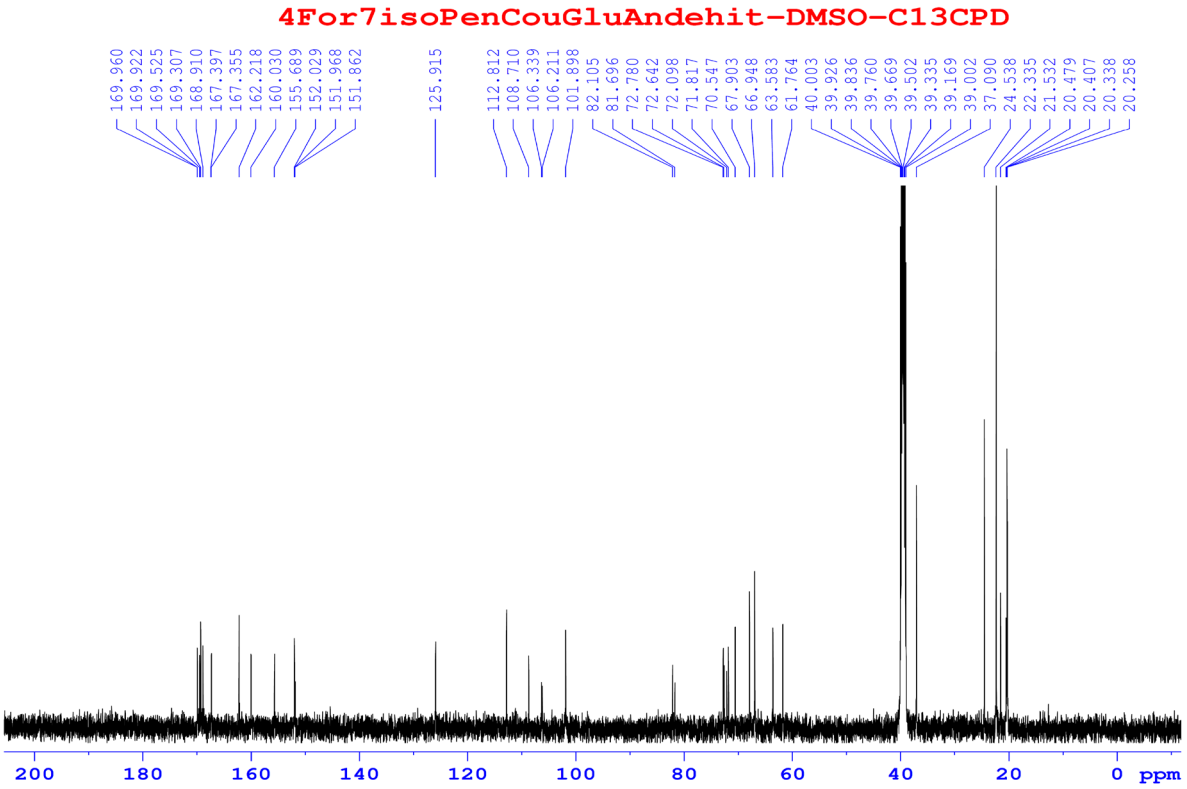
Mode: ESI, M+H

Mass Spectrometter
LTQ Orbitrap XL™



*(7) 4-(3'-Acetyl-5'-(N-(2'',3'',4'',6''-tetra-O-acetyl-β-D-glucopyranosyl)acetamido-2'-methyl-2',3'-dihydro-1',3',4'-thiadiazol-2'-yl)-7-isopentoxycoumarin (**9g**)*





Lab: Materials chemistry, Faculty of Chemistry, HUS-VNU
19 Le Thanh Tong, Hoan Kiem, Ha Noi

Tel: 844.38.253.053; **Fax**: 844.38.241.140 **Mail**: Chem.vnu@.edu.vn

Operator: Ms. Dao Thi Nhung
Mobile: 0948 119 043; Email: daothinhungtn@yahoo.com

Mass Spectrometter
LTQ Orbitrap XL™

Sample name : Glc7OiPn4ForCouThiadiaz

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Mode: ESI, M+H