

(Supporting Information)

**Design, synthesis and biological evaluation of esculetin derivatives
as anti-tumour agents**

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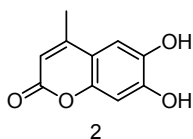
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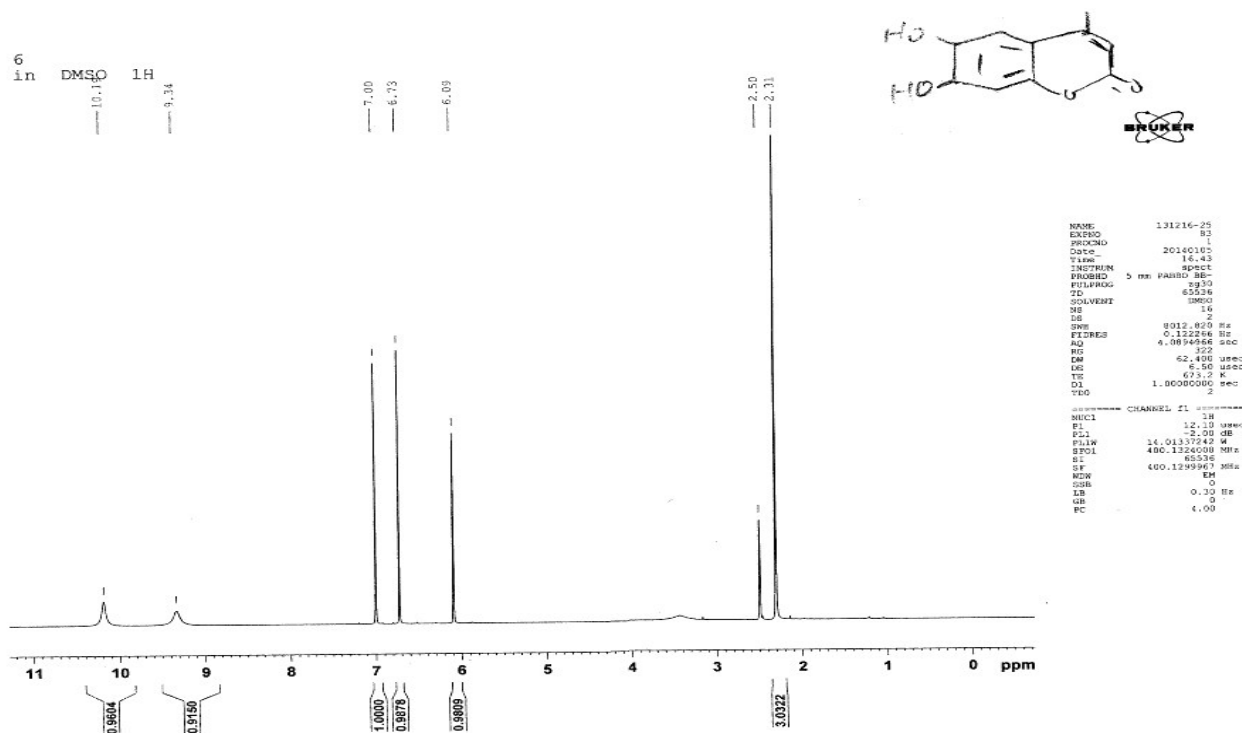
1. General Experimental

The ^1H NMR and ^{13}C NMR spectra were recorded in $\text{DMSO-}d_6$ using a Bruker ARX 400 spectrometer (400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR), and chemical shifts were expressed as ppm against TMS as an internal reference. High-resolution mass spectral (HRMS) analyses were measured with Hybrid Ion Trap-Orbitrap Mass Spectrometer (LTQ Orbitrap XL, Thermo). A UFLC system (Shimadzu, Kyoto, Japan) with tandem mass spectrometry (2010EV), using electrospray ionization (ESI) interface and a computer equipped with UFLC-MS solution software (version 3.41; Shimadzu). All reagents used in the synthesis were obtained commercially and used without further purification. The reactions were monitored by thin layer chromatography (TLC) on glass-packed precoated silica gel GF_{254} plates and visualized in an iodine chamber or with a UV lamp. Flash column chromatography was performed using silica gel (200~300 mesh) purchased from Qingdao Haiyang Chemical Co. Ltd.

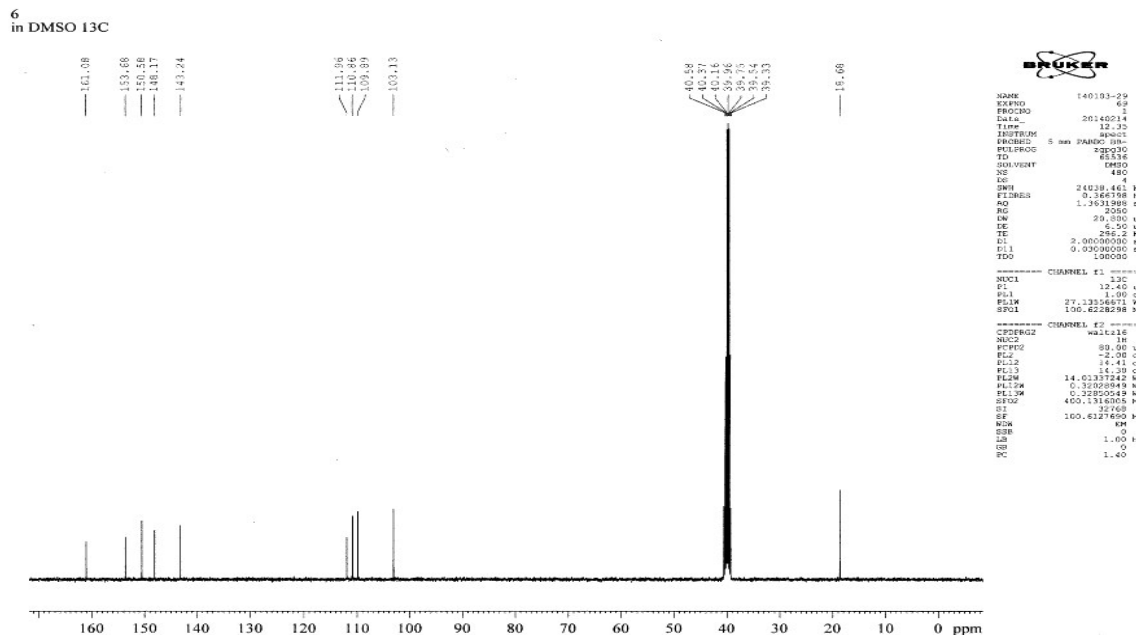
2. ^1H NMR and ^{13}C NMR spectra for compound 2



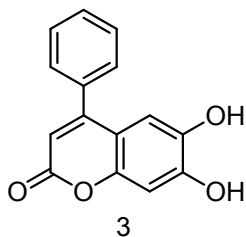
^1H NMR (400 MHz, $\text{DMSO-}d_6$)



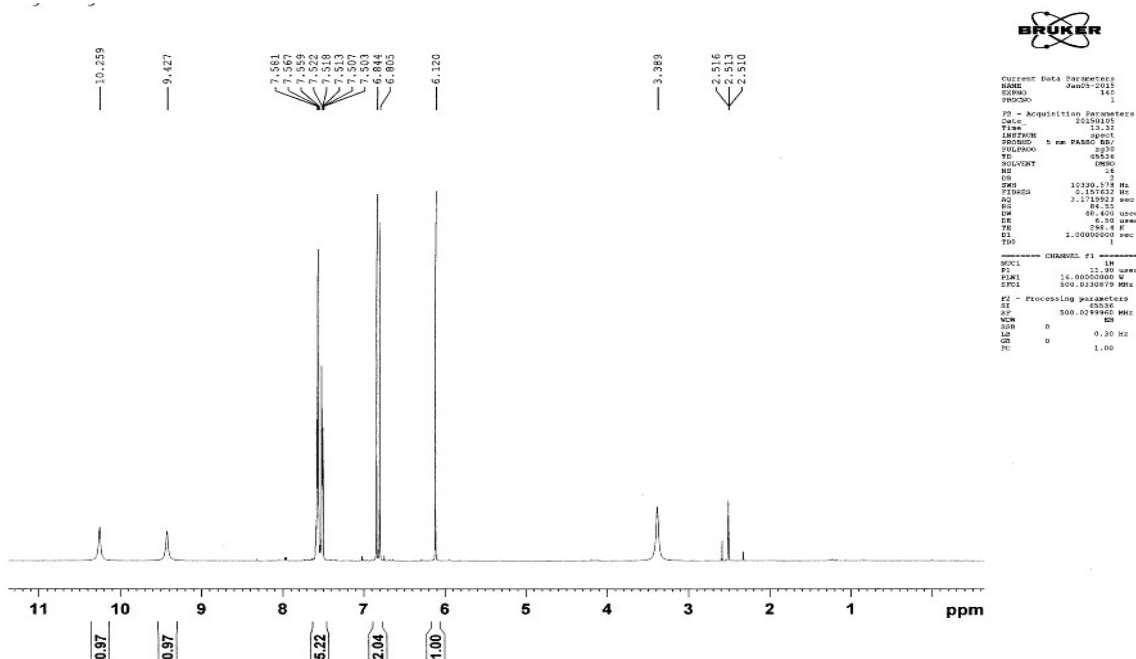
¹³C NMR (100 MHz, DMSO-d₆)



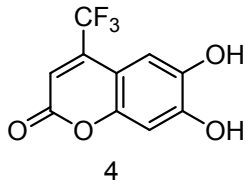
3. ¹H NMR Spectra for compound 3



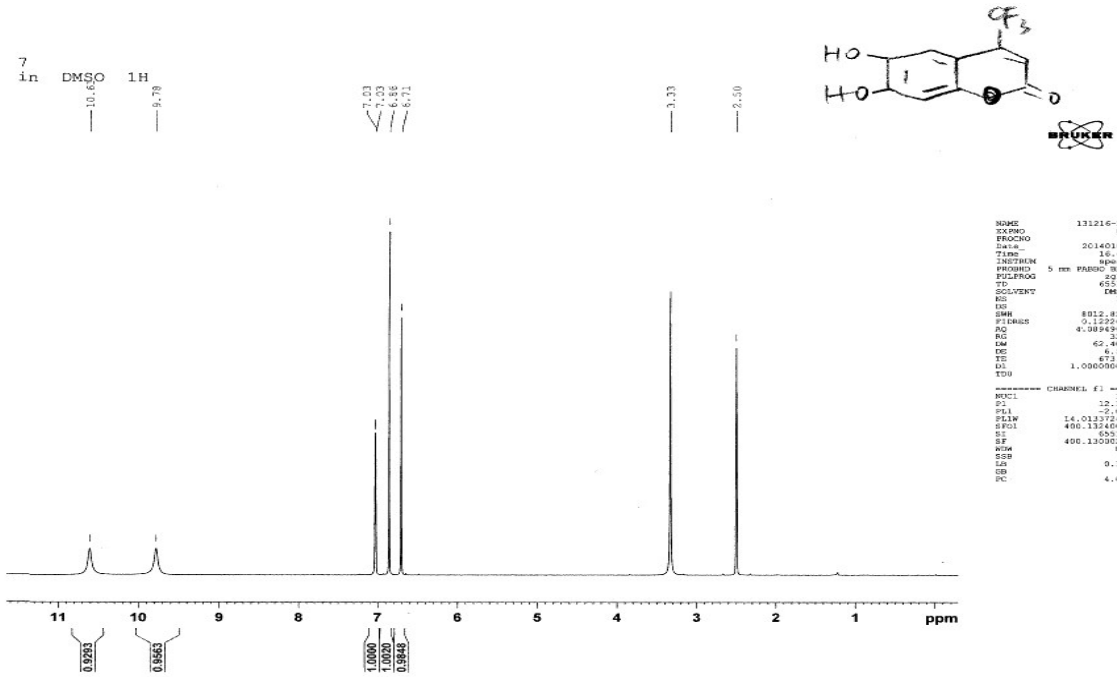
¹H NMR (400 MHz, DMSO-d₆)



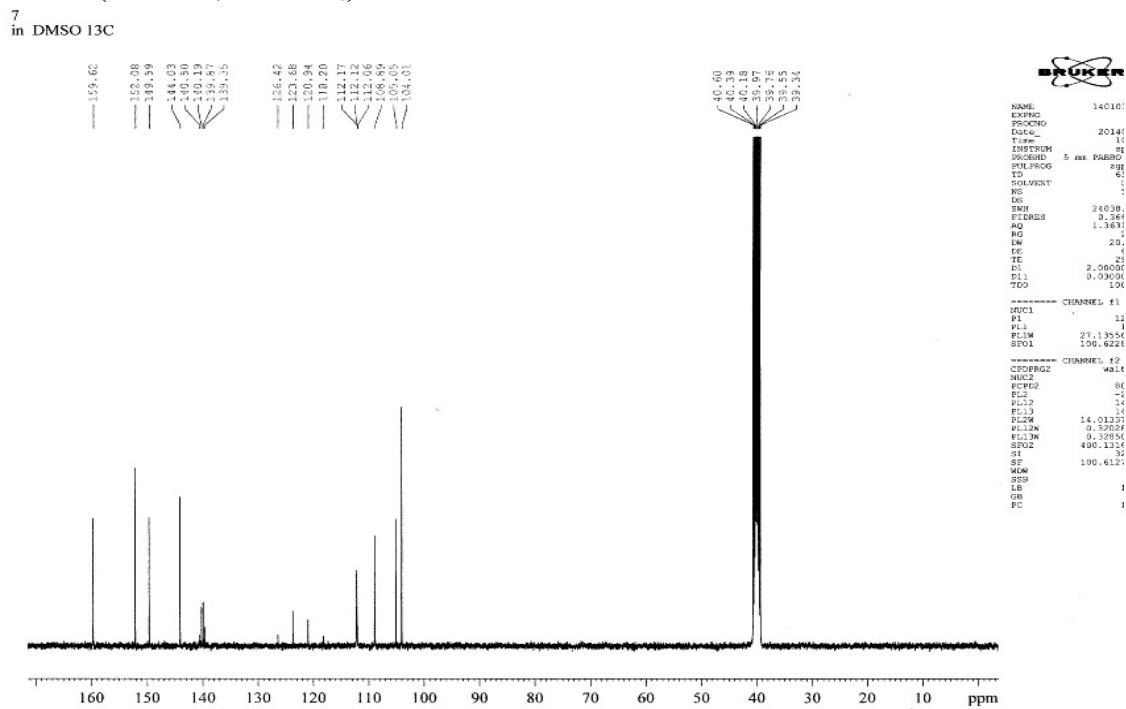
4. ¹H NMR and ¹³C NMR Spectra for compound 4



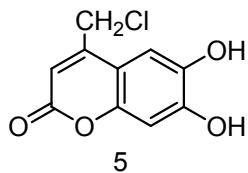
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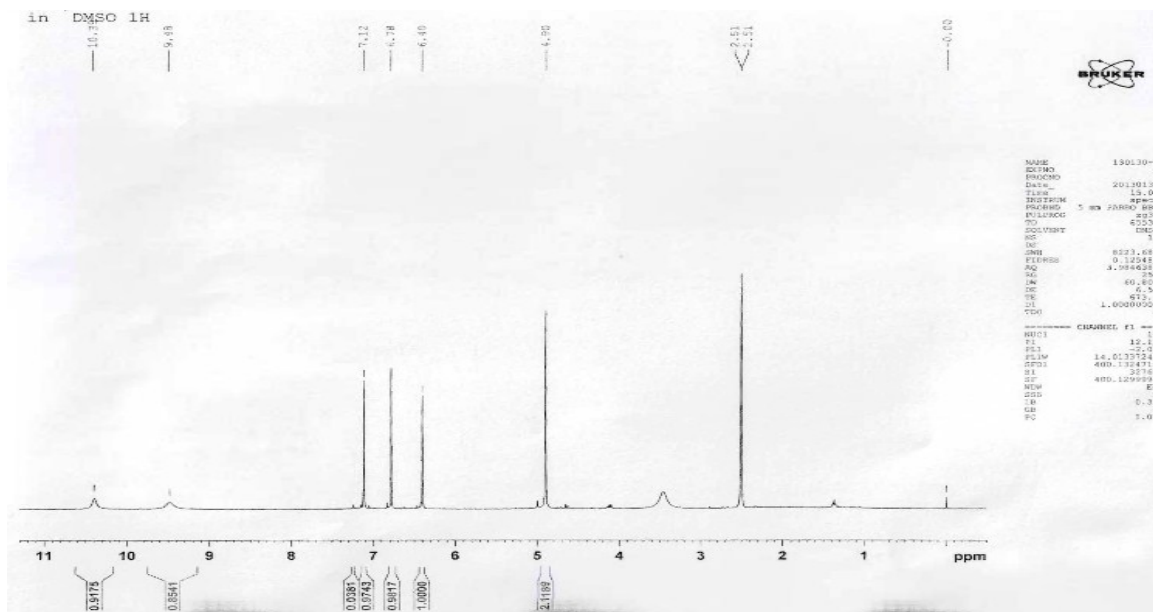
¹³C NMR (100 MHz, DMSO-d₆)



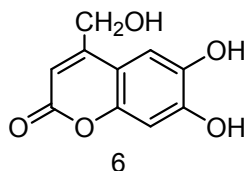
5. ¹H NMR Spectra for compound 5



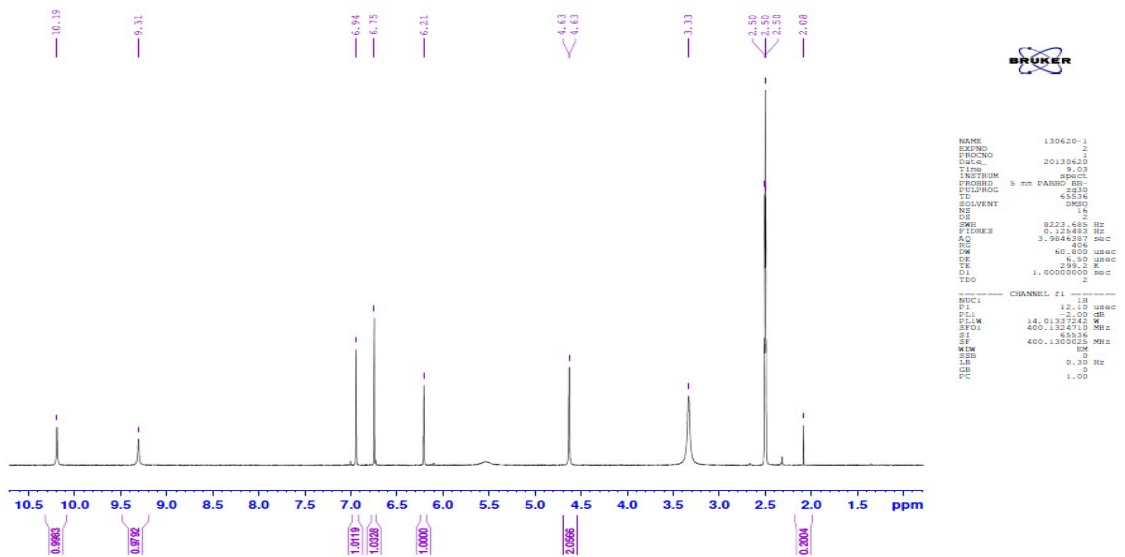
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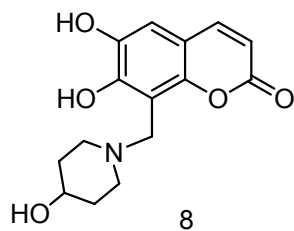
6. ¹H NMR spectra for compound 6



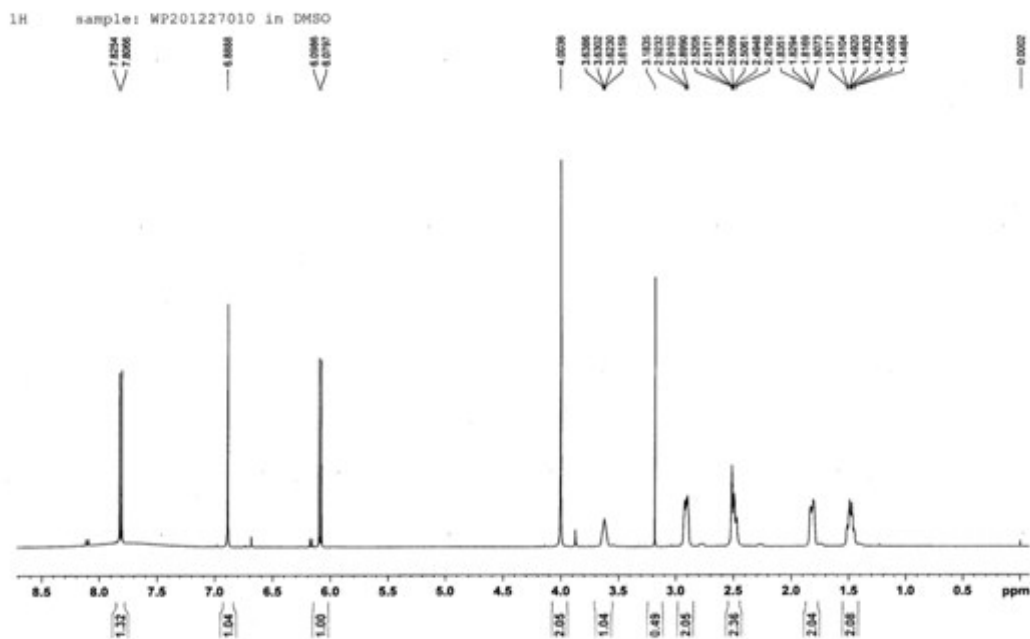
¹H NMR (400 MHz, DMSO-d₆)



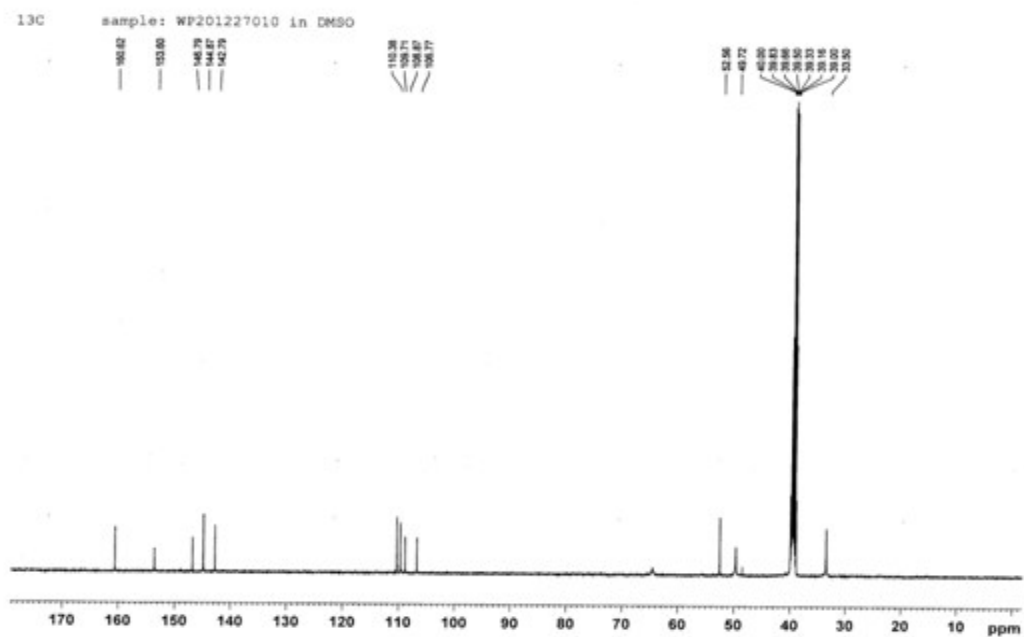
7. ^1H NMR, ^{13}C NMR, HSQC, HMBC and HRMS spectra for compound 8



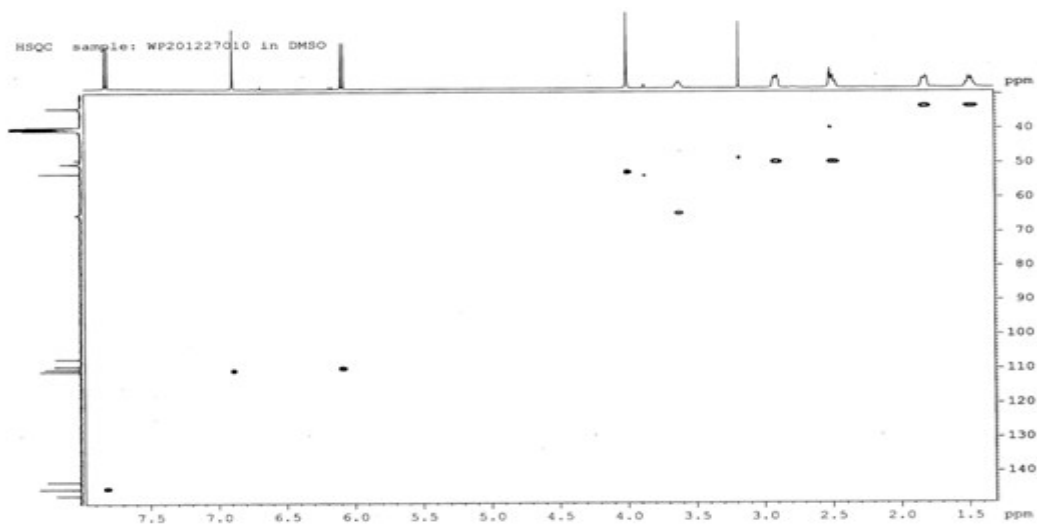
^1H NMR (400 MHz, $\text{DMSO}-d_6$)



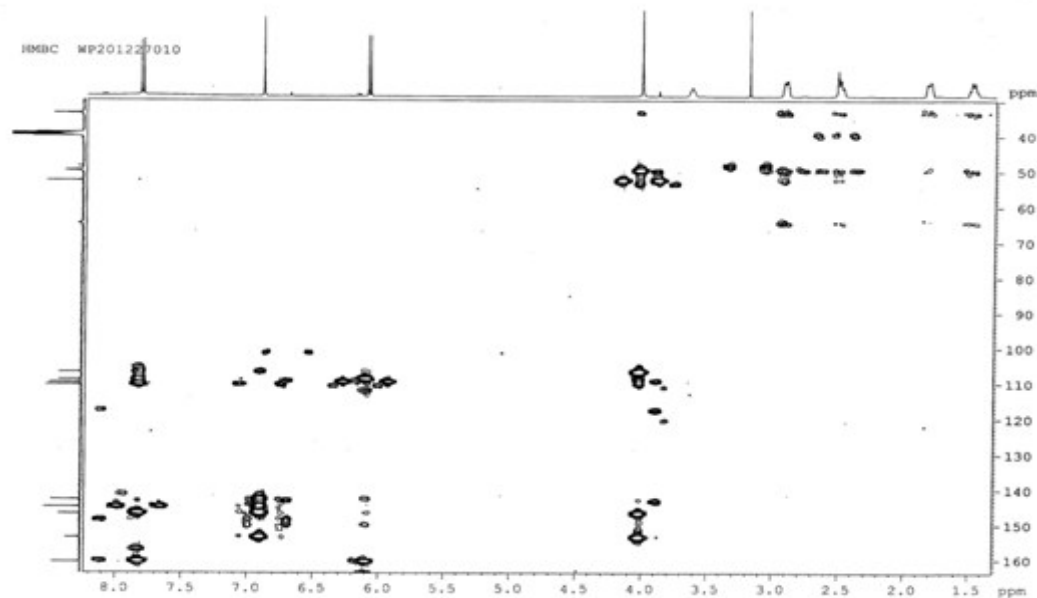
^{13}C NMR (100 MHz, $\text{DMSO}-d_6$)



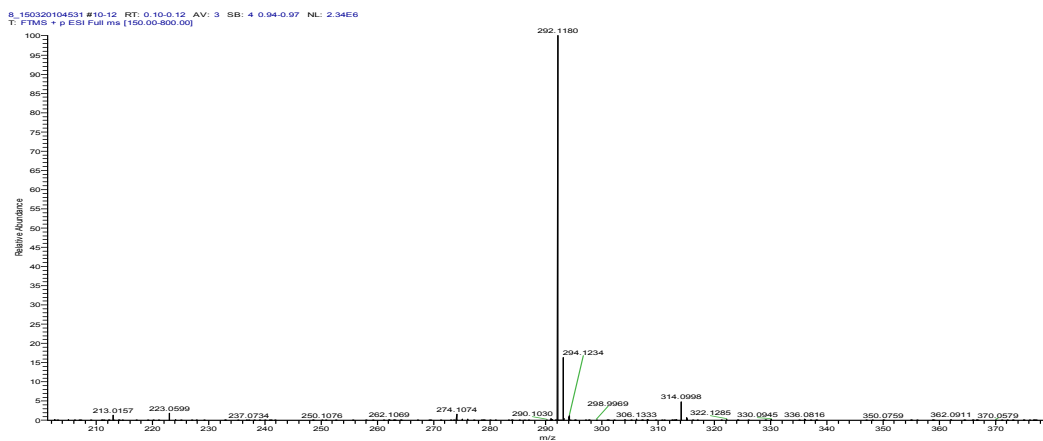
HSQC



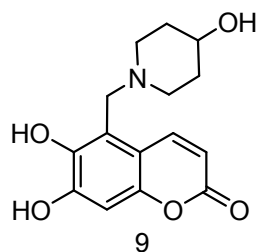
HMBC



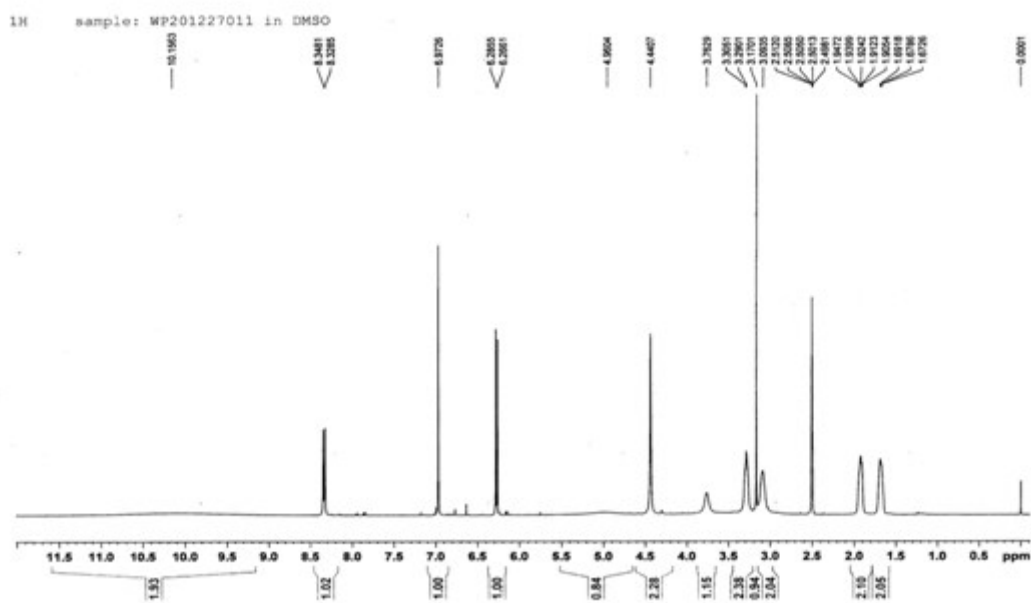
HRMS (ESI)



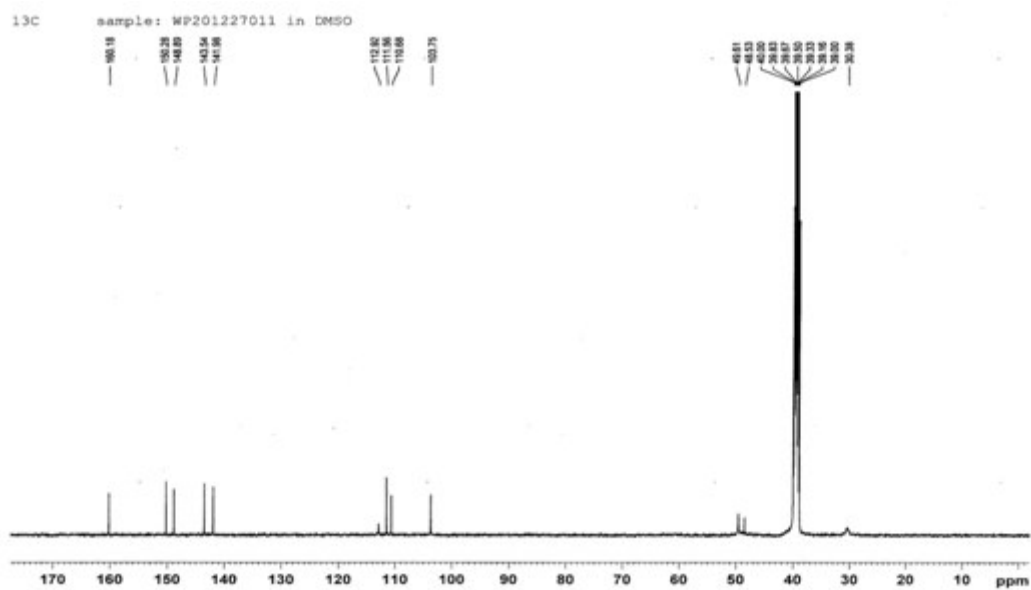
8. ^1H NMR, ^{13}C NMR, HSQC, HMBC and HRMS spectra for compound 9



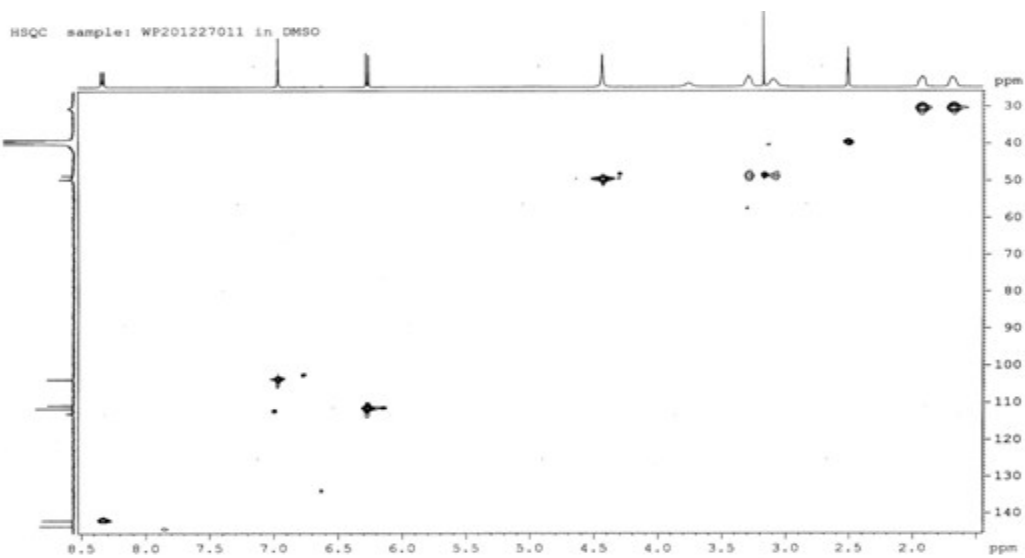
^1H NMR (400 MHz, $\text{DMSO-}d_6$)



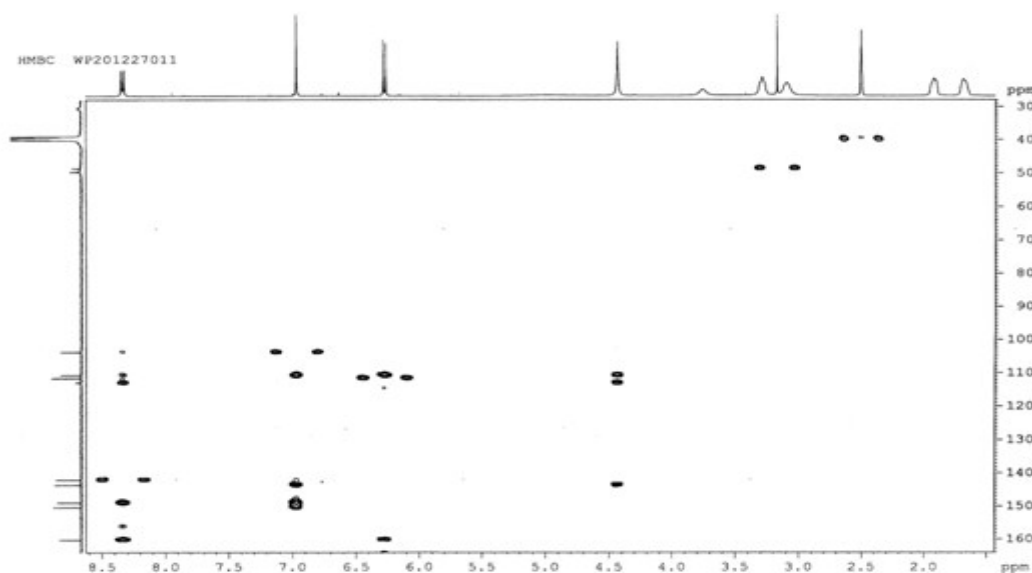
^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



HSQC

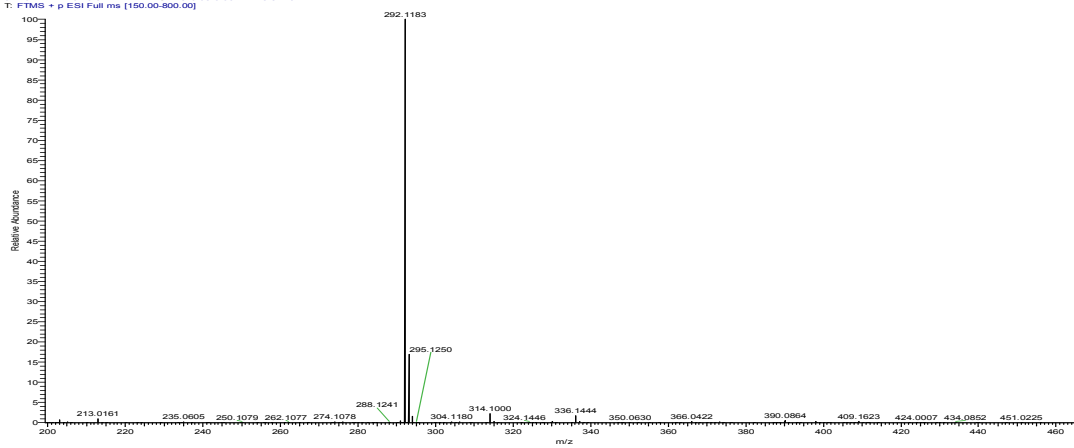


HMBC

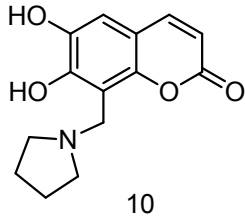


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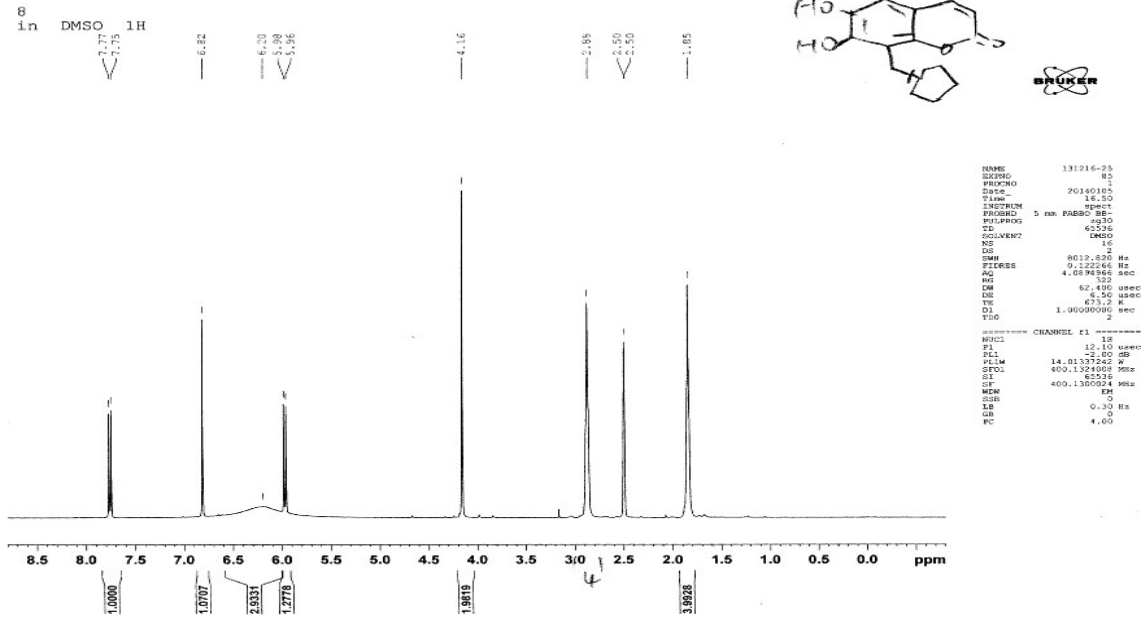
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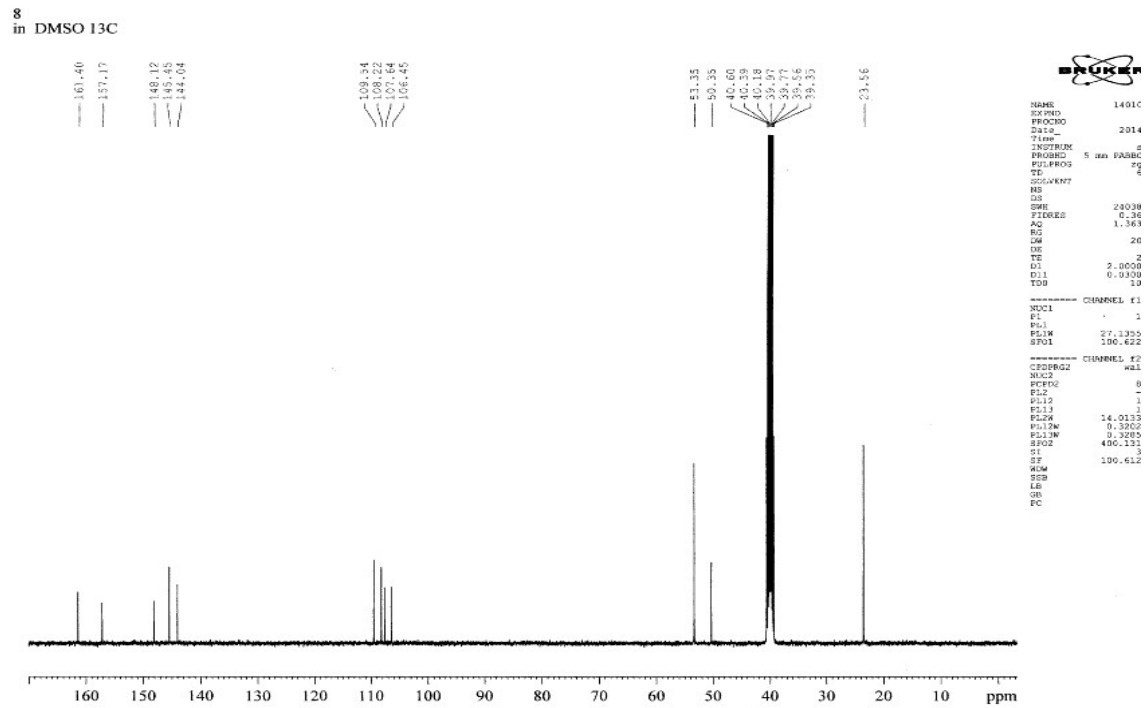
9. ¹H NMR, ¹³C NMR and HRMS spectra for compound 10



¹H NMR (400 MHz, DMSO-d₆)

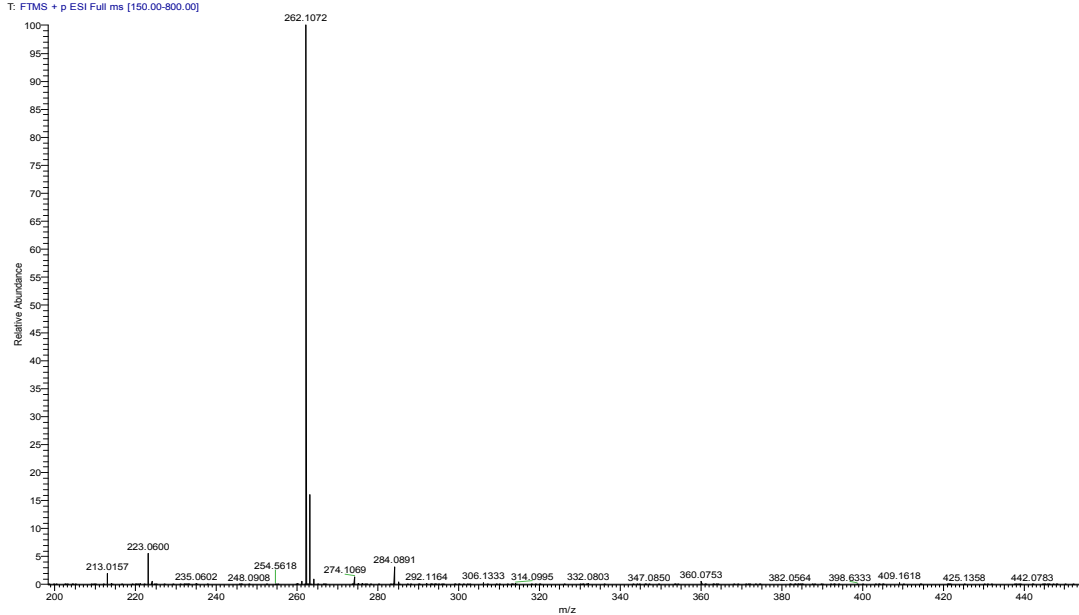


¹³C NMR (100 MHz, DMSO-d₆)

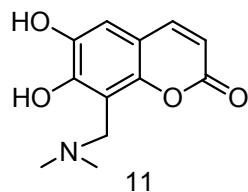


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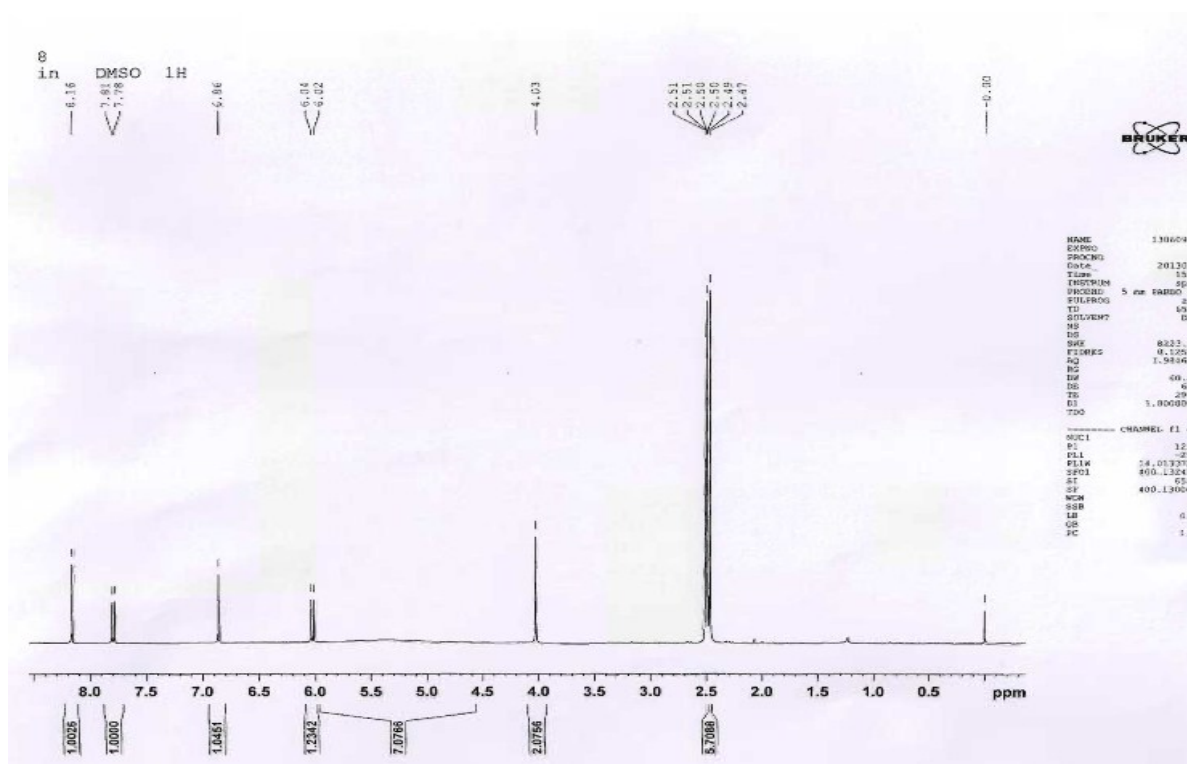
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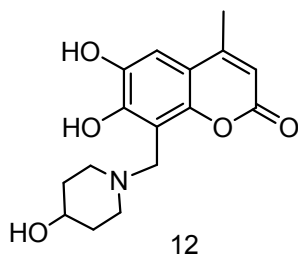
10. ¹H NMR spectra for compound 11



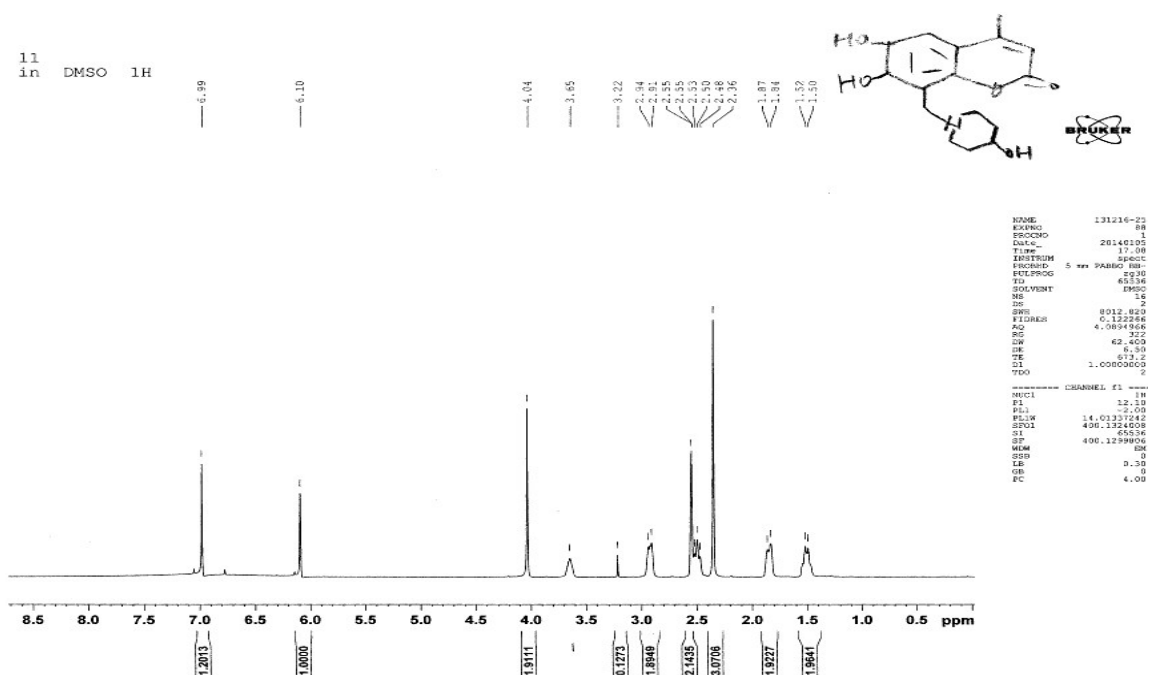
¹H NMR (400 MHz, DMSO-d₆)



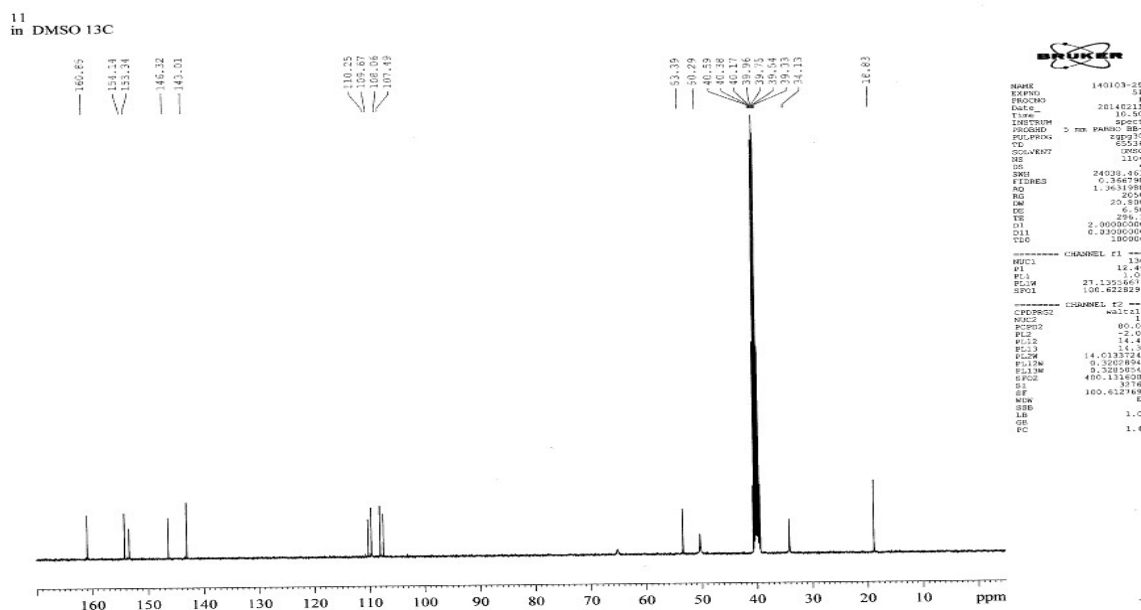
11. ¹H NMR, ¹³C NMR and HRMS spectra for compound 12



¹H NMR (400 MHz, DMSO-d₆)

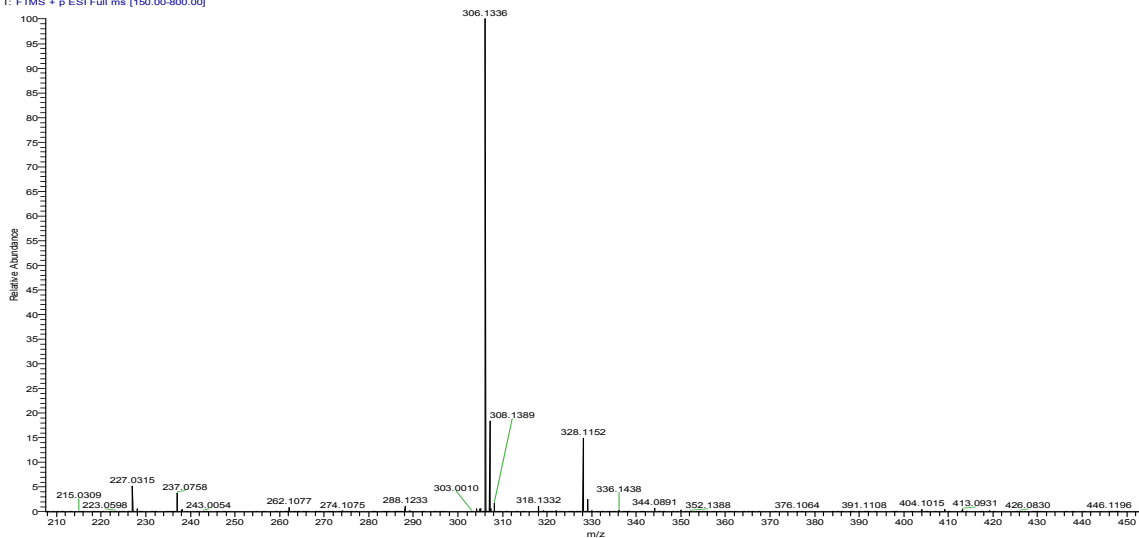


¹³C NMR (100 MHz, DMSO-d₆)

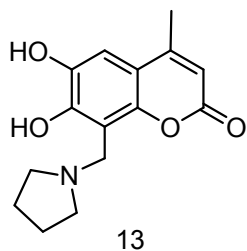


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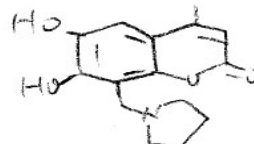
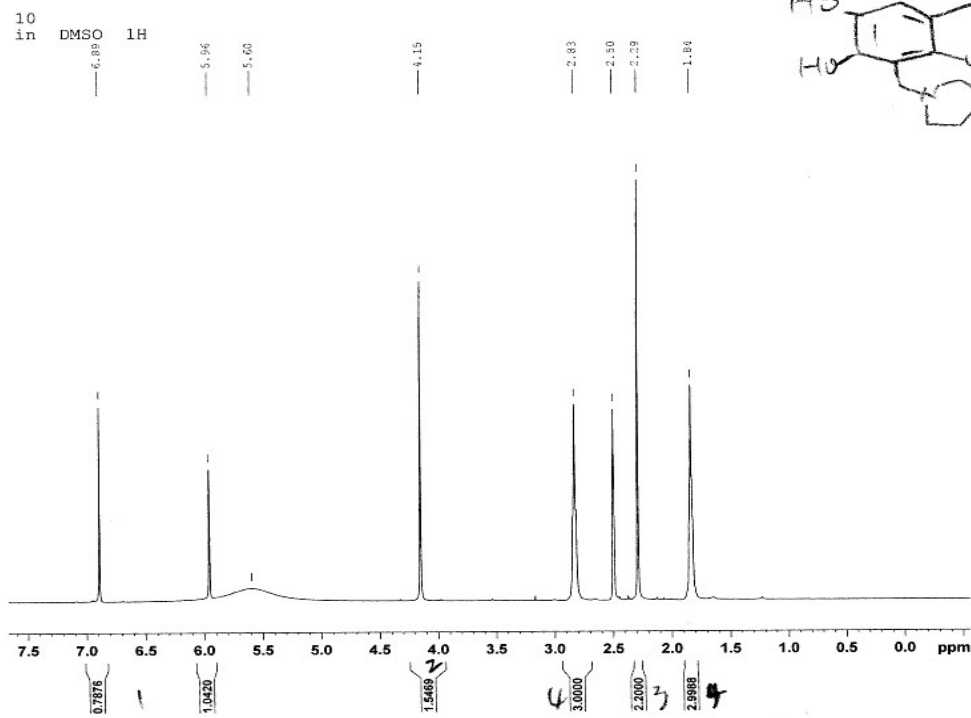
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12. ¹H NMR, ¹³C NMR and HRMS spectra for compound 13



¹H NMR (400 MHz, DMSO-*d*₆)



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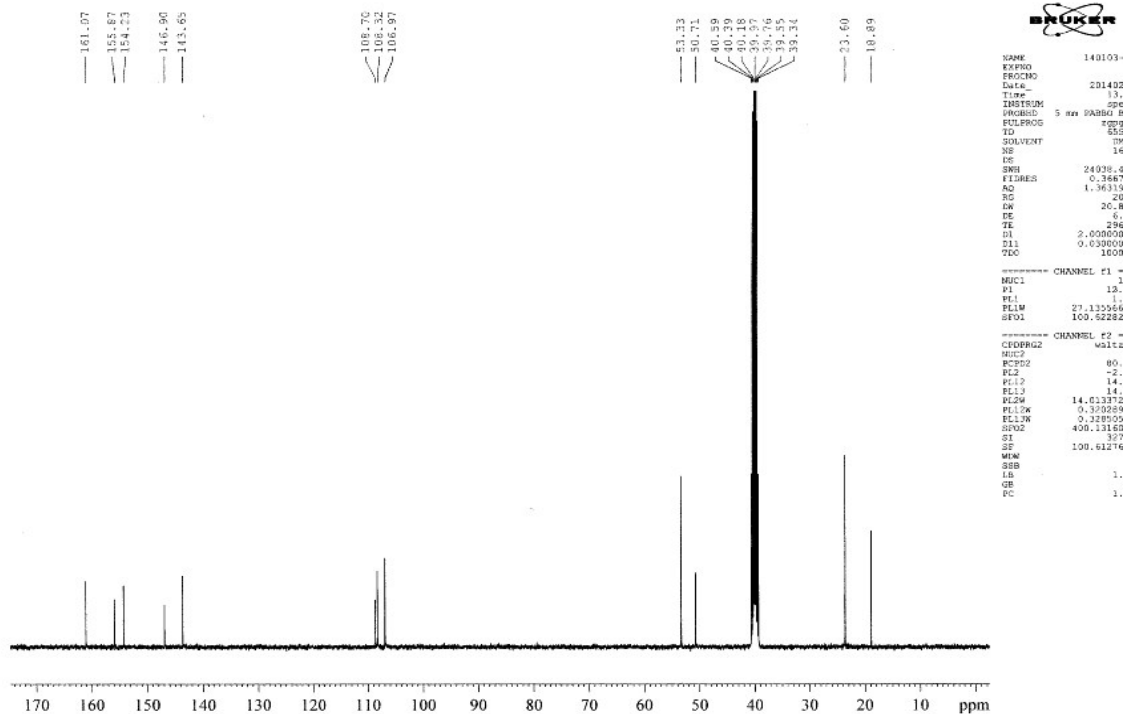
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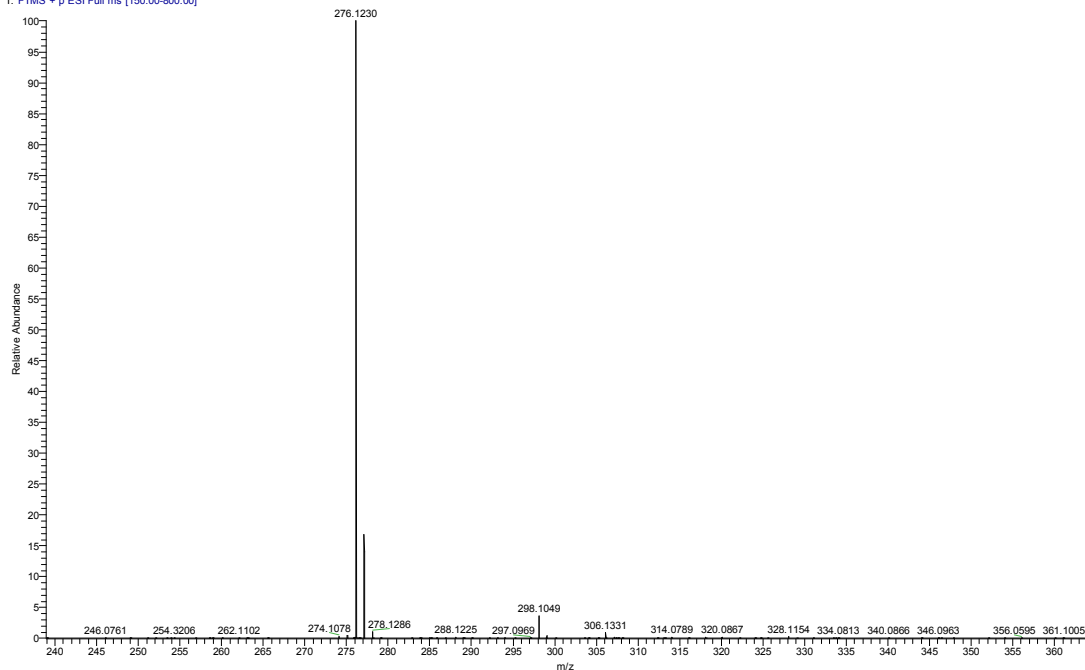
¹³C NMR (100 MHz, DMSO-d₆)

10
in DMSO 13C

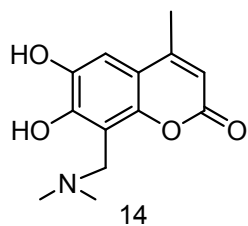


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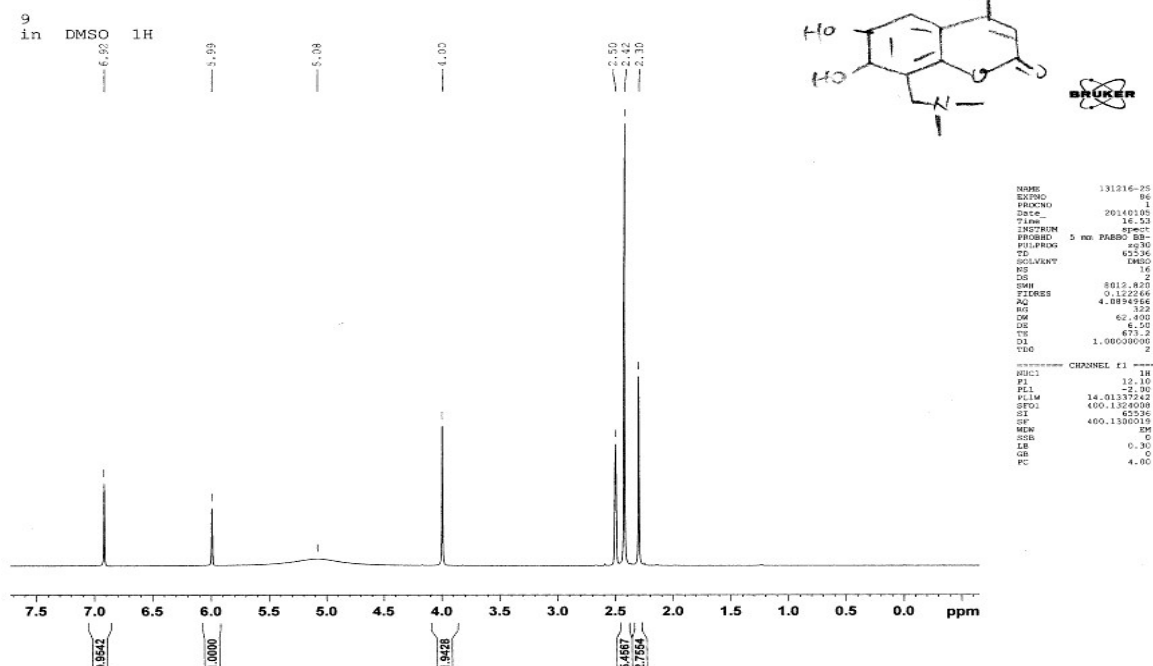
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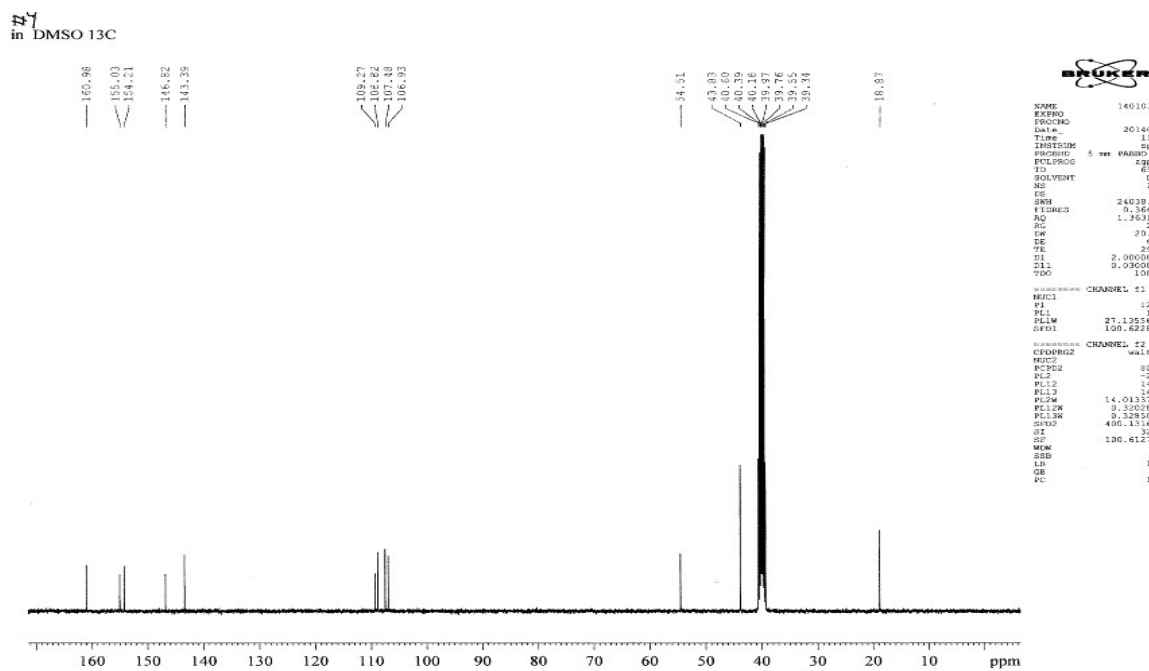
13. ¹H NMR, ¹³C NMR and HRMS spectra for compound 14



¹H NMR (400 MHz, DMSO-d₆)

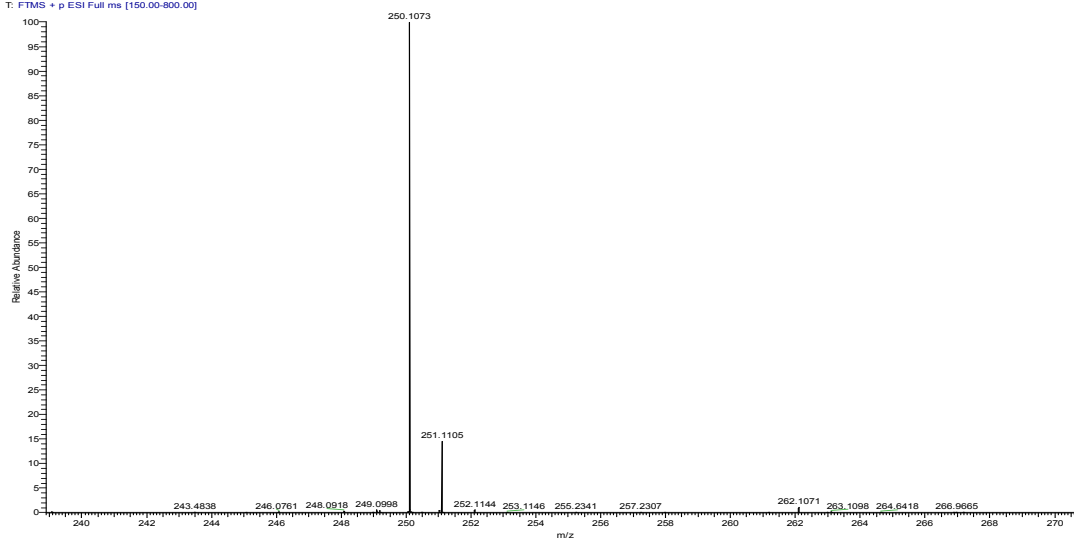


¹³C NMR (100 MHz, DMSO-d₆)

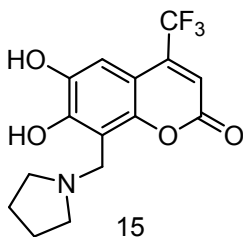


HRMS (ESI)

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14. ¹H NMR, ¹³C NMR and HRMS spectra for compound 15



¹H NMR (400 MHz, DMSO-d₆)

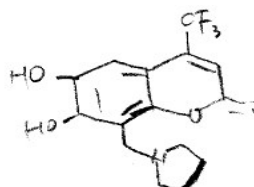
12
in DMSO 1H
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6.70
6.15

4.29

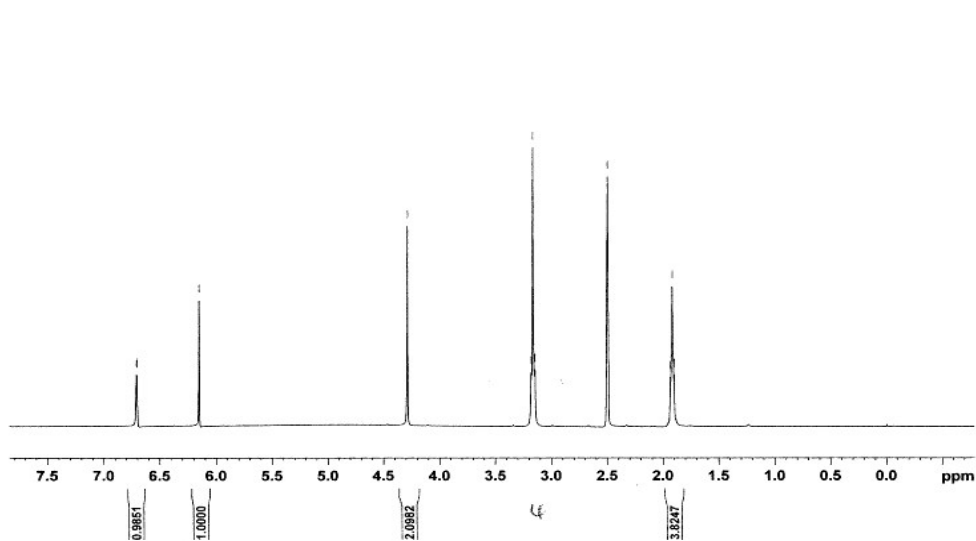
3.18
3.17
3.15

2.50

1.84
1.82
1.80



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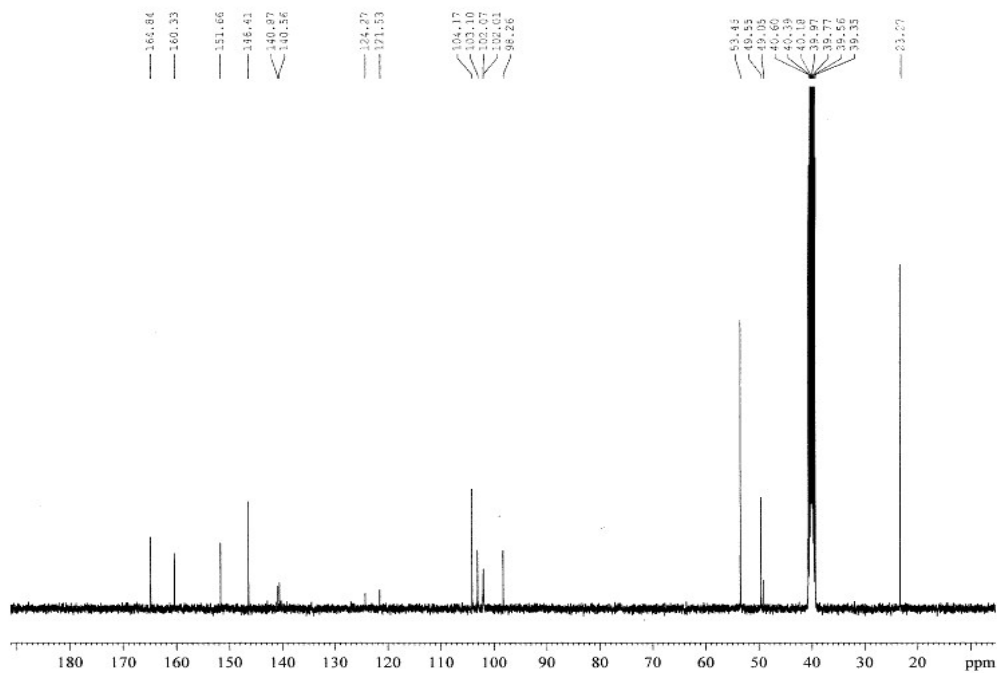


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SF           400.1300022
XDA          EM
SQR           0
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¹³C NMR (100 MHz, DMSO-d₆)

12
in DMSO 13C



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PROCRES       14.
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RG            20
DM            20.8
DE            6.
TE            296
D1            2.060800
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TD0           300

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P1             12.
PC1           27.135466
SFO1          100.62282

----- CHANNEL f2 -----
CHRG2         waitz
NUC2           13
PC2           12.
P12           27.135466
SFO2          100.62282

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SFR           100.61276
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HRMS (ESI)

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