Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Antibiotic activities of propanolamine containing 1,4-benzoxazin-3-ones against phytopathogenic bacteria

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1. Crystallographic data of compound 2a(The deposition number is CCDC 1938560)

Table 1. Crystallographic data of compound **2a**

Chemical formula	$C_{19}H_{22}N_2O_3$
Formula weight	326.40
Temperature[K]	298 K
Crystal system	Orthorhombic
Space group	Pbca
a [Å]	7.2797(5)
b [Å]	14.3957(12)
c [Å]	32.2490(3)
α [°]	90
β [°]	90
γ [°]	90
V[Å^3]	3379.5(5)
Z	8
ρ (calculated)[g/cm^3]	1.283
μ [mm^{-1}]	0.087
F(000)	1392.0
Crystal size [mm^3]	0.40 × 0.41 × 0.45
Colour, shape	brown crystal, block
Radiation [Å]	MoKα (λ = 0.71073)
Theta Min-Max [°]	2.526, 25.017
h,k,l	-8 ≤ h ≤ 8, -17 ≤ k ≤ 16, -21 ≤ l ≤ 38
Reflections collected	2987
Independent reflections	1701
Data/restraints/parameters	2987/0/220
Goodness-of-fit	1.041
Final R indexes [I>=2σ (I)]	R1= 0.0549, wR2= 0.1263
Final R indexes [all data]	R1= 0.1155, wR2= 0.1557

2. Protocols for Crystallographic analysis, antibacterial assay, in-vivo bioactivity and scanning electron microscopy.

Crystallographic analysis of 1,4-benzoxazin-3-one 2a

A single crystal of compound **2a** was obtained via recrystallisation from a $CDCl_3$ solution. X-ray crystal data for compound **2a** was acquired using a Bruker Apex-2 CCD diffractometer with graphite-monochromatic Mo-Kα radiation (λ = 0.71073 Å, μ = 0.828 mm-1) under ω-scan mode. A combination of absorption correction and Lorentz polarization was adopted. Structural solutions and F2-based full-matrix least-squares refinements were conducted using SHELXT-14 and SHELXL-14 software, respectively. Anisotropical refinement of the non-hydrogen atoms was then carried out. Subsequently, the scattering factors of the neutral atoms were analyzed, by incorporating an anomalous dispersion correction. The majority of H_2O molecules in the crystalline structure were removed using the SQUEEZE option in PLATON.

Crystallographic data of compound **2a**: brown crystal, $C_{19}H_{22}N_2O_3$, M_r = 326.38, orthorhombic, space group *Pbca*, a = 7.2797(5) Å, b = 14.3957(12) Å, c = 32.2490(3) Å; α = 90°, β = 90°, γ = 90°; μ = 0.087 mm^{-1}, V = 3379.5(5) $Å^3$, Z = 8, Dc = 1.283 g/cm^3, F(000) = 1392.0, Reflection collected/Independent reflection measured = 2987/1701, Goodness-of-fit on F^2 = 1.041, Fine, R_1 = 0.0549, wR_2 = 0.1557. CCDC 1938560 that contains the Crystallographic data was accessed freely at the Cambridge Crystallographic Data Centre.

In vitro antibacterial bioassays

In vitro antibacterial activities of all propanolamine containing 1,4-benzoxazin-3-ons against *R. solanacearum, Xac* and *Xoo* were determined by turbidimetric analysis using the following protocol. Media with dimethylsulfoxide were used blank controls, while those with BT or TC were treated as positive controls. NB solvents (5 mL) comprising different amounts of tested compounds (or the positive controls) were mixed with 40 μL preincubated bacterial solution (*Xoo*, *R. solanacearum* or *Xac*) and NB (10 g glucose, 5 g peptone, 3 g beef extract, 1 g yeast powder and 1 L distilled water; pH = 7.0–7.2). The compound concentrations of 50 and 100 μg/mL were used to determine the preliminary values of antibiotic activity. Compound concentrations

of 6.25, 12.5, 25, 50 and 100 μg/mL or 2.5, 5, 10, 20 and 40 μg/mL were used to determine the EC_{50} values of compounds in triplicate. To ensure that the bacteria had progressed into the log phase, the inoculated samples were incubated for 24-48 hours at 28 ± 1 °C with shaking (180 rpm). The optical density (OD_{595}) values of the NB media were then recorded using the Model 680 microplate reader (BIO-RAD, Hercules, CA), and the inhibition rate *I* (%) was calculated based on the following equation:

$$\text{Inhibition rate } I\ (\%) = (C - T)/C \times 100\%$$

where, C indicates the corrected absorbance value (OD_{595}) of the untreated NB media, while T indicates the corrected absorbance value (OD_{595}) of the treated NB media. EC_{50} values calculated by SPSS version 17.0 (SPSS, Chicago, IL).

In vivo study of the antibacterial activity of compound 4n against the BLB of rice

The protective and curative effects of compound **4n** against BLB in potted rice plants were assessed using a slight modification of Schaad's method.[31] The bactericides BT (20% in the form of wettable powder) and TC (20% in the form of suspending agent) that have been approved for treating rice BLB were used as positive controls. The curative effects of compound **4n** on the BLB in potted rice plants was evaluated under growth-chamber conditions. "Fengyouxiangzhan" rice seeds were sown and the resultant plants grown for 9 weeks, before their leaves were inoculated with *Xoo* under sterile conditions. A day after inoculation, 200 μg/mL **4n** compound solution was sprayed uniformly onto the rice leaves until they were fully soaked, with distilled water being sprayed as a negative control. For a period of 14 days, the inoculated plants were maintained in a growth chamber at 28 °C and 90% relative humidity. Finally, the leaf disease index (C and T) of were determined.

Percentage disease areas of leaves were determined by measuring the diseased spot area (DSA) of each leaf in comparison to its total leaf area. Each leaf was then classified using the grading system as follows: grade 1, DSA <5%; grade 3, DSA between 6−10%; grade 5, DSA between 11−20%; grade 7, DSA between 21−50%; grade 9, DSA >50%. The calculation of disease index is shown as follows:

Disease index = Σ (number of leaves of each grade × corresponding grade)/(total number of leaves × the superlative grade).[32]

The disease control efficiency (*I*) was determined as follows:

$$I\ (\%) = (C - T)/C \times 100$$

where, C represents the disease index of control group, while T represents that of treatment group.

Scanning electron microscopy (SEM)

1.5 mL of *Xoo* cells were incubated until they had entered a logarithmic growth phase, with the suspension then centrifuged and washed with PBS buffer (pH = 7.2) to afford a bacterial pellet that was resuspended in 1.5 mL of PBS buffer. This Xoo bacterial suspension was treated with 50 and 100 μg/mL compound **4n** in DMSO at rt for 6-8 hours. Following treatment, the bacterial cells were rinsed 3 times with PBS and, fixed with 2.5% glutaraldehyde for 8 h at 4 °C, followed by sequential treatment with ethanol and tert-butanol (2 times for 10 min). After freeze drying and gold sputter coating, the samples were imaged by the Nova NanoSEM 450 microscope.[33]

31. N.W. Schaad, Z.K. Wang, M. Di, J. McBeath, G.L. Peterson, M.R. Bonde, Seed. Sci. Technol., 1996, 24, 449−456.

32. P. Li, D.Y. Hu, D.D. Xie, J.X. Chen, L.H. Jin and B.A. Song, J. Agric. Food. Chem. 2018, 66, 3093−3100.

33. J. Zhou, Q.Q. Tao, P.Y. Wang, W.B. Shao, Z.B. Wu, Z. Li, S. Yang, Bioorg. Med. Chem. Lett., 2018, 28, 1742-1746.

3. ^{1}H NMR, ^{13}C NMR and HRMS spectrum of the compounds.

4-(oxiran-2-ylmethyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (1).

White liquid; yield 86.98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (dd, *J* = 7.7, 1.8 Hz, 1H, 1,4-benzoxazin-3-one-7-H), 6.95 – 6.86 (m, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 4.54 – 4.44 (m, 2H, 1,4-benzoxazin-3-one-2-2H), 4.41 (dd, *J* = 15.1, 3.0 Hz, 1H, 1,4-benzoxazin-3-one-N-CH), 3.53 (dd, *J* = 15.1, 5.9 Hz, 1H, 1,4-benzoxazin-3- one-N-CH), 3.11 (ddt, *J* = 5.9, 4.1, 2.8 Hz, 1H, CH), 2.72 (t, *J* = 4.4 Hz, 1H, 1,4-benzoxazin-3-one-N-CH_2-CH-CH), 2.57 (dd, *J* = 4.8, 2.6 Hz, 1H, 1,4-benzoxazin -3-one-N-CH_2-CH-CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 145.2, 129.0, 124.2, 123.0, 116.9, 115.9, 67.6, 49.9, 45.4, 43.8; HR-MS (ESI): *m/z* calcd for $C_{11}H_{12}O_3N$ ($[M+H]^+$) 206.08117, found 206.08054.

4-(3-((2,4-dimethylphenyl)amino)-2-hydroxypropyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (2a).

Yellow solid; yield 60.99%; m.p. 128-129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 – 7.12 (m, 1H, 1,4-benzoxazin-3-one-7-H), 7.01 (tt, *J* = 4.7, 2.7 Hz, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 6.92 (d, *J* = 9.8 Hz, 2H, Ar-3,5-2H), 6.58 (dd, *J* = 7.8, 2.3 Hz, 1H, Ar-6-H), 4.63 (d, *J* = 1.9 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.23 (tt, *J* = 6.3, 4.8 Hz, 1H, CH), 4.14 – 4.10 (m, 2H, 1,4-benzoxazin-3-one-N-CH_2), 3.40 – 3.35 (m, 1H, Ar-NH-CH), 3.23 – 3.18 (m, 1H, Ar-NH-CH), 2.23 (d, *J* = 2.2 Hz, 3H, Ar-4-CH_3), 2.17 (d, *J* = 2.3 Hz, 3H, Ar-2-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 145.4, 143.6, 131.2, 128.9, 127.4, 127.2, 124.5, 123.2, 123.0, 117.3, 115.5, 110.7, 68.8, 67.6, 48.0, 46.2, 20.4, 17.5; HR-MS (ESI): *m/z* calcd for $C_{19}H_{23}O_3N_2$ ($[M+H]^+$) 327.17032, found 327.16898.

4-(oxiran-2-ylmethyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (2b).

Gray solid; yield 94.99%; m.p. 100-101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (dq, *J* = 7.1, 1.9, 1.2 Hz, 1H, Ar-6-H), 6.99 – 6.91 (m, 3H, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 6.82 (td, *J* = 7.6, 1.5 Hz, 1H, 3H, 1,4-benzoxazin-3-one-7-H), 6.75 (dd, *J* = 8.0, 1.5 Hz, 1H, Ar-3-H), 6.67 (td, *J* = 7.6, 1.6 Hz, 1H, Ar-4-H), 6.61 (dd, *J* = 7.8, 1.5 Hz, 1H, Ar-5-H), 4.57 (s, 2H, 1,4-benzoxazin-3-one-2-2H), 4.17 (dt, *J* = 6.4, 4.9 Hz, 1H, CH), 4.05 (d, *J* = 5.8 Hz, 2H, N-CH_2), 3.80 (s, 3H, O-CH_3), 3.31 (dd, *J* = 13.2, 4.7 Hz, 1H, Ar-N-H), 3.19 (dd, *J* = 13.2, 6.7 Hz, 1H, Ar-N-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 160.6, 152.5, 145.3, 129.9, 129.3, 124.2, 122.8, 117.0, 116.2, 108.9, 104.6, 102.6, 67.7, 65.8, 61.7, 55.2, 53.3, 49.2, 46.4; HR-MS (ESI): *m/z* calcd for $C_{18}H_{21}O_4N_2$ ($[M+H]^+$) 329.14958, found 329.14877.

4-(2-hydroxy-3-((4-methoxyphenyl)amino)propyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (2c).

Brown solid; yield 90.20%; m.p. 94-95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 – 7.11 (m, 1H, 1,4-benzoxazin-3-one-7-H), 7.00 (dd, *J* = 5.1, 3.3 Hz, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 6.80 – 6.74 (m, 2H, Ar-2,6-2H), 6.67 – 6.61 (m, 2H, Ar-3,5-2H), 4.61 (s, 2H, 1,4-benzoxazin-3-one-2-2H), 4.16 (tt, *J* = 6.5, 4.6 Hz, 1H, CH), 4.13 – 4.04 (m, 2H, N-CH_2), 3.73 (s, 3H, O-CH_3), 3.28 (dd, *J* = 12.9, 4.3 Hz, 1H, Ar-N-CH), 3.13 (dd, *J* = 12.9, 6.3 Hz, 1H, Ar-N-CH); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 165.9, 152.8, 145.4, 142.2, 129.0, 124.4, 123.0, 117.2, 115.5, 115.1, 115.0, 68.7, 67.6, 55.8, 49.0, 46.2; HR-MS (ESI): *m/z* calcd for $C_{18}H_{21}O_4N_2$ ($[M+H]^+$) 329.14958, found 329.14883.

4-(3-((2-chlorophenyl)amino)-2-hydroxypropyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (2d).

White solid; yield 48.92%; m.p. 109-110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar-3-H), 7.10 (ddd, *J* = 9.6, 6.2, 2.0 Hz, 2H, Ar-5,6-2H), 7.01 – 6.94 (m, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 6.70 – 6.61 (m, 2H, 1,4-benzoxazin-3-one-7-H, Ar-4-H), 4.80 – 4.71 (m, 1H, NH), 4.59 (s, 2H, 1,4-benzoxazin-3-one-2-2H), 4.23 – 4.16 (m, 1H, OH), 4.08 (d, *J* = 5.8 Hz, 2H, 1,4-benzoxazin-3-one-N-CH_2), 3.40 – 3.30 (m, 2H, Ar-NH-$\underline{CH_2}$), 3.24 (dt, *J* = 13.1, 5.8 Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 145.4, 143.8, 129.3, 128.9, 128.0, 124.5, 123.0, 120.0, 118.0, 117.3, 115.5, 111.7, 68.8, 67.6, 47.4, 46.2; HR-MS (ESI): *m/z* calcd for $C_{17}H_{18}O_3N_2Cl$ ($[M+H]^+$) 333.10005, found 333.10162.

4-(2-hydroxy-3-(piperazin-1-yl)propyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (3).

Yellow solid; yield 34.87%; m.p. 120-121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.32 (m, 1H, 1,4-benzoxazin-3-one-7-H), 7.02 (dddd, *J* = 12.0, 7.1, 4.5, 3.0 Hz, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 4.63 (d, *J* = 2.2 Hz, 2H, 1,4-benzoxazin-3- one-2-2H), 4.15 (dd, *J* = 14.3, 3.9 Hz, 1H, CH), 4.05 (ddt, *J* = 9.5, 6.7, 4.2 Hz, 1H, 1,4-benzoxazin-3-one-N-CH), 3.88 (dd, *J* = 14.3, 6.6 Hz, 1H, 1,4-benzoxazin- 3-one-N-CH), 2.92 (dq, *J* = 5.9, 3.0, 2.5 Hz, 4H, piperazin-2,6-4H), 2.68 – 2.59 (m, 2H, piperazin-N-CH_2), 2.54 – 2.40 (m, 4H, piperazin-3,5-4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 145.2, 129.2, 123.9, 122.7, 116.9, 116.1, 67.6, 65.2, 62.5, 54.5, 46.2, 45.8; HR-MS (ESI): *m/z* calcd for $C_{15}H_{22}O_3N_3$ ($[M+H]^+$) 292.16557, found 292.16544.

4-(2-hydroxy-3-(4-(3-methoxyphenyl)piperazin-1-yl)propyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4a).

White solid; yield 70.12%; m.p. 78-79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (ddd, *J* = 7.0, 3.8, 1.8 Hz, 1H, Ar-5-H), 7.16 (td, *J* = 8.2, 4.4 Hz, 1H, 1,4-benzoxazin-3-one-8-H), 7.01 (ddtd, *J* = 12.1, 7.2, 4.5, 2.5 Hz, 3H, 1,4-benzoxazin-3-one-1,6,7-3H), 6.56 – 6.36 (m, 3H,Ar-2,4,6-3H), 4.60 (t, *J* = 4.1 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.20 – 4.02 (m, 2H, N-CH_2), 3.89 (ddd, *J* = 10.0, 6.6, 3.3 Hz, 1H, CH), 3.77 (d, *J* = 4.5 Hz, 3H, O-CH_3), 3.16 (dq, *J* = 6.7, 3.5, 3.0 Hz, 4H, piperazin-3,5-4H), 2.74 (dt, *J* = 10.3, 5.3 Hz, 2H, piperazin-N-CH_2), 2.62 – 2.46 (m, 4H, piperazin-2,6-4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 160.6, 152.5, 145.3, 129.9, 129.3, 124.2, 122.8, 117.0, 116.2, 108.9, 104.6, 102.6, 67.7, 65.8, 61.7, 55.2, 53.3, 49.2, 46.4; HR-MS (ESI): *m/z* calcd for $C_{22}H_{28}O_4N_3$ ($[M+H]^+$) 398.20743, found 398.20688.

4-(3-(4-(4-fluorophenyl)piperazin-1-yl)-2-hydroxypropyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4b).

Yellow solid; yield 74.72%; m.p. 105-106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.36 (m, 1H, Ar-3-H), 7.09 – 6.95 (m, 5H, Ar-5-H, 1,4-benzoxazin-3-one-5,6,7,8-4H), 6.92 – 6.86 (m, 2H, Ar-2,6-2H), 4.65 (d, *J* = 2.1 Hz, 2H, 1,4-

benzoxazin-3-one-2-2H), 4.20 (dd, *J* = 14.4, 3.9 Hz, 1H, CH), 4.10 (ddt, *J* = 8.7, 6.5, 4.3 Hz, 1H, 1,4-benzoxazin-3-one-N-CH), 3.92 (dd, *J* = 14.3, 6.5 Hz, 1H, 1,4-benzoxazin-3-one-N-CH), 3.13 (dt, *J* = 6.5, 3.3 Hz, 4H, piperazin3,5-4H), 2.82 (ddd, *J* = 10.6, 5.9, 3.7 Hz, 2H, piperazin-N-CH_2), 2.68 – 2.51 (m, 4H, piperazin2,6-4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 158.4, 156.0, 147.8, 145.3, 129.3, 124.2, 122.8, 117.8, 117.8, 117.0, 116.2, 115.7, 115.4, 67.6, 65.7, 61.8, 53.3, 50.2, 46.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.30; HR-MS (ESI): *m/z* calcd for $C_{21}H_{25}O_3N_3F$ ($[M+H]^+$) 386.18745, found 386.18692.

4-(3-(4-(2,4-difluorobenzyl)piperazin-1-yl)-2-hydroxypropyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4c).

White solid; yield 48.50%; m.p. 64-65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 2H, Ar-6,3-2H), 7.04 – 6.96 (m, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 6.81 (dtd, *J* = 25.1, 9.5, 9.0, 2.6 Hz, 2H, Ar-5-H, 1,4-benzoxazin-3-one-7-H), 4.61 (d, *J* = 1.8 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.13 (dd, *J* = 14.3, 3.9 Hz, 1H, CH), 4.01 (dq, *J* = 10.8, 4.2, 3.4 Hz, 1H, N-CH), 3.85 (dd, *J* = 14.4, 6.6 Hz, 1H, N-CH), 3.53 (s, 2H, Ar-CH_2), 2.64 (d, *J* = 8.5 Hz, 2H, piperazin-N-CH_2), 2.46 (qd, *J* = 12.5, 7.1 Hz, 8H, piperazin-2,3,5,6-8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 145.3, 129.3, 124.2, 122.8, 120.5, 120.5, 120.4, 120.3, 117.0, 116.2, 111.2, 110.9, 103.9, 103.6, 103.4, 67.7, 65.6, 61.4, 54.7, 52.8, 46.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.70, -113.67; HR-MS (ESI): *m/z* calcd for $C_{22}H_{26}O_3N_3F_2$ ($[M+H]^+$) 418.19367, found 418.19299.

4-(3-(4-(3-chlorobenzyl)piperazin-1-yl)-2-hydroxypropyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4d).

Yellow liquid; yield 63.22%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 1H, Ar-6-H), 7.24 (q, *J* = 1.5 Hz, 1H, Ar-4-H), 7.17 – 7.13 (m, 2H, Ar-2,3-2H), 7.10 (ddd, *J* = 6.0, 3.0, 1.6 Hz, 1H, 1,4-benzoxazin-3-one-7-H), 6.97 – 6.89 (m, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 4.54 (d, *J* = 2.2 Hz, 2H, 1,4-benzoxazin- 3-one-2-2H), 4.05 (dd, *J* = 14.3, 3.9 Hz, 1H, CH), 3.99 – 3.92 (m, 1H, N-CH), 3.79 (dd, *J* = 14.3, 6.6 Hz, 1H, N-CH), 3.39 (d, *J* = 1.6 Hz, 2H, Ar-CH_2), 2.58 (d, *J* = 7.5 Hz, 2H, piperazin-N-CH_2), 2.52 – 2.29 (m, 8H, piperazin-2,3,5,6-8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 145.3, 140.2, 134.2, 129.5, 129.3, 129.1, 127.3, 127.2, 124.2, 122.8, 117.0, 116.2, 67.7, 65.6, 62.3, 61.5, 53.0, 46.3; HR-MS (ESI): *m/z* calcd for $C_{22}H_{27}O_3N_3Cl$ ($[M+H]^+$) 4416.17355, found 416.17322.

4-(3-(4-(4-chlorobenzyl)piperazin-1-yl)-2-hydroxypropyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4e).

Yellow solid; yield 42.40%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 1H, 1,4-benzoxazin-3-one-7-H), 7.30 – 7.22 (m, 4H, Ar-2,3,5,6-4H), 7.01 (qdt, *J* = 7.4, 5.0, 2.9 Hz, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 4.61 (d, *J* = 2.1 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.13 (dd, *J* = 14.4, 3.8 Hz, 1H, CH), 4.01 (ddt, *J* = 8.5, 6.5, 4.2 Hz, 1H, N-CH), 3.86 (dd, *J* = 14.4, 6.6 Hz, 1H, N-CH), 3.46 (s, 2H, Ar-CH_2), 2.64 (d, *J* = 6.7 Hz, 2H, piperazin-N-CH_2), 2.59 – 2.30 (m, 8H, piperazin-2,3,5,6-4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 145.3, 136.6, 132.8, 130.4, 129.3, 128.4, 124.2, 122.8,

117.0, 116.2, 67.7, 65.6, 62.2, 61.4, 53.1, 46.4; HR-MS (ESI): *m/z* calcd for $C_{22}H_{27}O_3N_3Cl$ ([M+H]$^+$) 416.17355, found 4.17291.

4-(2-hydroxy-3-(4-(3-nitrobenzyl)piperazin-1-yl)propyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4f).

Yellow solid; yield 47.47%; m.p. 105-107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (t, *J* = 2.0 Hz, 1H, Ar-2-H), 8.11 (dd, *J* = 8.2, 2.3 Hz, 1H, Ar-4-H)), 7.66 (d, *J* = 7.6 Hz, 1H, Ar-6-H)), 7.49 (t, *J* = 7.9 Hz, 1H, Ar-5-H)), 7.38 – 7.32 (m, 1H, 1,4-benzoxazin-3-one-7-H), 7.01 (ddt, *J* = 11.5, 6.9, 3.7 Hz, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 4.62 (d, *J* = 2.1 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.14 (dd, *J* = 14.4, 3.7 Hz, 1H, CH), 4.02 (ddd, *J* = 14.2, 7.6, 4.2 Hz, 1H, 1,4-benzoxazin-3-one-N-H), 3.87 (dd, *J* = 14.4, 6.6 Hz, 1H, 1,4-benzoxazin-3-one-N-H), 3.59 (s, 2H, Ar-CH_2), 2.66 (q, *J* = 8.2 Hz, 2H, piperazin-N-CH_2), 2.59 – 2.39 (m, 8H, piperazin-2,3,5,6-8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 148.4, 145.3, 140.6, 135.0, 129.3, 129.2, 124.2, 123.7, 122.8, 122.3, 117.0, 116.2, 67.7, 65.6, 62.0, 61.4, 53.2, 46.3; HR-MS (ESI): *m/z* calcd for $C_{22}H_{27}O_5N_4$ ([M+H]$^+$) 427.19760, found 427.19708.

4-(2-hydroxy-3-(4-methylpiperazin-1-yl)propyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4g).

Yellow liquid; yield 64.96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 7.1, 2.2 Hz, 1H, 1,4-benzoxazin-3-one-7-H), 7.04 – 6.97 (m, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 4.60 (d, *J* = 2.7 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.13 (dd, *J* = 14.3, 3.8 Hz, 1H, N-CH), 4.03 (ddd, *J* = 9.0, 6.7, 4.4 Hz, 1H, CH), 3.87 (dd, *J* = 14.3, 6.6 Hz, 1H, N-CH), 2.64 (t, *J* = 8.7 Hz, 2H, piperazin-N-CH_2-2H), 2.46 (qd, *J* = 11.3, 10.1, 5.7 Hz, 8H, piperazin-2,3,5,6-8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 145.3, 129.3, 124.1, 122.7, 117.0, 116.1, 67.7, 65.6, 61.5, 55.2, 53.2, 46.3, 46.0; HR-MS (ESI): *m/z* calcd for $C_{16}H_{24}O_3N_3$ ([M+H]$^+$) 306.18122, found 306.18073.

4-(3-(4-acetylpiperazin-1-yl)-2-hydroxypropyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4h).

Yellow solid; yield 87.20%; m.p. 126-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 1H, 1,4-benzoxazin-3-one-7-H), 7.00 (dtt, *J* = 8.9, 4.4, 2.4 Hz, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 4.60 (t, *J* = 2.2 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.14 (dd, *J* = 14.2, 3.9 Hz, 1H, N-CH), 4.10 – 4.03 (m, 1H, CH), 3.90 (ddd, *J* = 14.2, 6.6, 1.9 Hz, 1H, N-CH), 3.59 (dt, *J* = 6.7, 3.5 Hz, 2H, piperazin-3-2H), 3.49 – 3.42 (m, 2H, piperazin-5-2H), 2.62 – 2.39 (m, 6H, piperazin-2,6-4H, piperazin-N-CH_2), 2.07 (d, *J* = 2.1 Hz, 3H, N-CO-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 165.3, 145.3, 129.2, 124.2, 122.8, 117.0, 116.0, 67.6, 65.8, 61.7, 53.4, 53.0, 46.3, 46.2, 41.4, 21.3; HR-MS (ESI): *m/z* calcd for $C_{17}H_{24}O_4N_3$ ([M+H]$^+$) 334.17613, found 334.17548.

4-(2-hydroxy-3-(4-(2-hydroxypropyl)piperazin-1-yl)propyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4i).

Yellow solid; yield 76.83%; m.p. 104-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 1H, 1,4-benzoxazin-3-one-7-H), 7.00 (pq, *J* = 6.2, 2.8 Hz, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 4.61 (d, *J* = 2.4 Hz, 2H, 1,4-benzoxazin- 3-one-2-2H), 4.13 (dd, *J* = 14.3, 3.8 Hz, 1H, 1,4-benzoxazin- 3-one-N-CH_2-CH), 4.03 (ddd, *J* = 8.8, 6.6, 4.3 Hz, 1H, 1,4-

benzoxazin-3-one-N-CH), 3.90 – 3.78 (m, 2H, 1,4-benzoxazin-3-one-N-CH, CH), 2.76 – 2.32 (m, 10H, piperazin-2,3,5,6-8H, piperazin-N-CH, piperazin-N-CH), 2.31 – 2.20 (m, 2H, piperazin-N-CH, piperazin-N-CH), 1.12 (d, *J* = 6.1 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 145.3, 129.3, 124.1, 122.7, 117.0, 116.1, 67.7, 65.6, 62.3, 61.6, 53.3, 46.3, 29.7, 20.0; HR-MS (ESI): *m/z* calcd for $C_{18}H_{28}O_4N_3$ ($[M+H]^+$) 305.20743, found 305.20688.

4-(2-hydroxy-3-(4-(2-hydroxy-2-phenylethyl)piperazin-1-yl)propyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4j).

White liquid; yield 70.52%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 5H, Ar-2,6,3,5,4 -5H), 7.22 – 7.17 (m, 1H, 1,4-benzoxazin-3-one-7-H), 6.93 (tdd, *J* = 11.2, 6.4, 3.0 Hz, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 4.66 (ddd, *J* = 9.5, 4.4, 2.9 Hz, 1H, Ar-CH), 4.55 – 4.51 (m, 2H, 1,4-benzoxazin-3-one-2-2H), 4.11 – 4.02 (m, 1H, CH), 4.01 – 3.93 (m, 1H, 1,4-benzoxazin-3-one-N-CH), 3.84 – 3.76 (m, 1H, 1,4-benzoxazin-3-one-N-CH), 2.77 – 2.54 (m, 4H, piperazin-N-CH_2, piperazin-N-CH_2), 2.51 – 2.30 (m, 8H, piperazin-2,3,5,6-8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 145.3, 141.9, 135.5, 129.3, 128.9, 128.4, 128.1, 127.6, 125.9, 124.2, 122.8, 117.0, 116.1, 69.9, 68.8, 67.7, 66.1, 65.6, 61.5, 60.5, 53.3, 46.3; HR-MS (ESI): *m/z* calcd for $C_{23}H_{30}O_4N_3$ ($[M+H]^+$) 412.22308, found 412.22375.

4-(3-(4-((2-chlorophenyl)sulfonyl)piperazin-1-yl)-2-hydroxypropyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4k).

Yellow liquid; yield 63.75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar-6-H), 7.57 – 7.47 (m, 2H, Ar-3,4-2H), 7.41 (ddd, *J* = 7.9, 6.9, 1.8 Hz, 1H, Ar-5-H), 7.29 – 7.25 (m, 1H, 1,4-benzoxazin-3-one-7-H), 7.05 – 6.93 (m, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 4.60 (d, *J* = 1.6 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.11 (dd, *J* = 14.3, 3.9 Hz, 1H, CH), 4.01 (ddt, *J* = 8.7, 6.5, 4.2 Hz, 1H, 1,4-benzoxazin-3-one-N-CH), 3.87 (dd, *J* = 14.3, 6.5 Hz, 1H, 1,4-benzoxazin-3-one-N-CH), 3.31 (dt, *J* = 6.6, 3.3 Hz, 4H, piperazin-3,5-4H), 2.66 (dt, *J* = 10.5, 5.0 Hz, 2H, piperazin-N-CH_2), 2.57 – 2.41 (m, 4H, piperazin-2,6-4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 145.3, 135.9, 133.8, 132.3, 132.1, 129.2, 127.1, 124.3, 122.8, 117.1, 116.0, 67.7, 65.7, 61.4, 52.8, 46.1, 45.7; HR-MS (ESI): *m/z* calcd for $C_{21}H_{25}O_5N_3ClS$ ($[M+H]^+$) 466.11980, found 466.11935.

methyl-1-(2-hydroxy-3-(4-(2-hydroxy-3-(3-oxo-2,3-dihydro-4*H*-benzo[*b*][1,4]oxazin-4-yl)propyl)piperazin-1-yl)propyl)-1*H*-indole-6-carboxylate (4l).

White liquid; yield 77.84%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H, indole-4-H), 7.77 (dd, *J* = 8.4, 1.4 Hz, 1H, indole-7-H), 7.60 (d, *J* = 8.2 Hz, 1H, indole-5-H), 7.35 (d, *J* = 3.1 Hz, 1H, indole-2-H), 7.30 (ddd, *J* = 7.0, 2.7, 1.3 Hz, 1H, 1,4-benzoxazin-3-one-7-4H), 7.02 – 6.94 (m, 3H, 1,4-benzoxazin-3-one-5,6,8-4H), 6.52 (dd, *J* = 3.2, 0.9 Hz, 1H, indole-3-H), 4.58 (d, *J* = 3.3 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.25 (dd, *J* = 14.7, 3.9 Hz, 1H, 1,4-benzoxazin-3-one-N-CH_2-CH), 4.15 (dd, *J* = 14.6, 6.1 Hz, 1H, indole-N-CH), 4.08 (dd, *J* = 14.4, 4.0 Hz, 1H, indole-N-CH), 4.06 – 3.98 (m, 2H, 1,4-benzoxazin-3-one-N-CH_2), 3.91 (s, 3H, CH_3), 3.84 (ddd, *J* = 14.3, 6.6, 1.3 Hz, 1H, indole-N-CH_2-CH), 2.57 (s, 4H, piperazin-N-CH_2, piperazin-N-CH_2), 2.49 – 2.23 (m, 8H, piperazin-2,3,5,6-8H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 168.3, 165.9, 165.3, 145.3, 135.9, 132.3, 129.3, 128.7, 124.6, 124.2, 123.2, 123.0, 122.8, 120.5, 117.2, 117.0, 116.1, 115.5, 111.9, 101.9, 69.6, 67.7, 67.5, 63.6, 52.0, 49.9, 46.2, 44.2; HR-MS (ESI): *m/z* calcd for $C_{26}H_{35}O_6N_4$ ($[M+H]^+$) 523.25511, found 523.25476.

4-(3-(4-(3-(6-fluoro-1*H*-indol-1-yl)-2-hydroxypropyl)piperazin-1-yl)-2-hydroxypropyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4m).

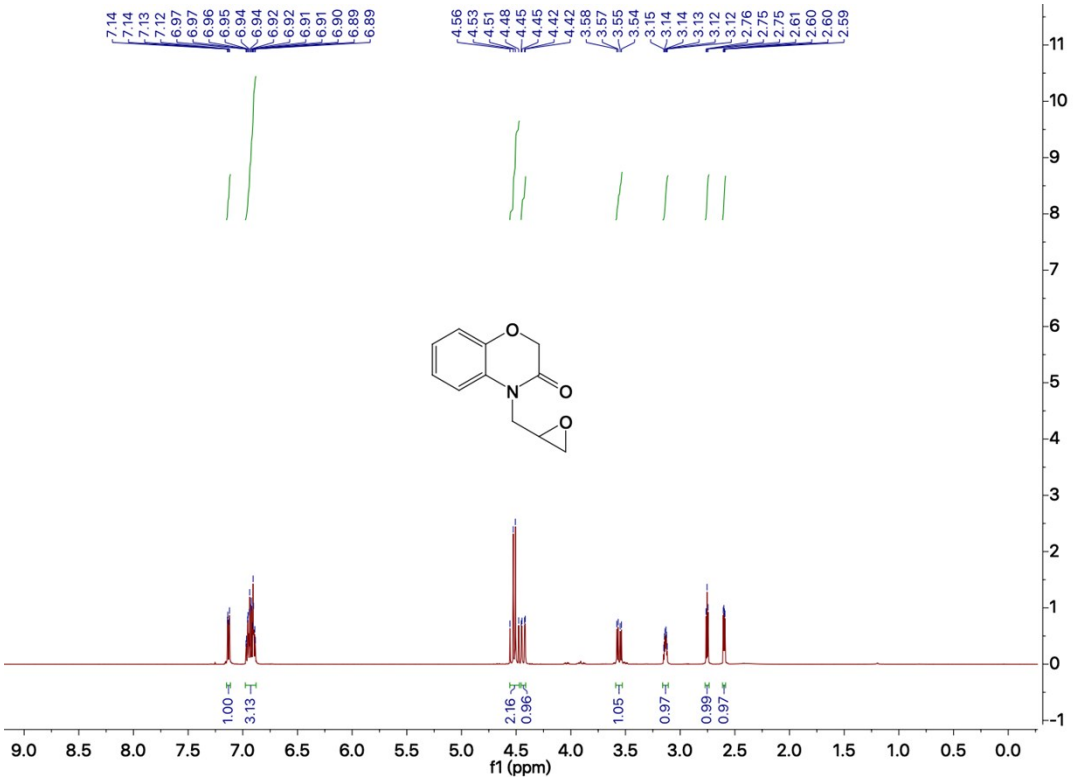
Pale red solid; yield 46.59%; m.p. 89-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 8.6, 5.4 Hz, 1H, indole-4-H), 7.34 – 7.30 (m, 1H, indole-2-H), 7.14 (d, *J* = 3.2 Hz, 1H, indole-5-H), 7.07 – 6.97 (m, 4H, 1,4-benzoxazin-3-one-5,6,7,8-4H), 6.86 (ddd, *J* = 9.6, 8.6, 2.3 Hz, 1H, indole-7-H), 6.47 (dd, *J* = 3.2, 0.9 Hz, 1H, indole-3-H), 4.60 (d, *J* = 2.5 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.18 – 4.05 (m, 3H, 1,4-benzoxazin-3-one-N-CH_2-CH, 1,4-benzoxazin-3-one-N-CH_2), 4.04 – 3.98 (m, 2H, indole-N-CH_2), 3.85 (ddd, *J* = 14.4, 6.6, 1.3 Hz, 1H, indole-N-CH_2-CH), 2.62 (s, 4H, piperazin-N-CH_2, piperazin-N-CH_2), 2.49 – 2.25 (m, 8H, piperazin-2,3,5,6-8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 161.0, 158.6, 145.3, 136.7, 129.3, 124.9, 124.2, 122.8, 121.7, 121.6, 117.0, 116.1, 108.3, 108.1, 101.7, 96.2, 95.9, 67.7, 66.2, 65.6, 61.5, 61.0, 53.2, 50.0, 46.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.06; HR-MS (ESI): *m/z* calcd for $C_{26}H_{32}O_4N_4F$ ($[M+H]^+$) 483.24021, found 483.23828.

4-(3-(4-(3-(9*H*-carbazol-9-yl)-2-hydroxypropyl)piperazin-1-yl)-2-hydroxypropyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4n).

Yellow liquid; yield 63.80%; $[\alpha]^{25}_D$ = 0.991 (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 7.7, 1.1 Hz, 2H, carbazole-5,6-2H), 7.48 – 7.42 (m, 4H, carbazole-2,3,8,9-4H), 7.33 – 7.28 (m, 1H, 1,4-benzoxazin-3-one-7-H), 7.23 (ddd, *J* = 7.9, 6.0, 2.2 Hz, 2H, carbazole-4,7-2H), 6.99 (dddd, *J* = 8.0, 4.9, 3.3, 1.9 Hz, 3H, 1,4-benzoxazin-3-one-5,6,8-3H), 5.28 (s, 1H, carbazole-N-CH_2-CH-OH), 4.59 (d, *J* = 2.2 Hz, 2H, 1,4-benzoxazin-3-one-2-2H), 4.36 (d, *J* = 5.3 Hz, 2H, carbazole-N-CH_2), 4.23 – 4.14 (m, 1H, 1,4-benzoxazin-3-one-N-CH_2-CH), 4.09 (dd, *J* = 14.4, 3.9 Hz, 1H, 1,4-benzoxazin-3-one-N-CH), 3.97 (ddtd, *J* = 8.7, 6.4, 4.3, 2.2 Hz, 1H, 1,4-benzoxazin-3-one-N-CH), 3.83 (dd, *J* = 14.4, 6.6 Hz, 1H, carbazole-N-CH_2-CH), 2.57 (t, *J* = 8.5 Hz, 4H, piperazin-N-CH_2, piperazin-N-CH_2), 2.49 – 2.25 (m, 8H, piperazin-2,3,5,6-8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 145.3, 141.0, 129.3, 125.8, 124.2, 123.0, 122.8, 120.3, 119.2, 117.0, 116.1, 109.2, 67.7, 66.4, 66.3, 65.6, 65.6, 61.7, 61.4, 61.4, 53.2, 47.1, 46.2; HR-MS (ESI): *m/z* calcd for $C_{30}H_{35}O_4N_4$ ($[M+H]^+$) 515.26528, found 515.26434.

4. Spectrograms of ^{1}H NMR and ^{13}C NMR and ^{19}F NMR and HRMS of compounds

^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 1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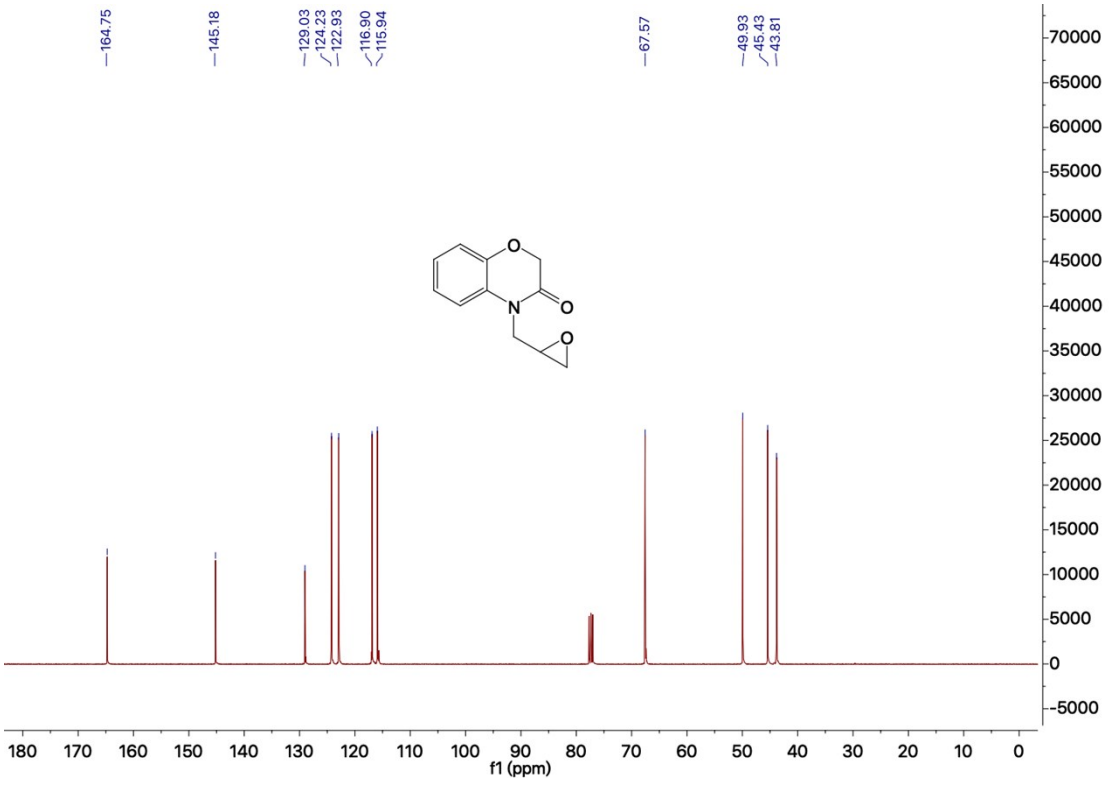
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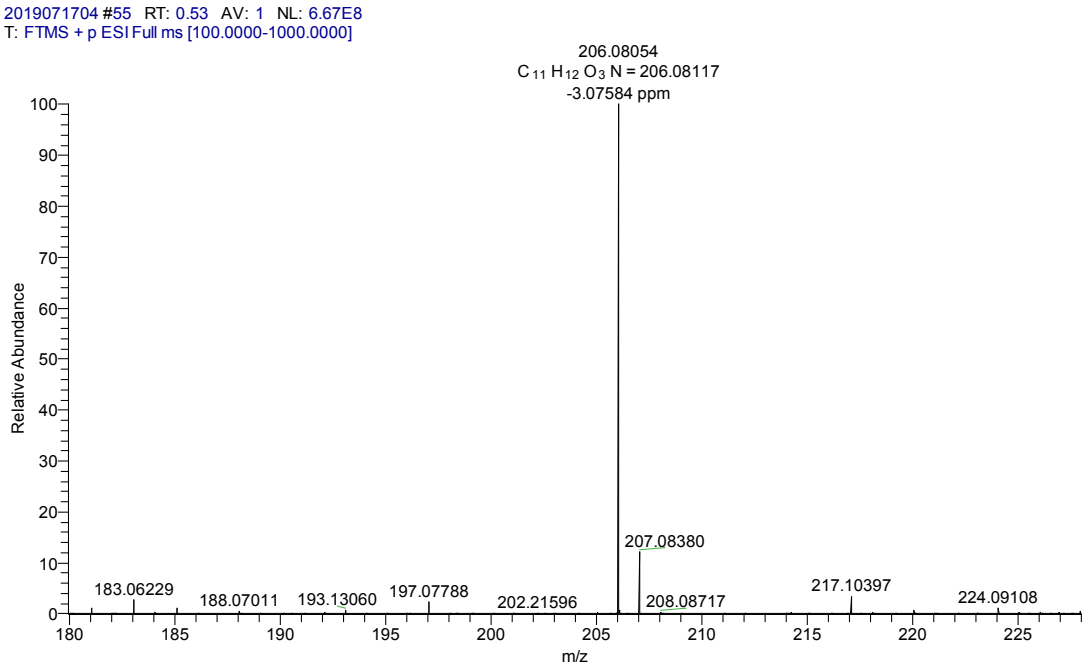
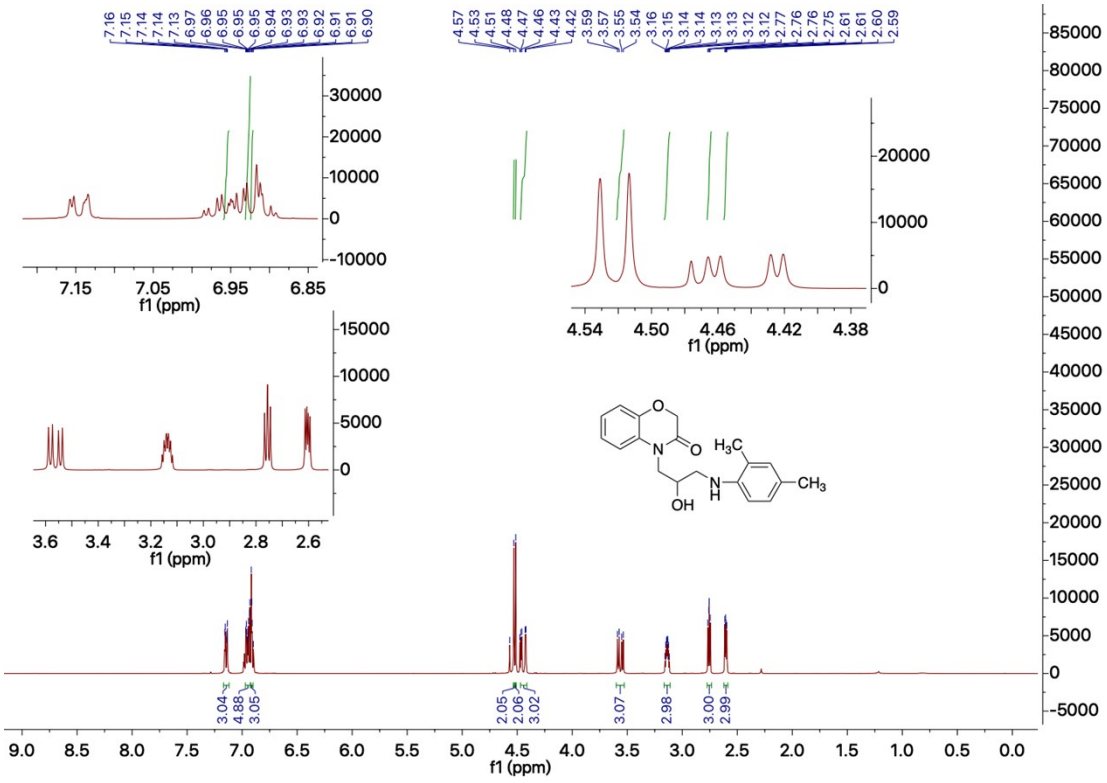
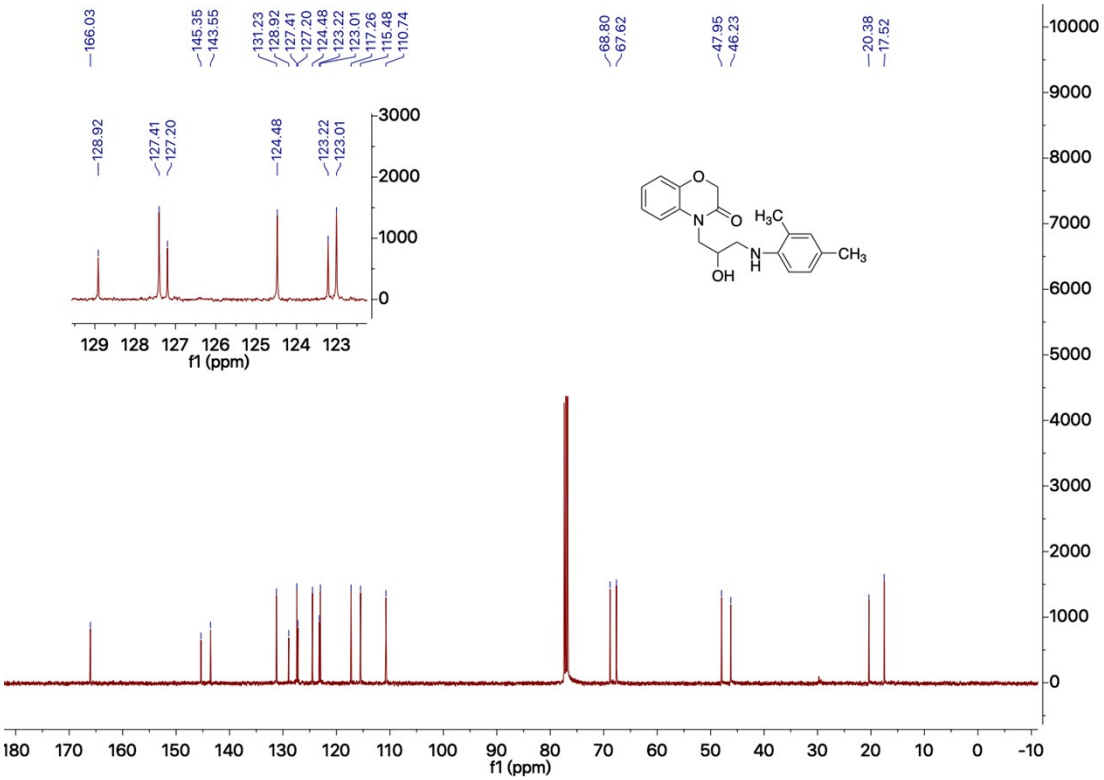
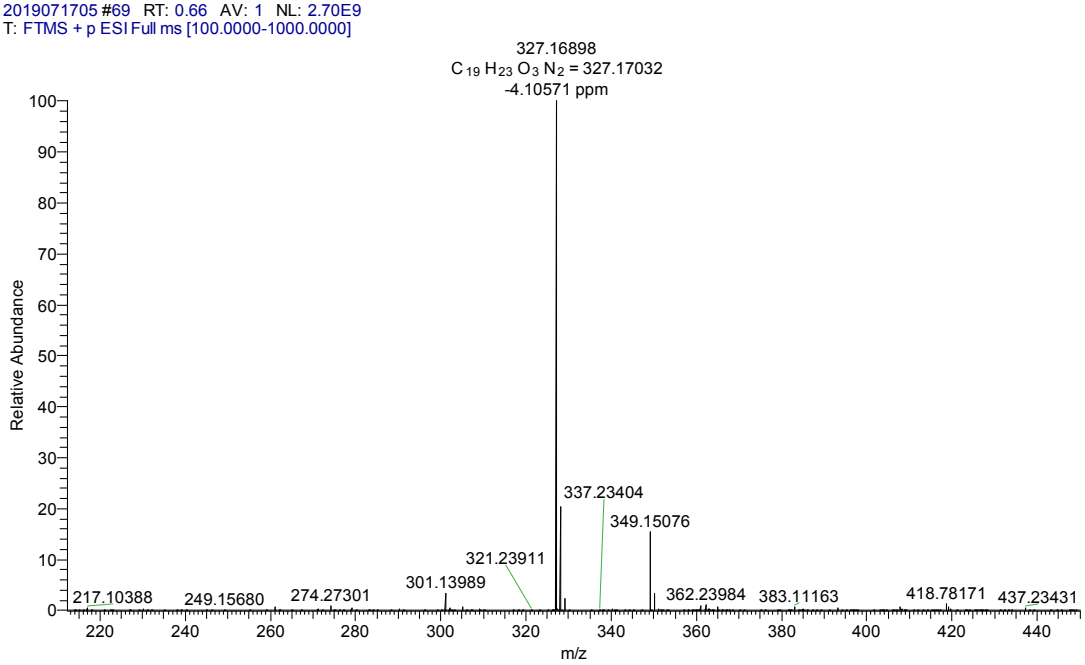


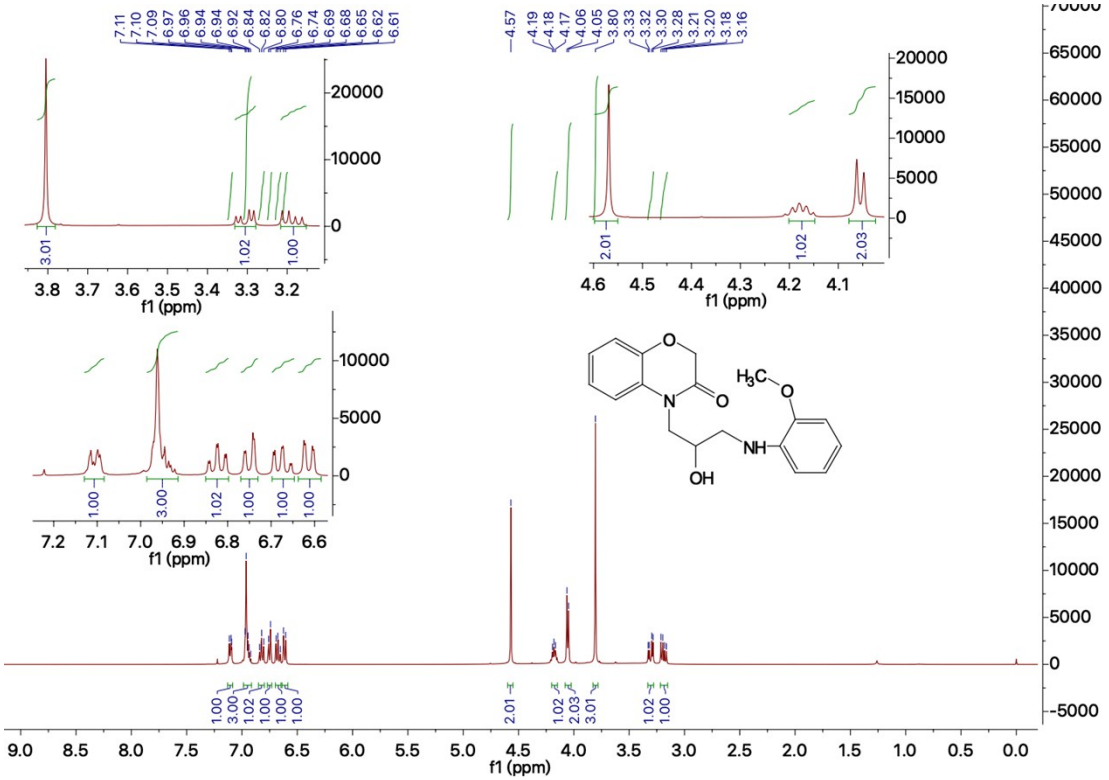
^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 2a







^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 2b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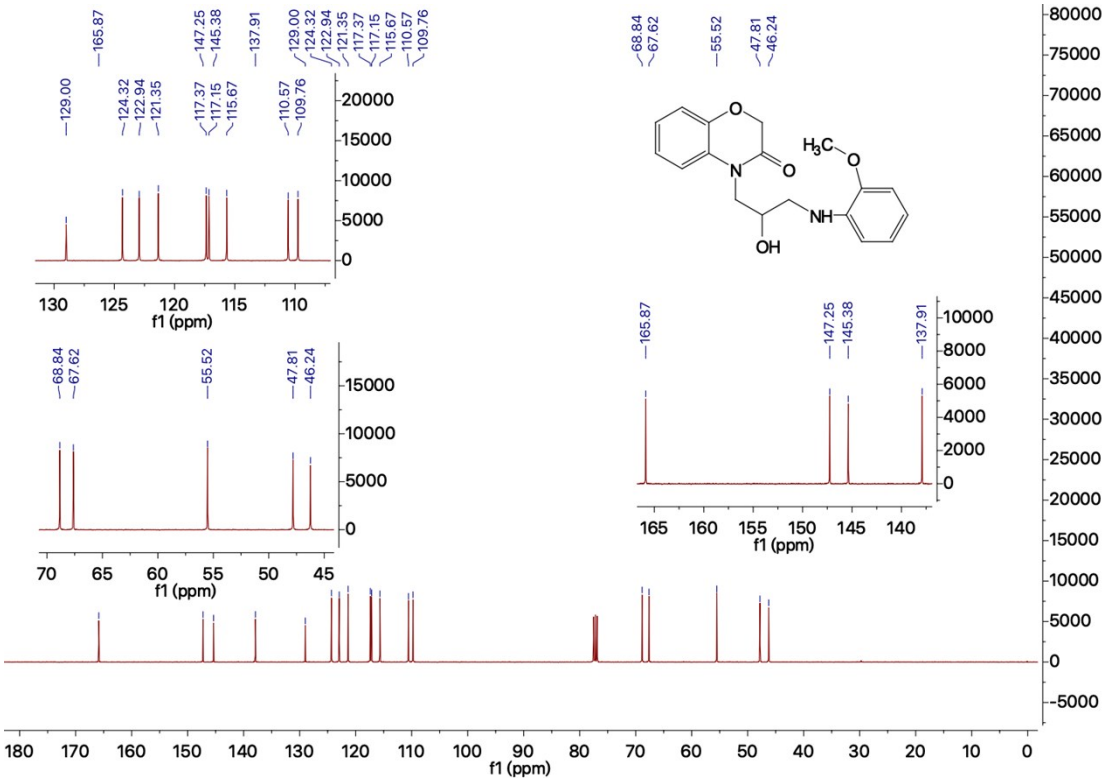
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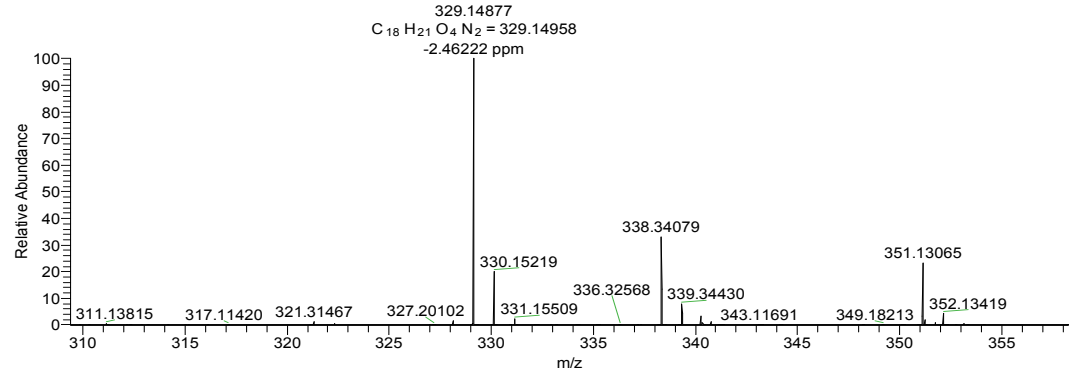
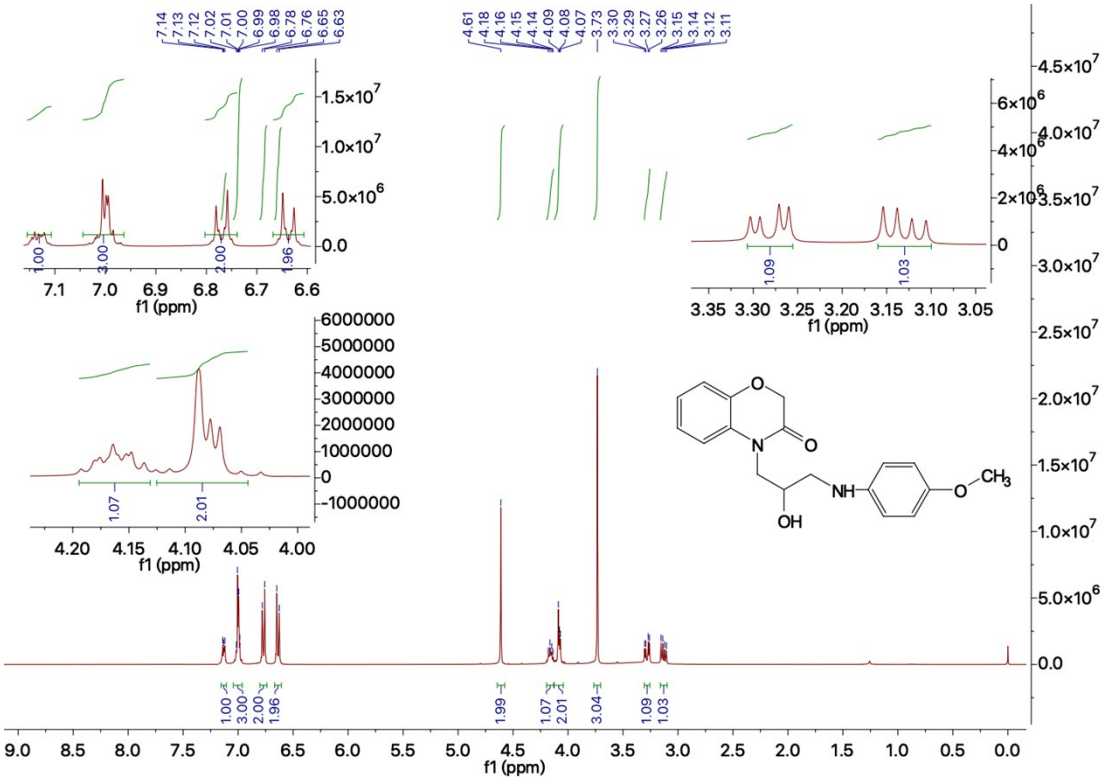
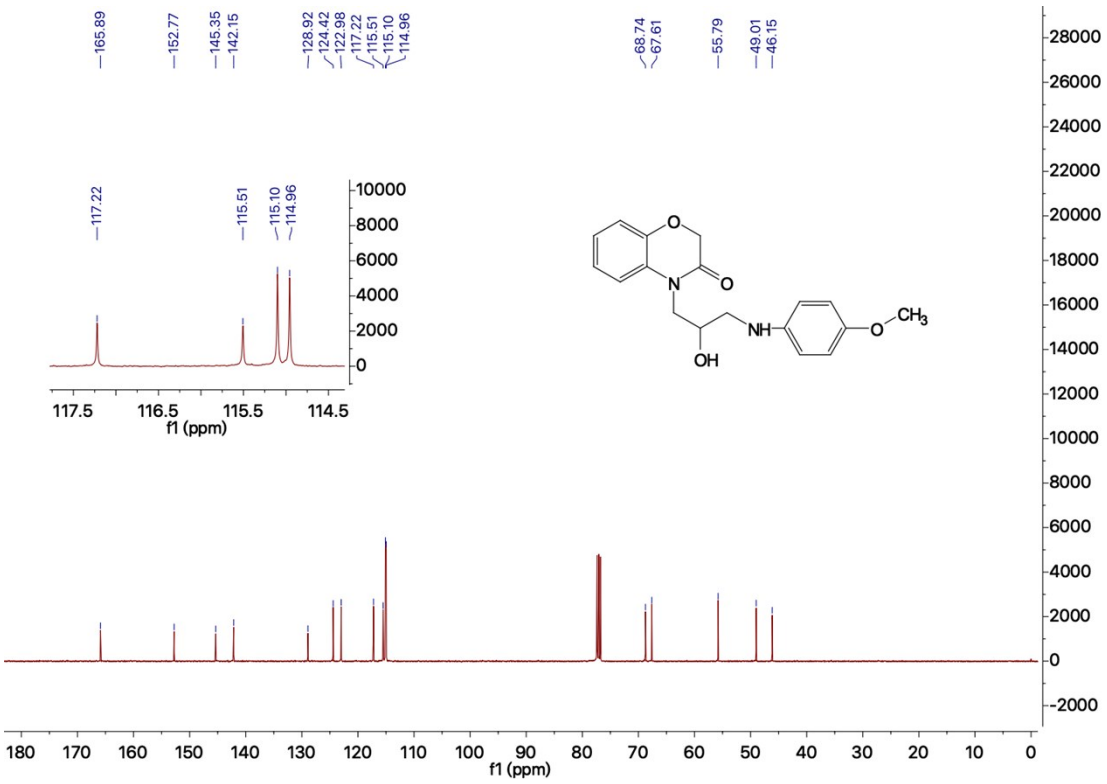
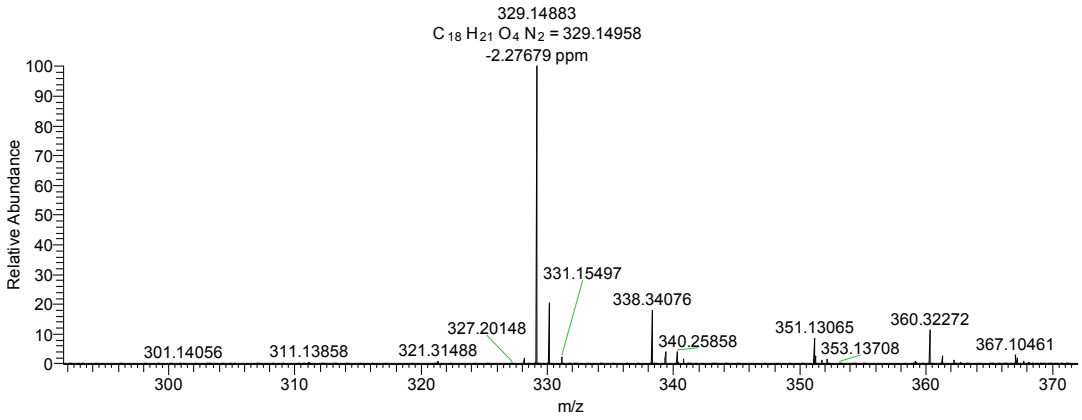


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 2c

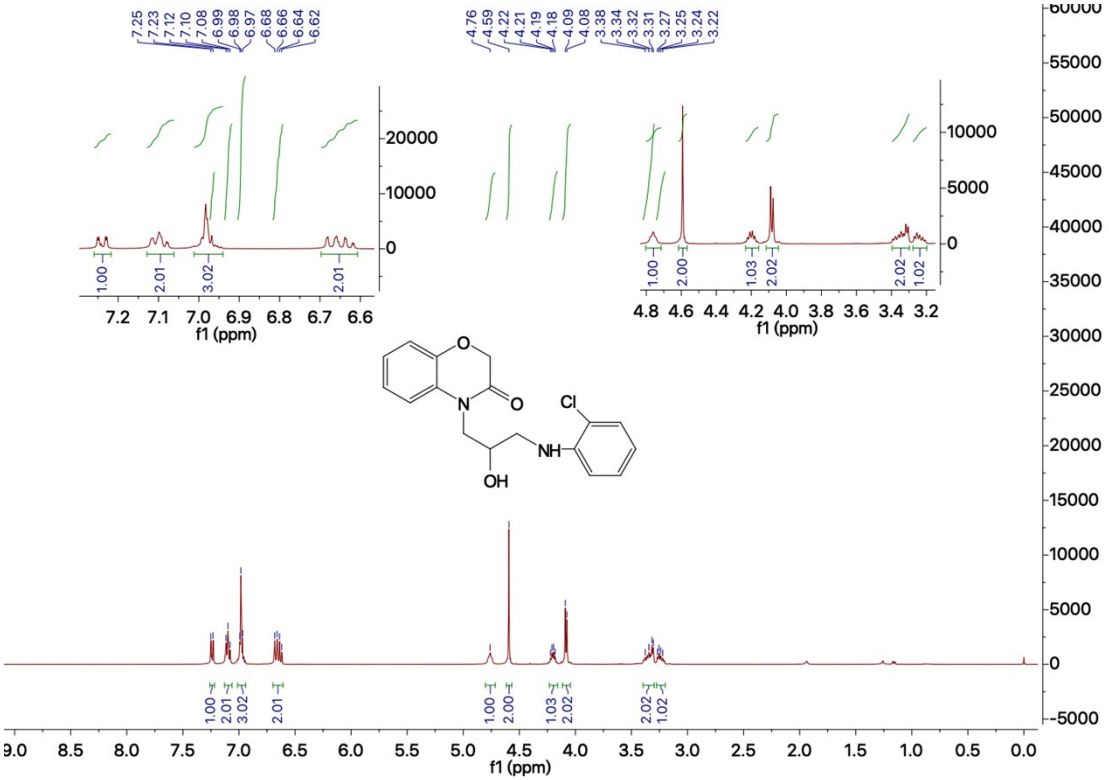


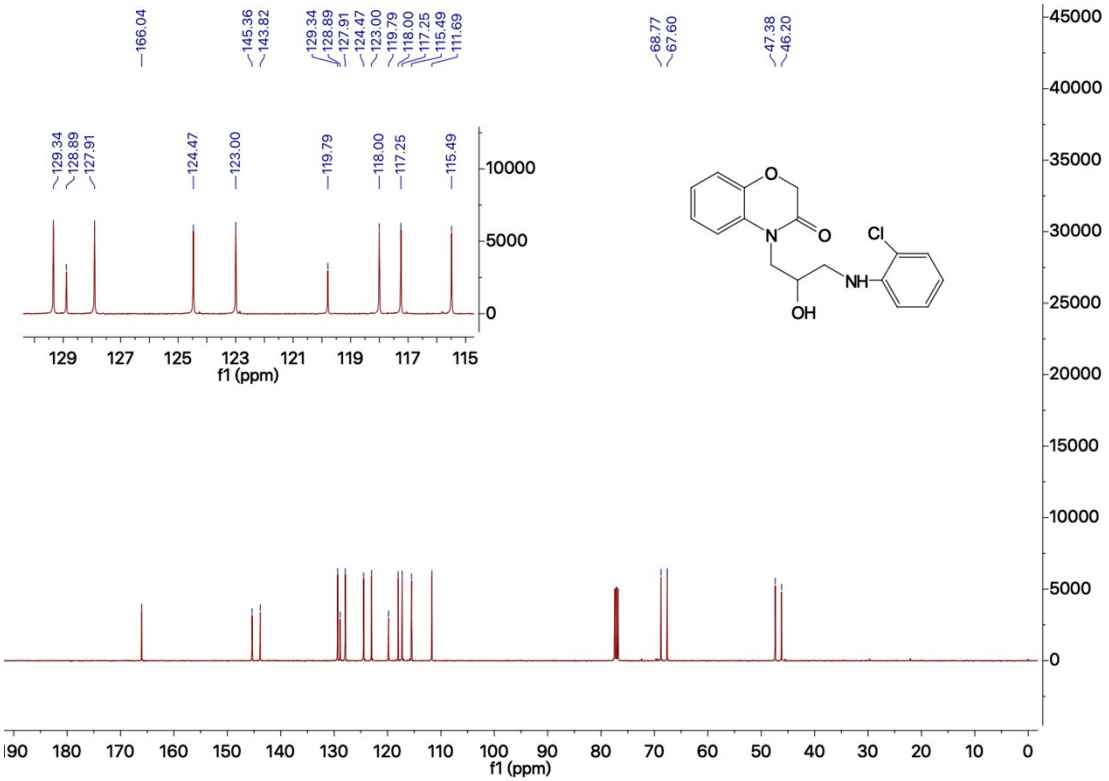


2018120744 #81 RT: 0.80 AV: 1 NL: 5.51E8
T: FTMS + p ESI Full ms [100.0000-1000.0000]

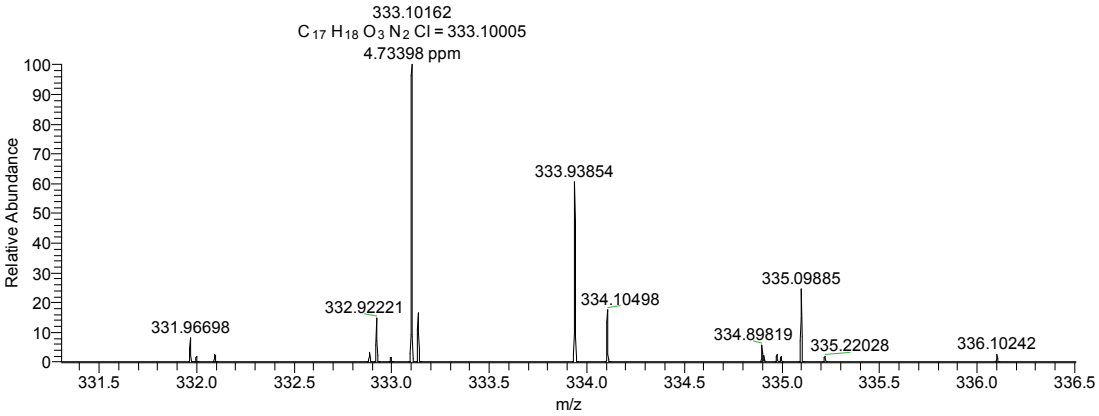


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 2d

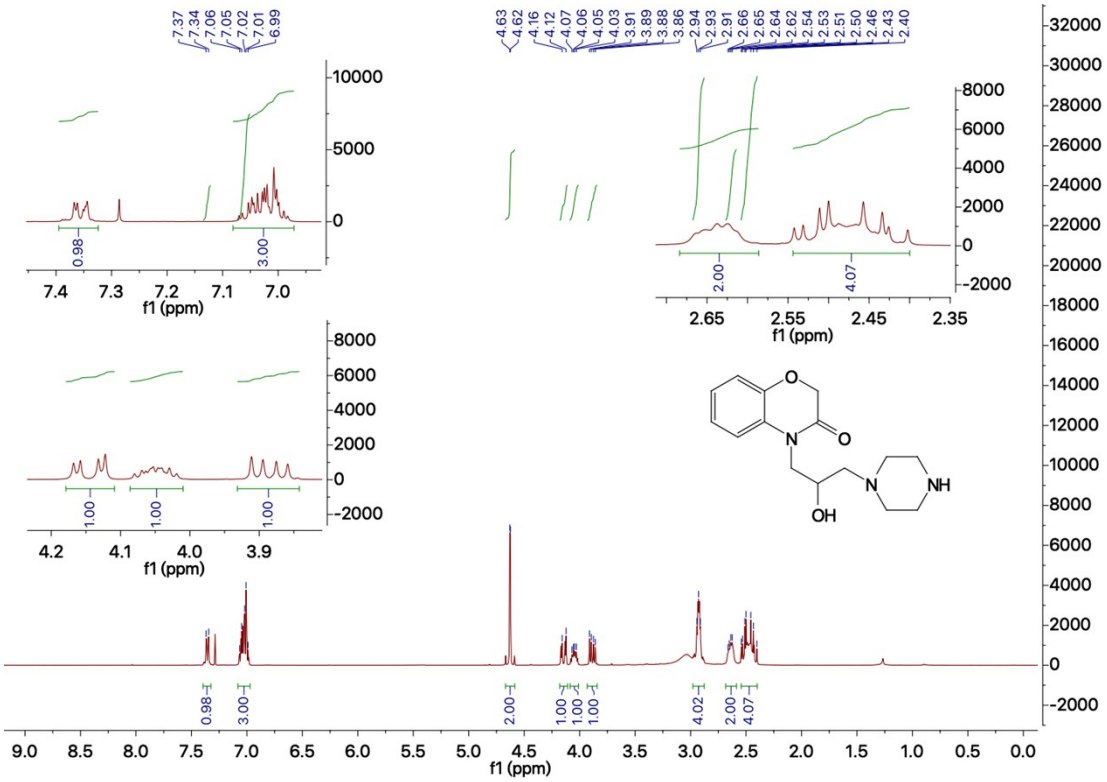

7.25
7.23
7.12
7.10
7.08
6.99
6.98
6.97
6.68
6.66
6.64
6.62
4.76
4.59
4.22
4.21
4.19
4.18
4.09
4.08
3.38
3.34
3.32
3.31
3.27
3.25
3.24
3.22
1.00
2.01
3.02
2.01
1.00
2.00
1.03
2.02
2.02
1.02
f1 (ppm)
O
N
O
Cl
NH
OH

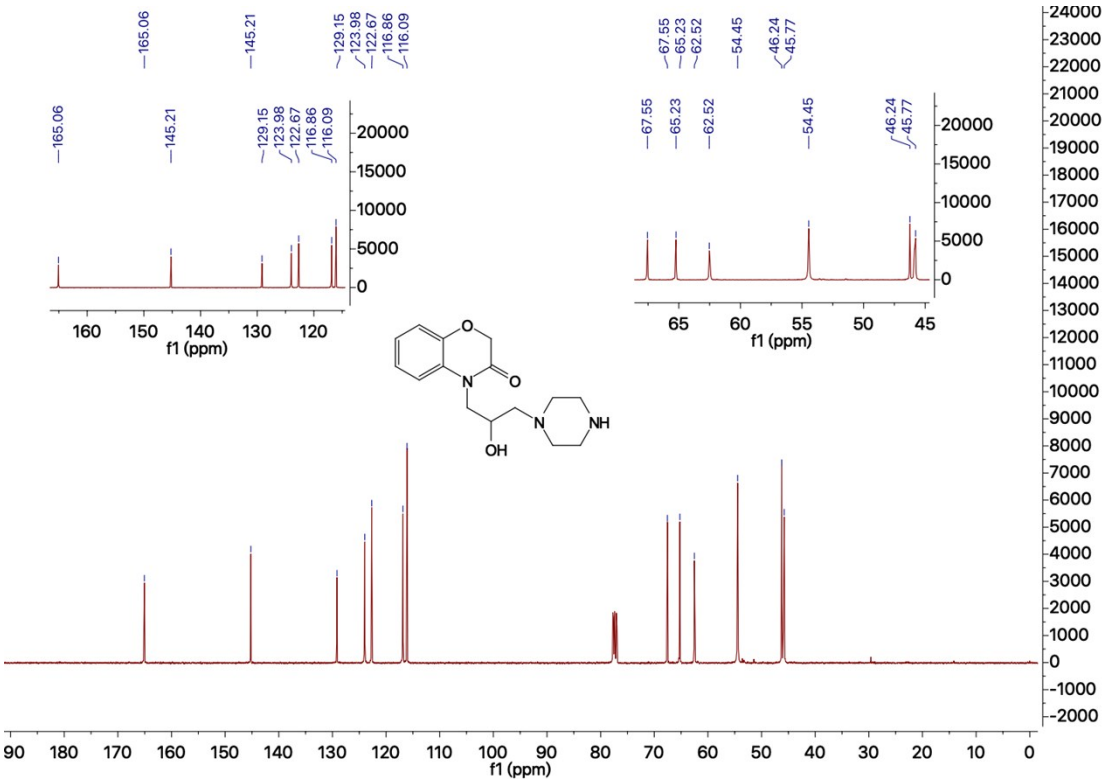

166.04
145.36
143.82
129.34
128.89
127.91
124.47
123.00
119.79
118.00
117.25
115.49
111.69
68.77
67.60
47.38
46.20
f1 (ppm)
O
N
O
Cl
NH
OH

2019062802 #44 RT: 0.43 AV: 1 NL: 5.95E5
T: FTMS - p ESI Full ms [100.0000-1000.0000]

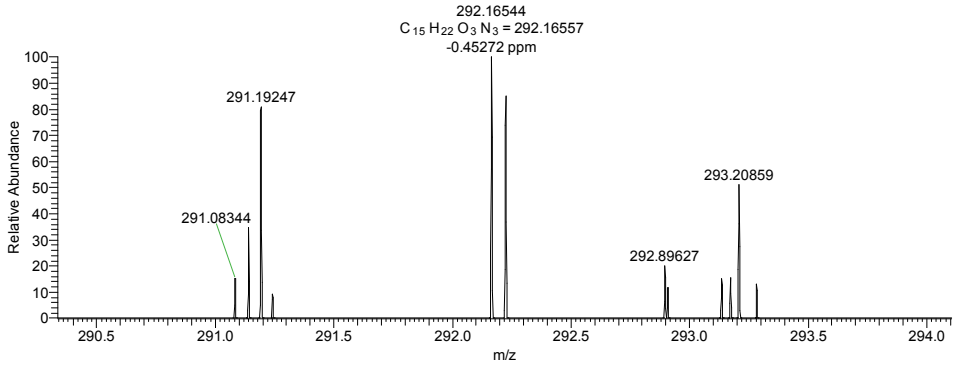


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 3

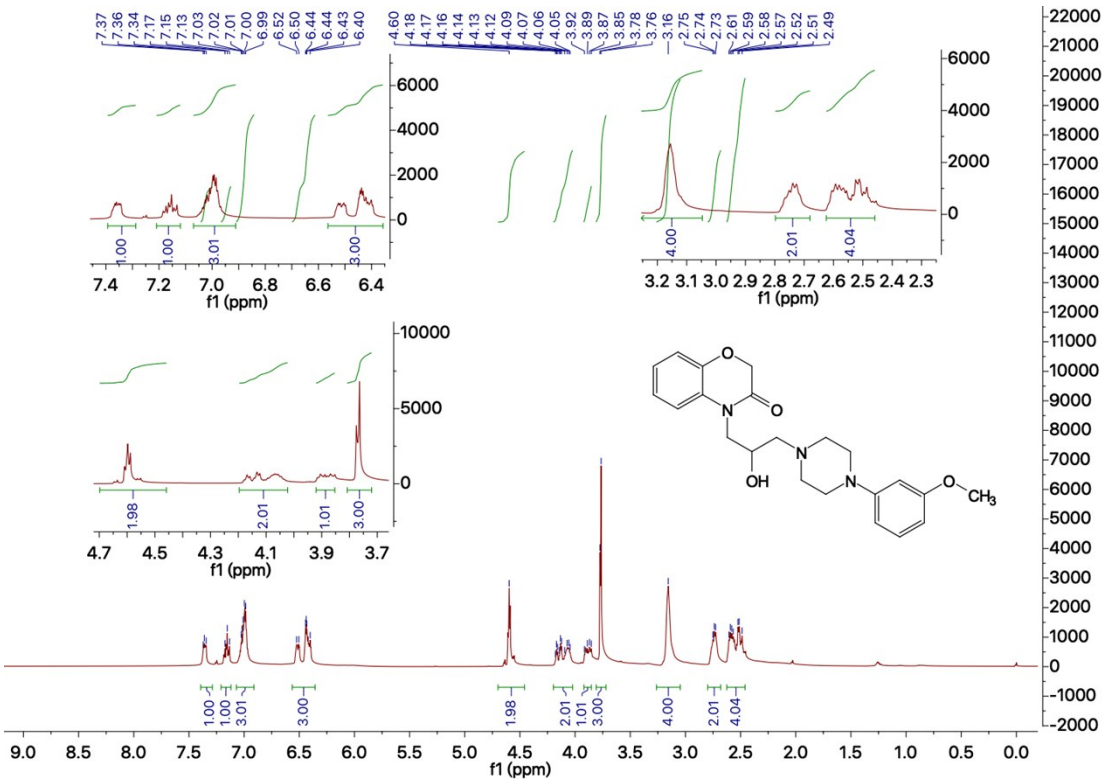


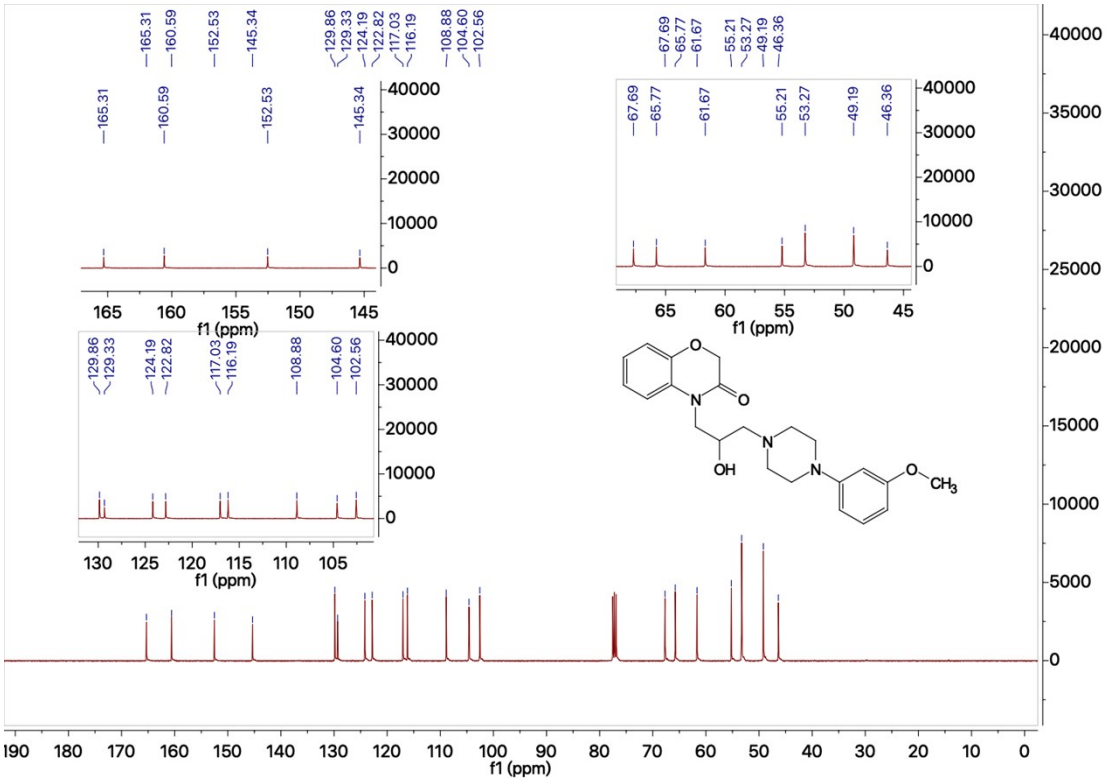


2018120741 #131 RT: 1.29 AV: 1 NL: 1.95E5
T: FTMS + p ESI Full ms [100.0000-1000.0000]

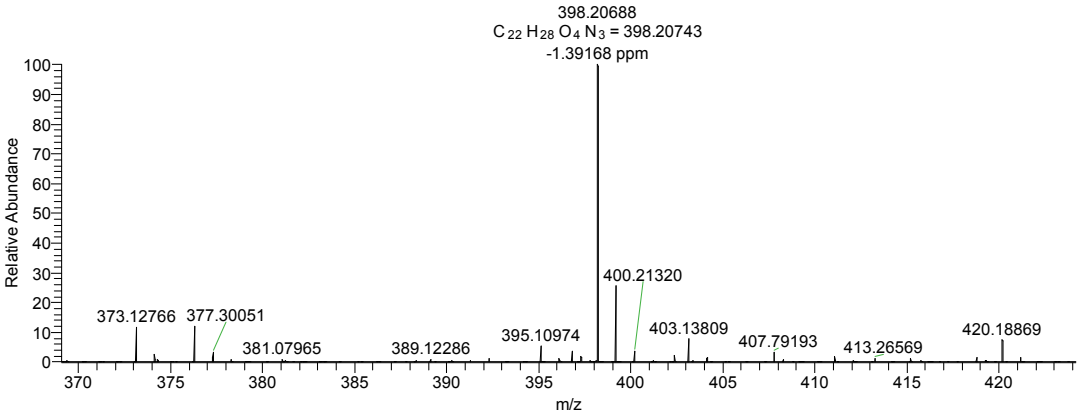


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4a

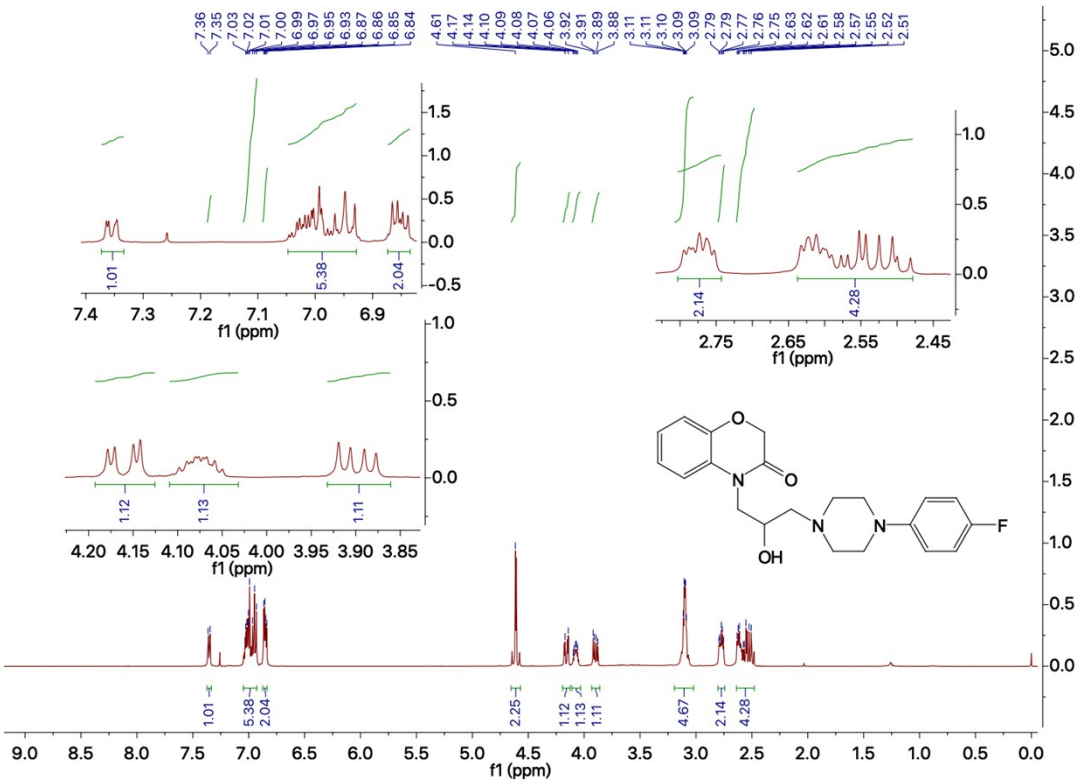

7.37 7.36 7.34 7.17 7.15 7.13 7.03 7.02 7.01 7.00 6.99 6.52 6.50 6.44 6.44 6.43 6.40
4.60 4.18 4.17 4.16 4.14 4.13 4.12 4.09 4.07 4.06 4.05 3.92 3.89 3.87 3.85 3.78 3.76 3.16 2.75 2.74 2.73 2.61 2.59 2.58 2.57 2.52 2.51 2.49
1.00 1.00 3.01 3.00
4.00 2.01 4.04
1.98 2.01 1.01 3.00
1.00 1.00 3.01 3.00 1.98 2.01 1.01 3.00 4.00 2.01 4.04
f1 (ppm)
O
N
O
OH
N
N
O
CH3

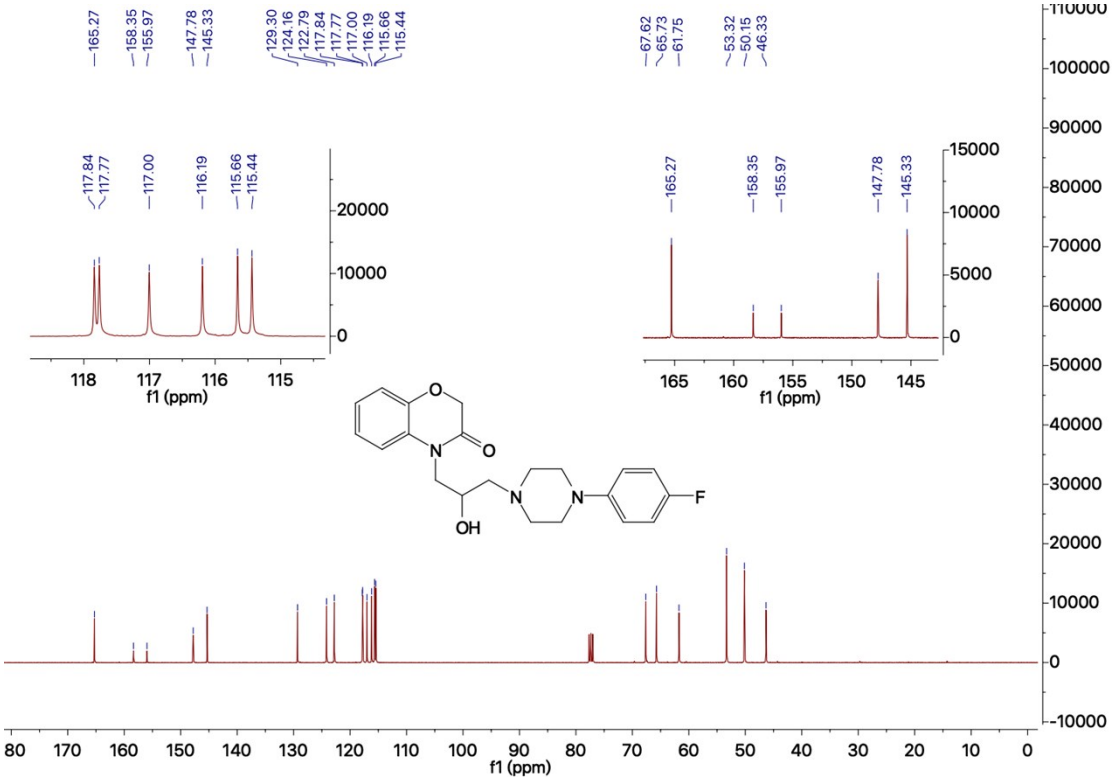

165.31 160.59 152.53 145.34 129.86 129.33 124.19 122.82 117.03 116.19 108.88 104.60 102.56
67.69 65.77 61.67 55.21 53.27 49.19 46.36
f1 (ppm)
O
N
O
OH
N
N
O
CH3

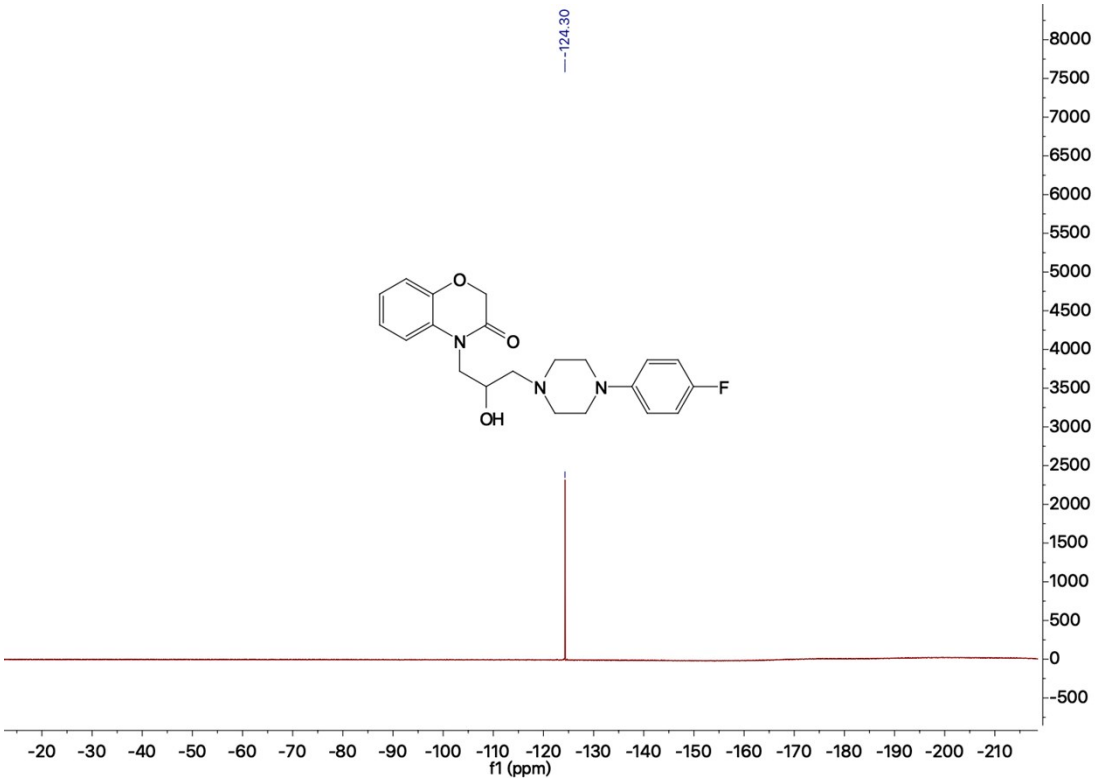
2018120740 #121 RT: 1.19 AV: 1 NL: 9.26E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]



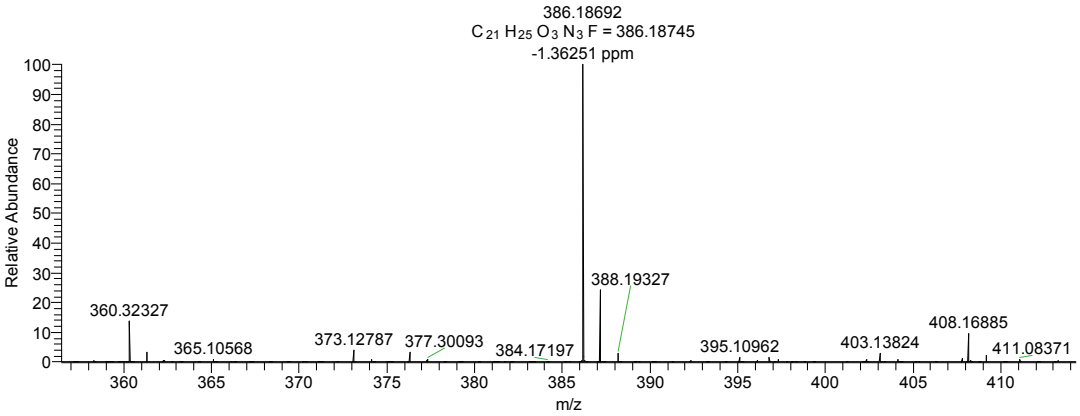
^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS spectra of the compound 4b



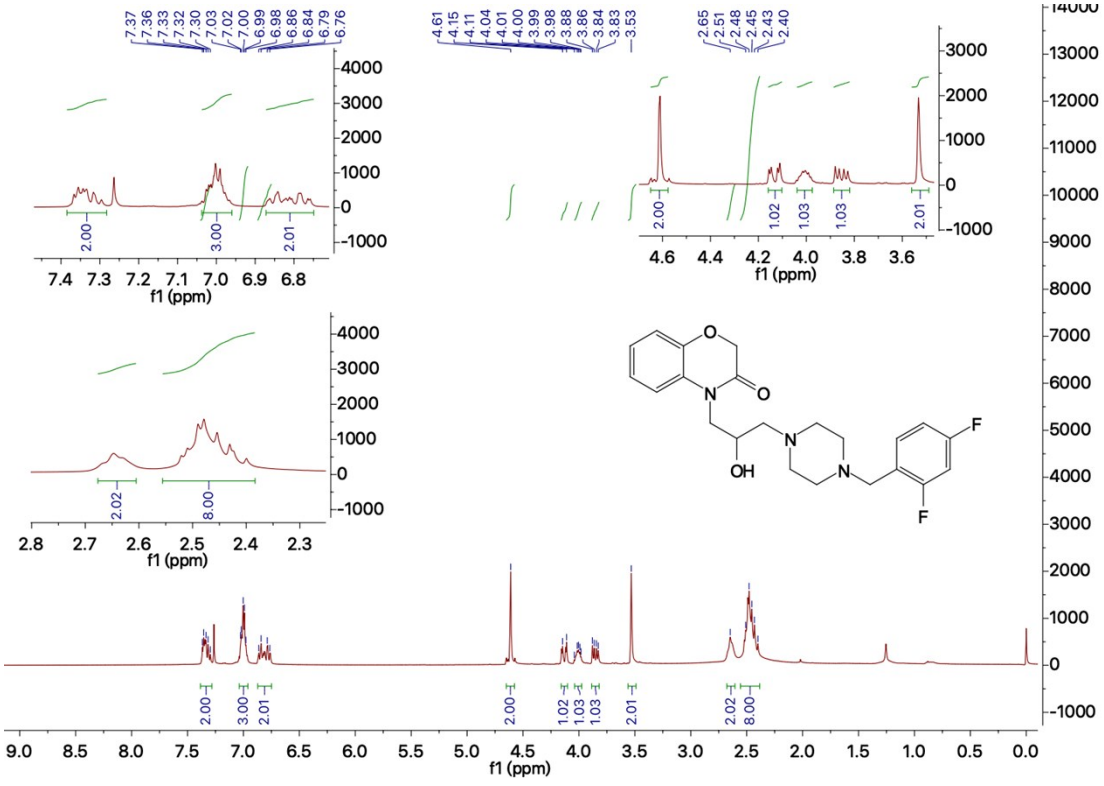

165.27
158.35
155.97
147.78
145.33
129.30
124.16
122.79
117.84
117.77
117.00
116.19
115.66
115.44
67.62
65.73
61.75
53.32
50.15
46.33
f1 (ppm)
O
N
O
OH
F

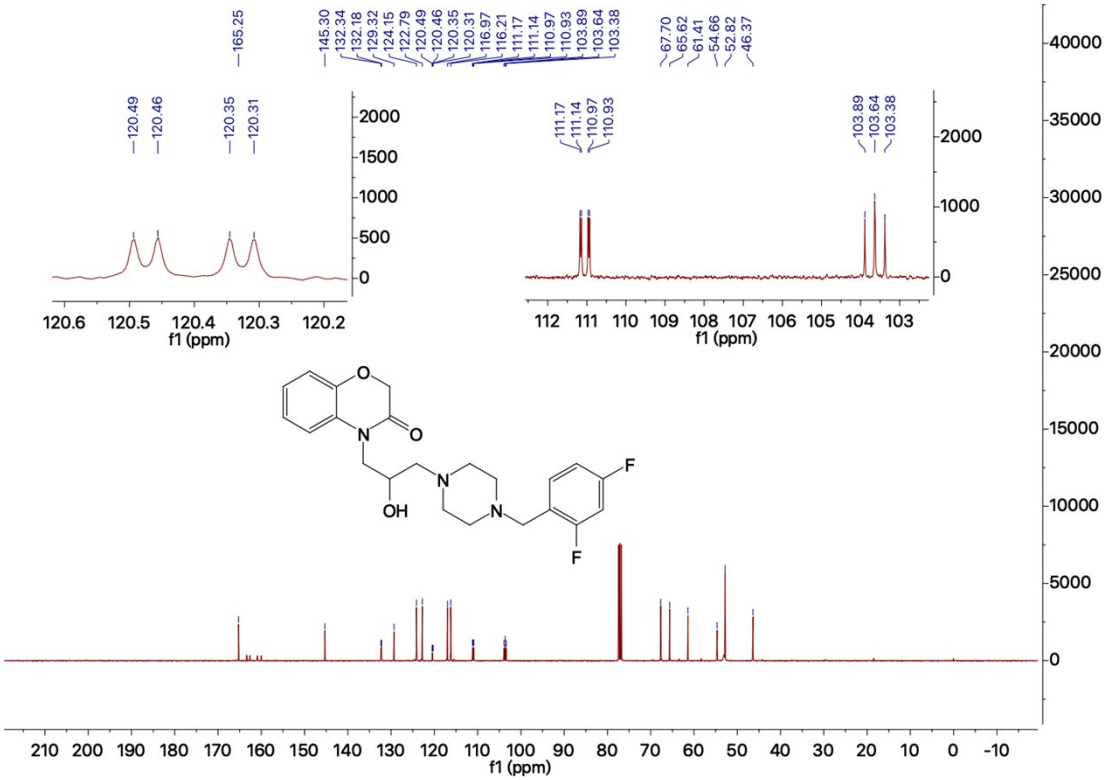

124.30
f1 (ppm)
O
N
O
OH
F

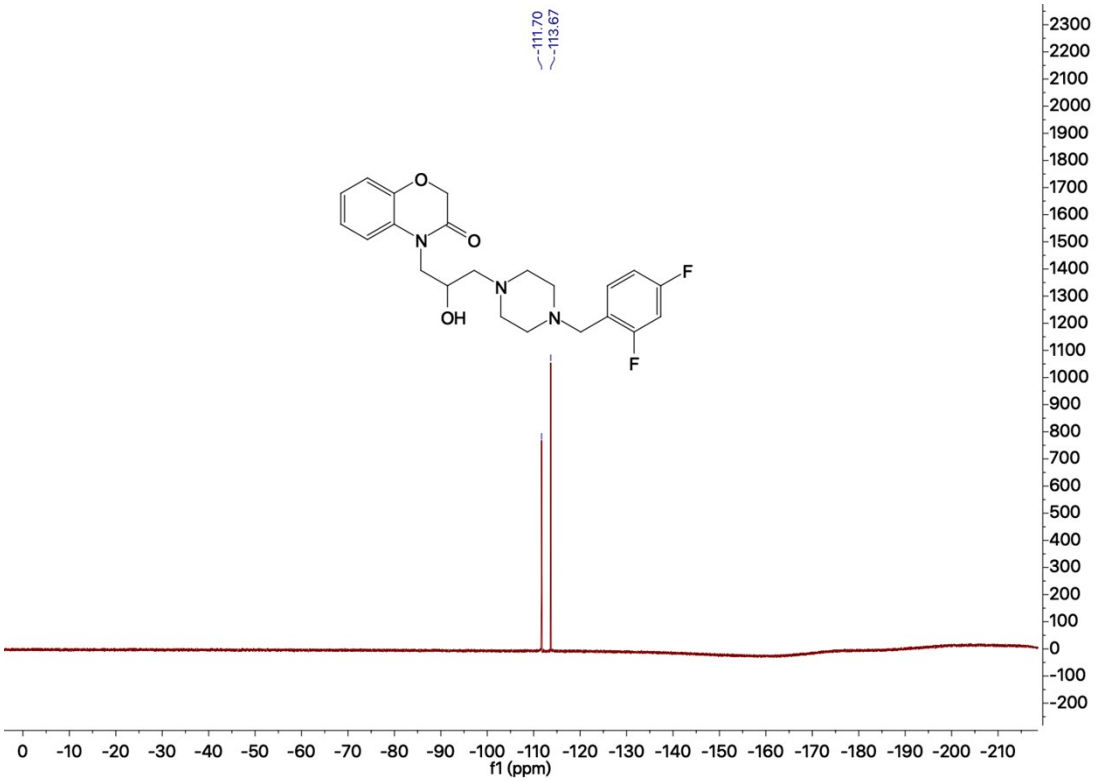
2018120743 #115 RT: 1.13 AV: 1 NL: 2.34E8
T: FTMS + p ESI Full ms [100.0000-1000.0000]



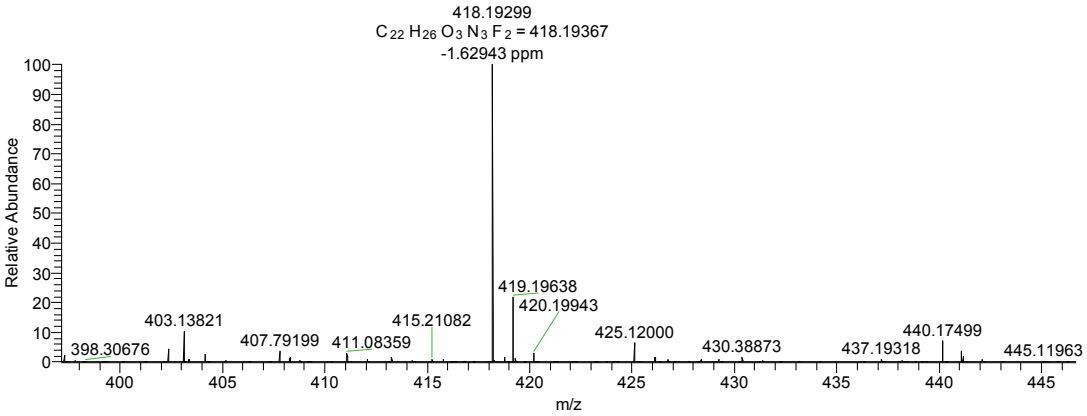
^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS spectra of the compound 4c



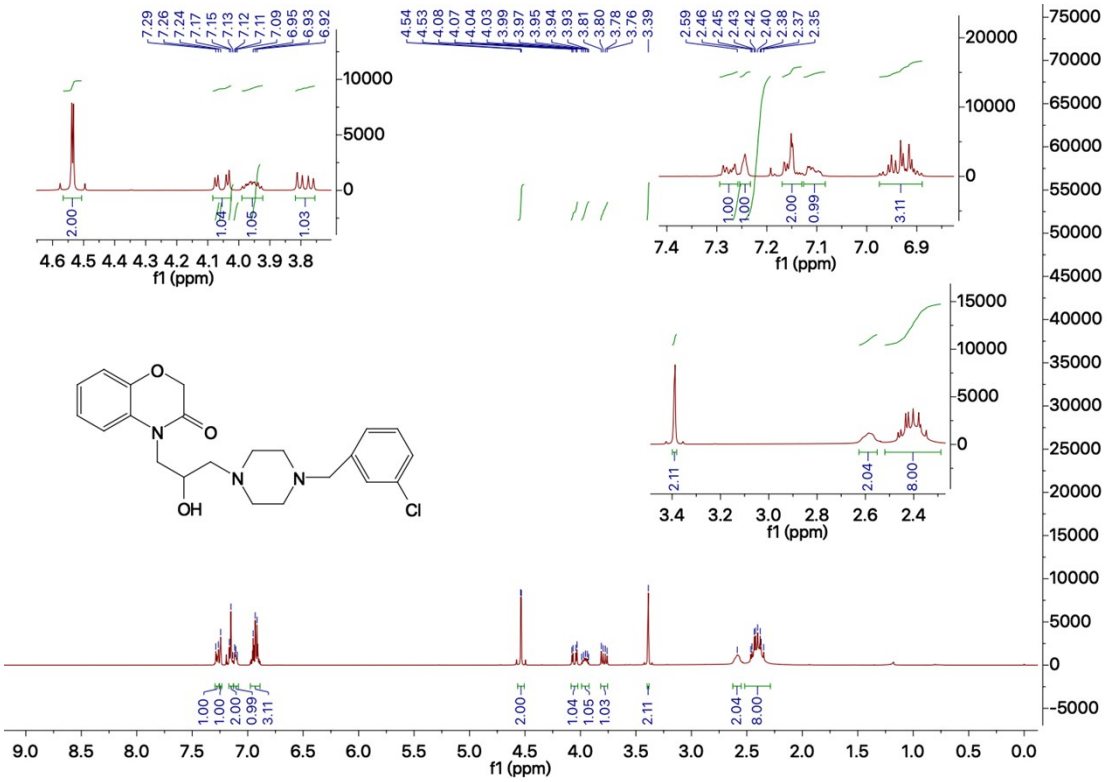

165.25
145.30
132.34
132.18
129.32
124.15
122.79
120.49
120.46
120.35
120.31
116.97
116.21
111.17
111.14
110.97
110.93
103.89
103.64
103.38
67.70
65.62
61.41
54.66
52.82
46.37
120.49
120.46
120.35
120.31
111.17
111.14
110.97
110.93
103.89
103.64
103.38
f1 (ppm)
f1 (ppm)
O
N
O
OH
N
N
F
F
f1 (ppm)

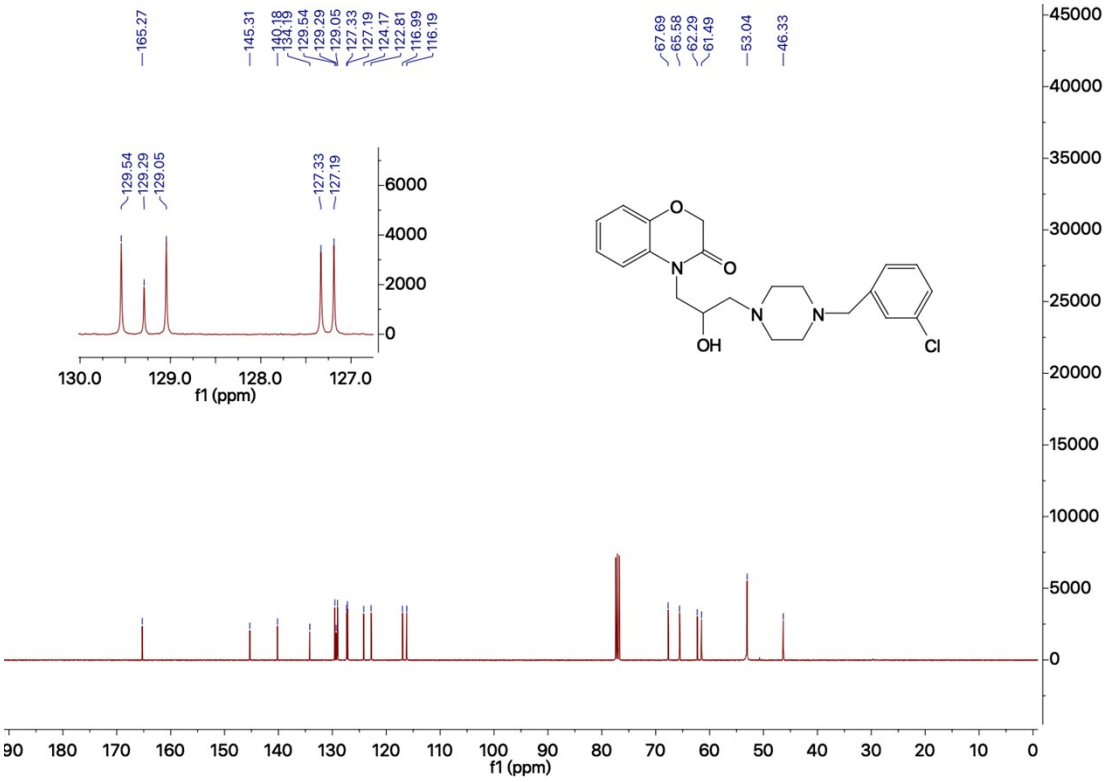

-111.70
-113.67
O
N
O
OH
N
N
F
F
f1 (ppm)

2018120756 #121 RT: 1.20 AV: 1 NL: 4.52E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

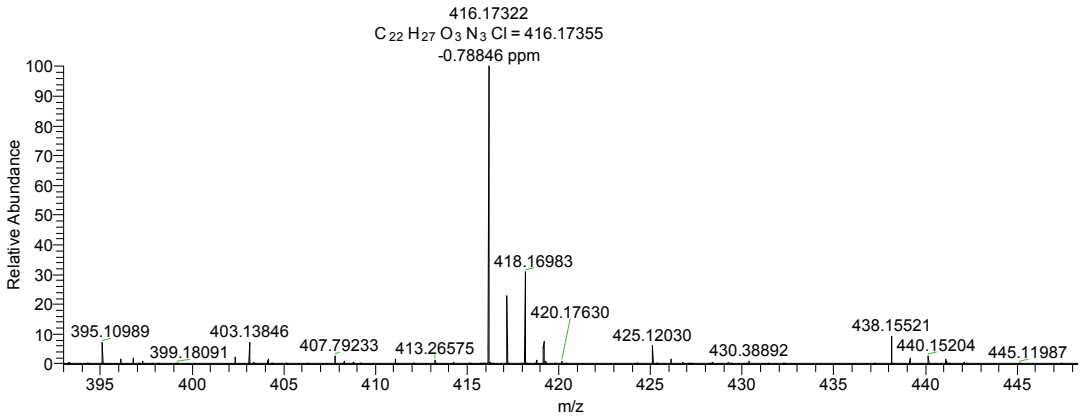


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4d

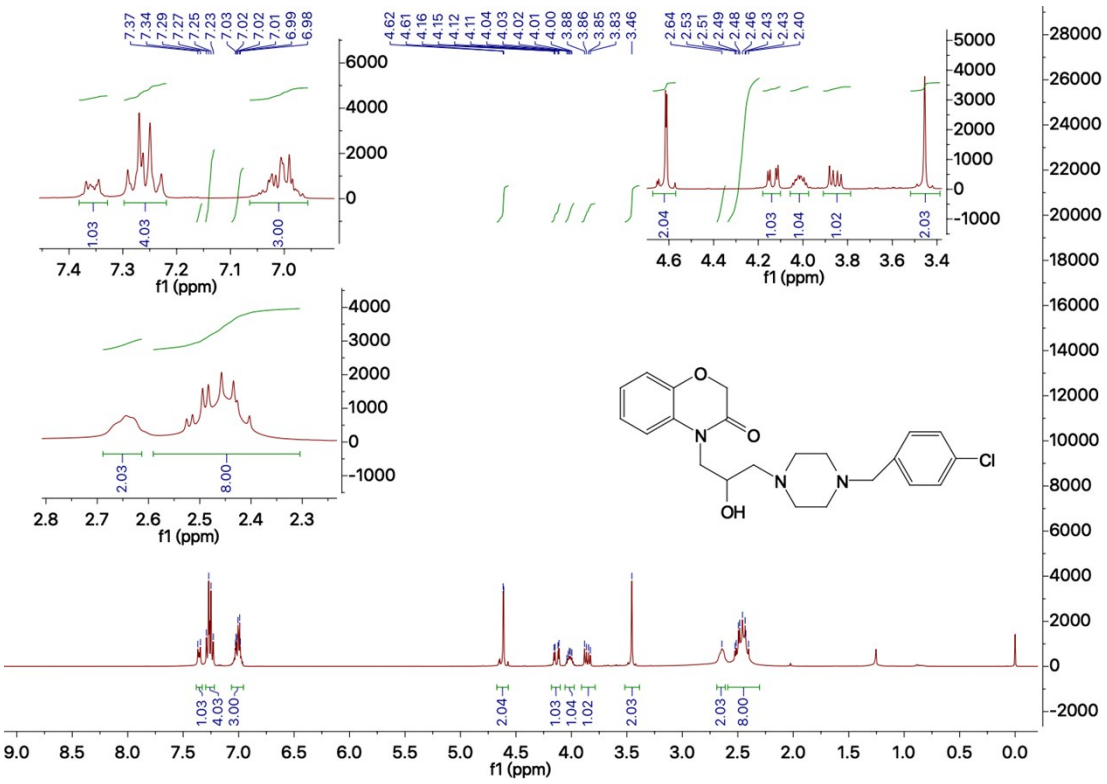


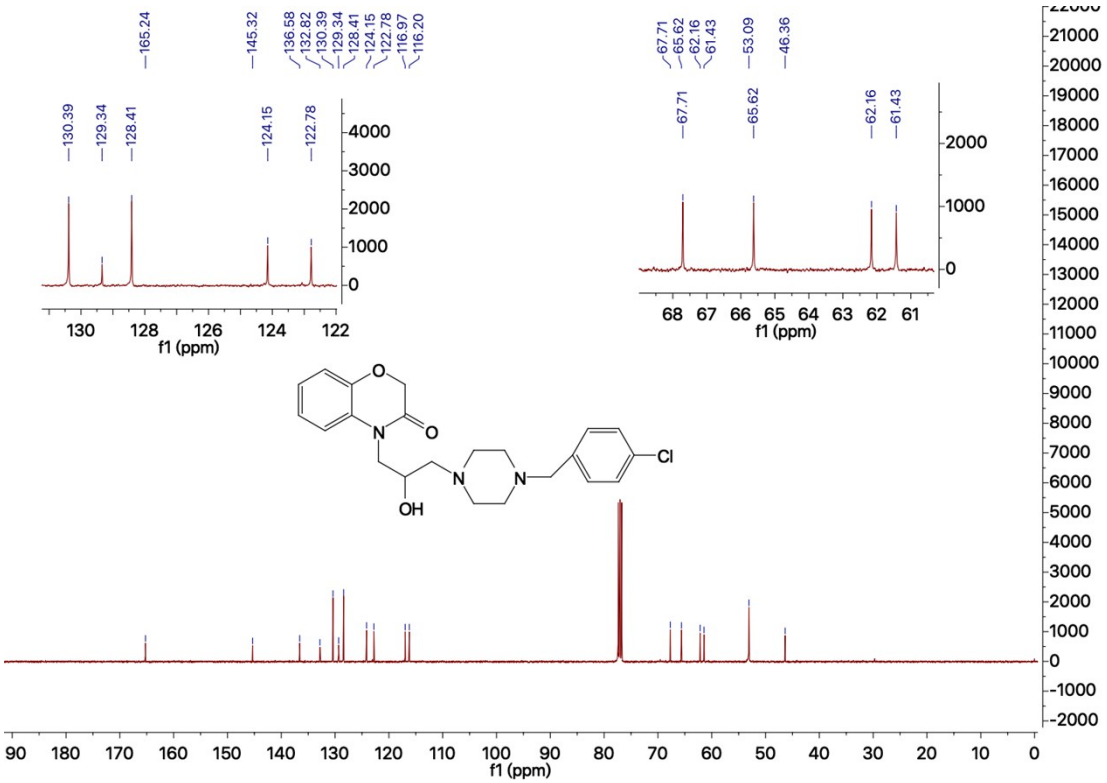


2018120750 #147 RT: 1.45 AV: 1 NL: 9.16E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

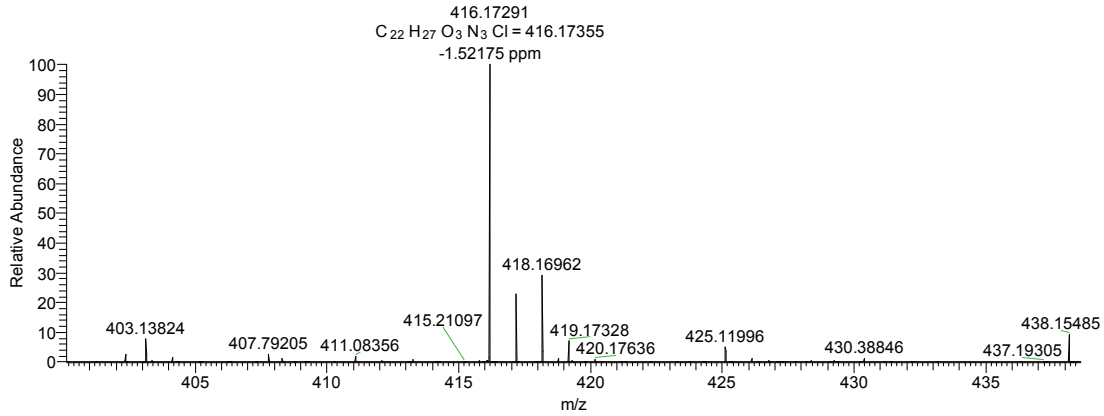


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4e

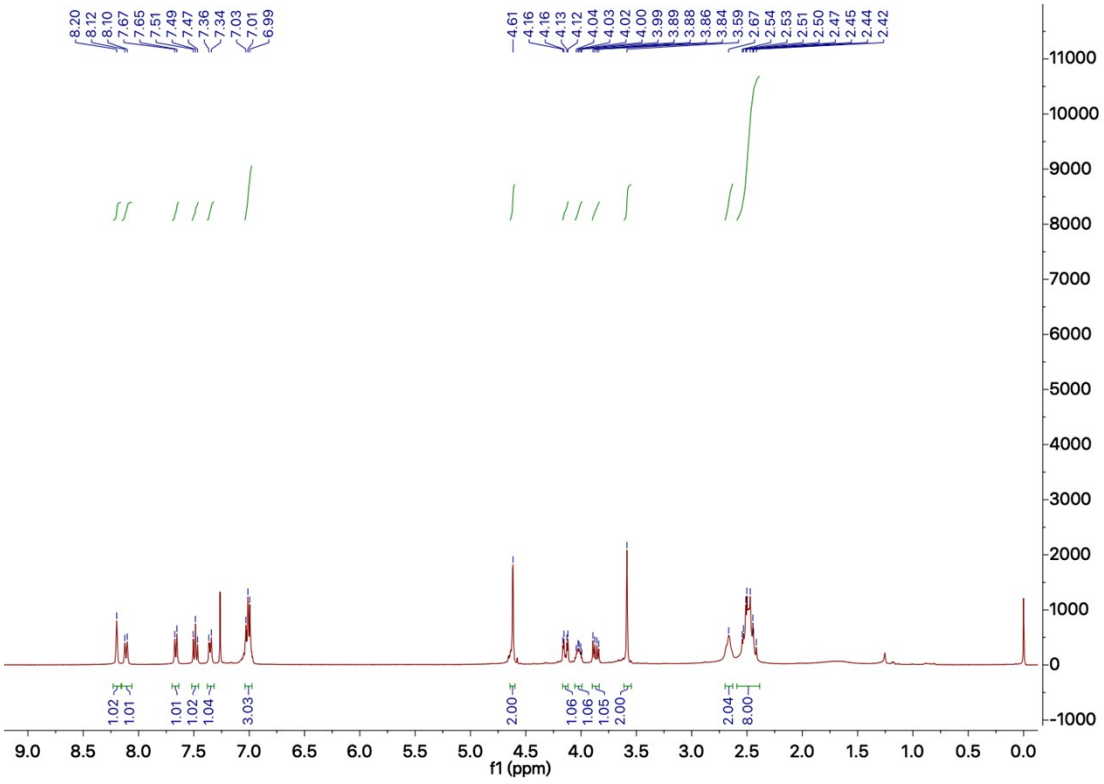

7.37
7.34
7.29
7.27
7.25
7.23
7.03
7.02
7.02
7.01
6.99
6.98
4.62
4.61
4.16
4.15
4.12
4.11
4.04
4.03
4.02
4.01
4.00
3.88
3.86
3.85
3.83
3.46
2.64
2.53
2.51
2.49
2.48
2.46
2.43
2.43
2.40
1.03
4.03
3.00
2.04
1.03
1.04
1.02
2.03
2.03
8.00
f1 (ppm)
O
N
O
N
N
Cl
OH

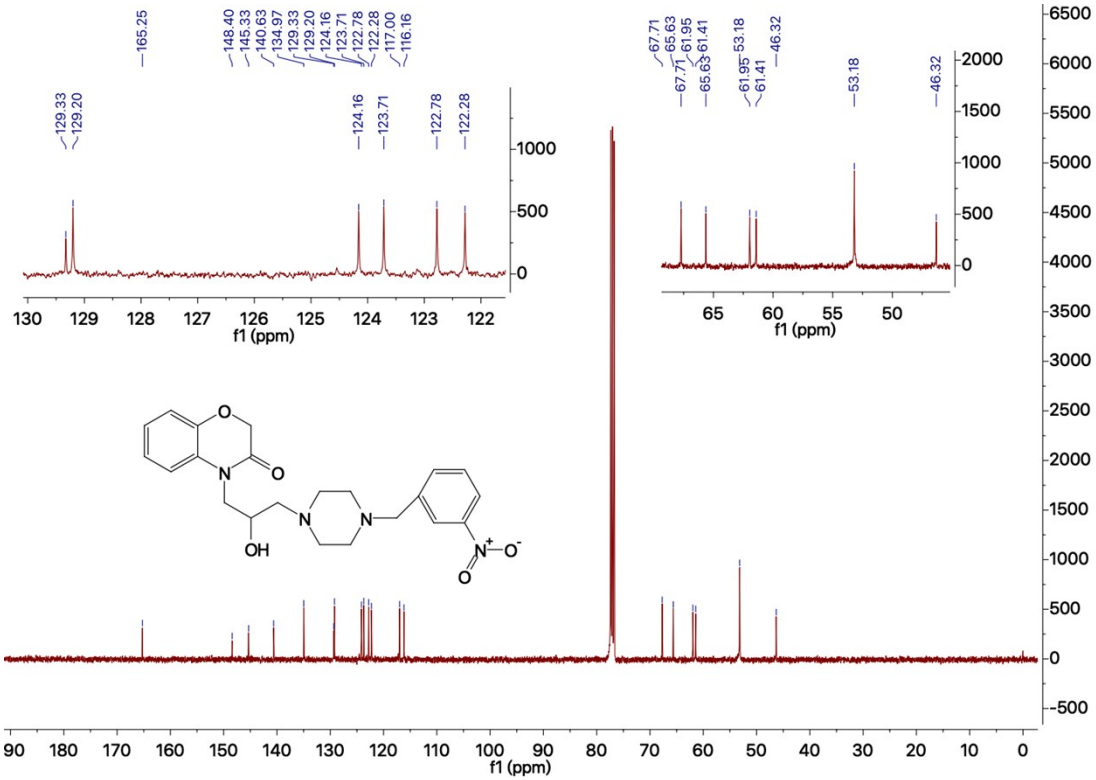

165.24
145.32
136.58
132.82
130.39
129.34
128.41
124.15
122.78
116.97
116.20
67.71
65.62
62.16
61.43
53.09
46.36
130.39
129.34
128.41
124.15
122.78
67.71
65.62
62.16
61.43
f1 (ppm)
O
N
O
N
N
Cl
OH

2018120751 #131 RT: 1.30 AV: 1 NL: 7.67E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

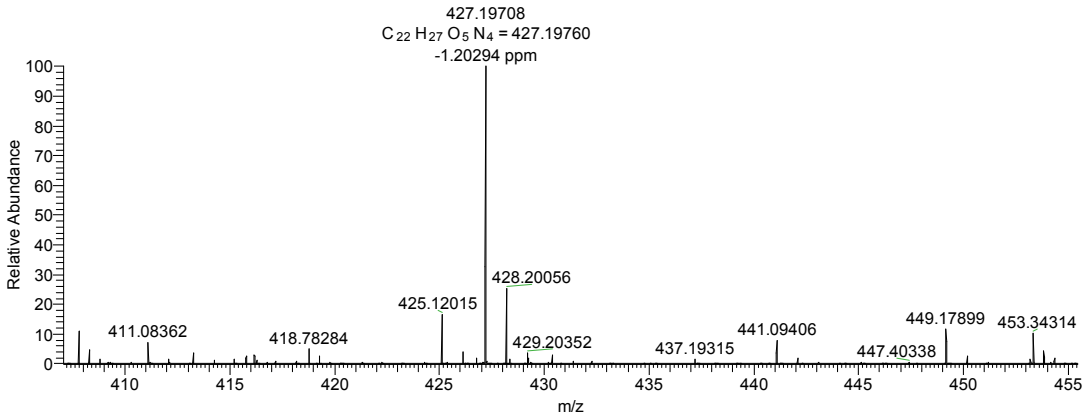


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4f

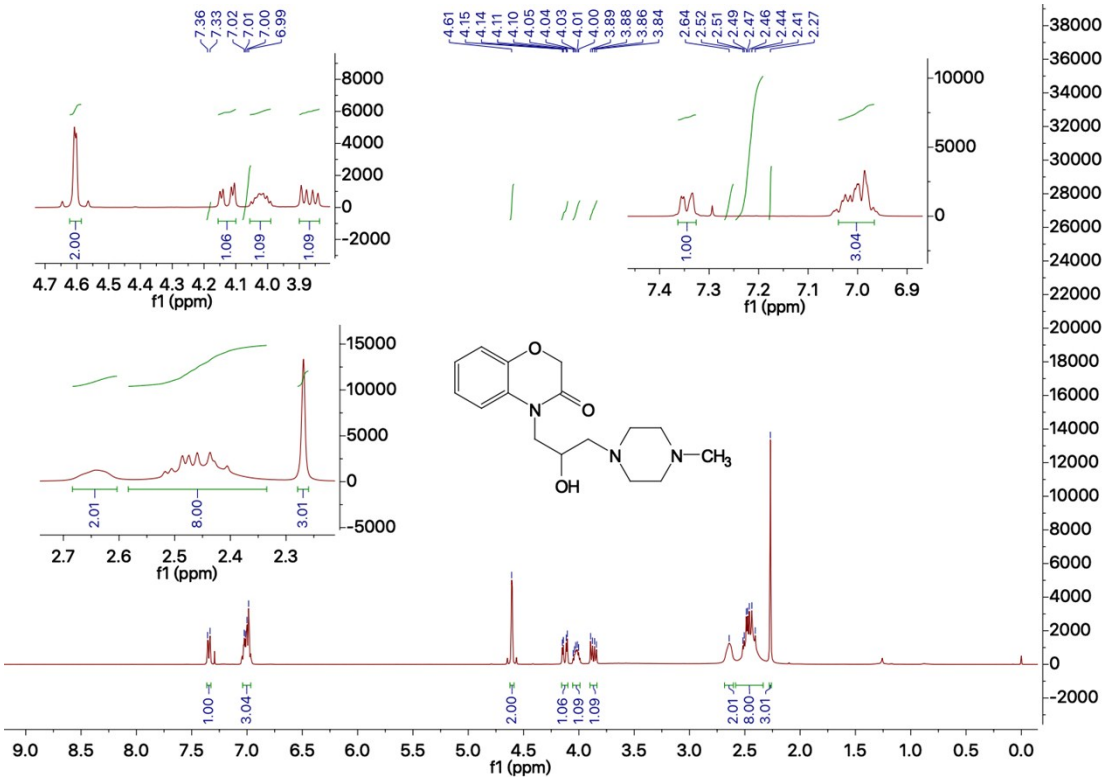


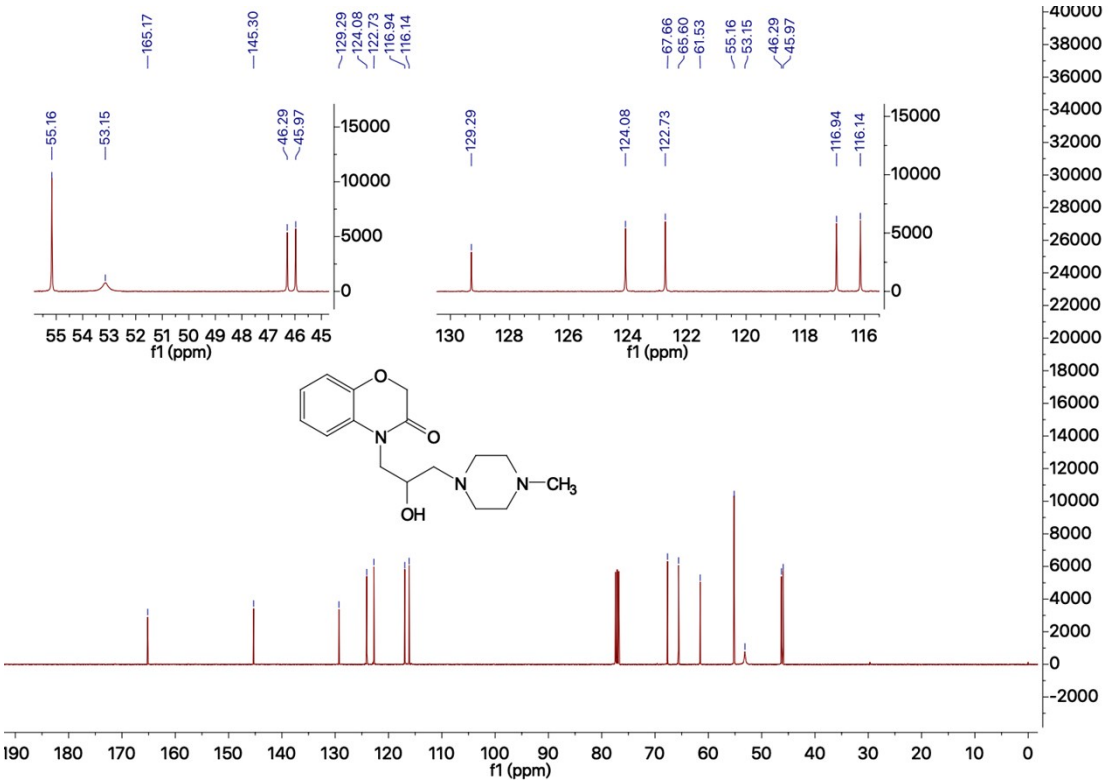


2018120752 #125 RT: 1.23 AV: 1 NL: 2.61E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

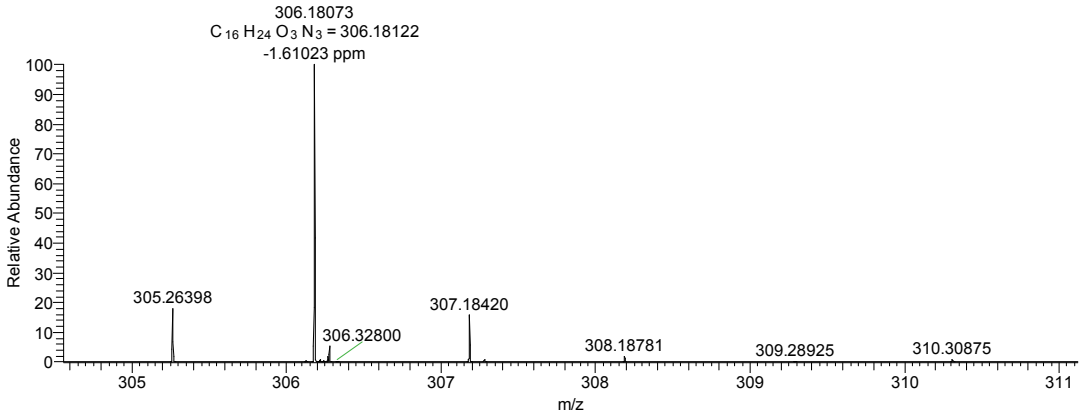


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4g

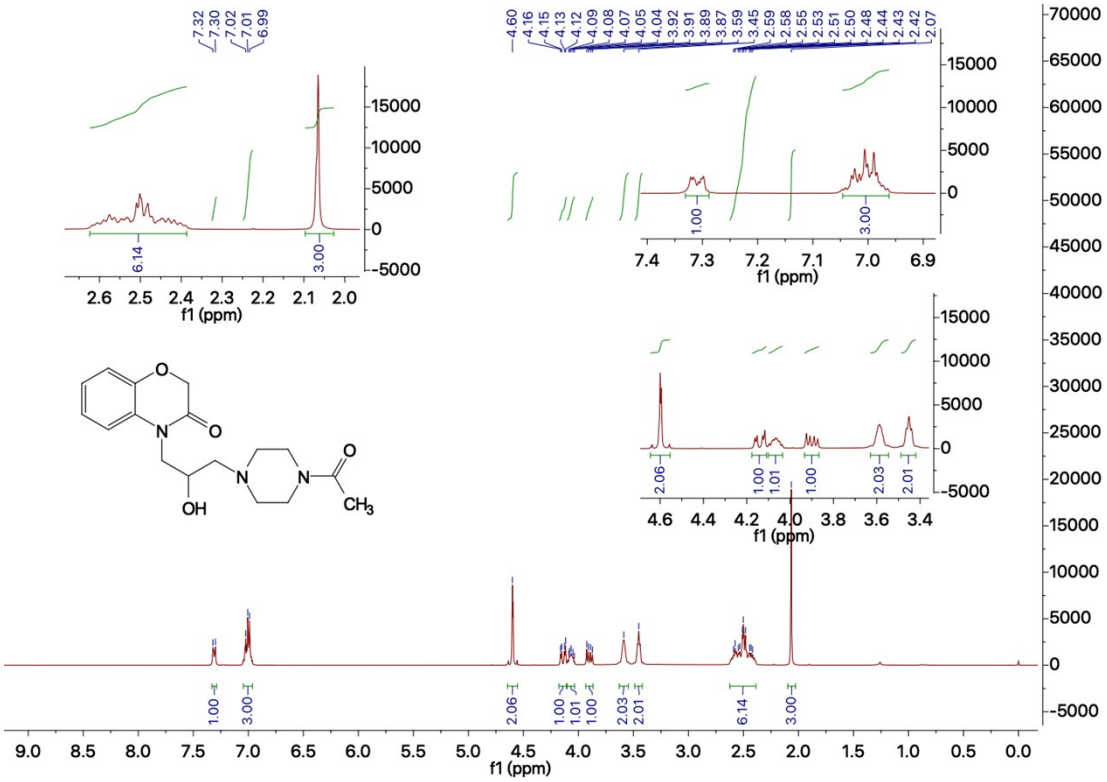

7.36
7.33
7.02
7.01
7.00
6.99
4.61
4.15
4.14
4.11
4.10
4.05
4.04
4.03
4.01
4.00
3.89
3.88
3.86
3.84
2.64
2.52
2.51
2.49
2.47
2.46
2.44
2.41
2.27
2.00
1.06
1.09
1.09
1.00
3.04
2.01
8.00
3.01
f1 (ppm)
O
N
O
OH
N
N—CH3

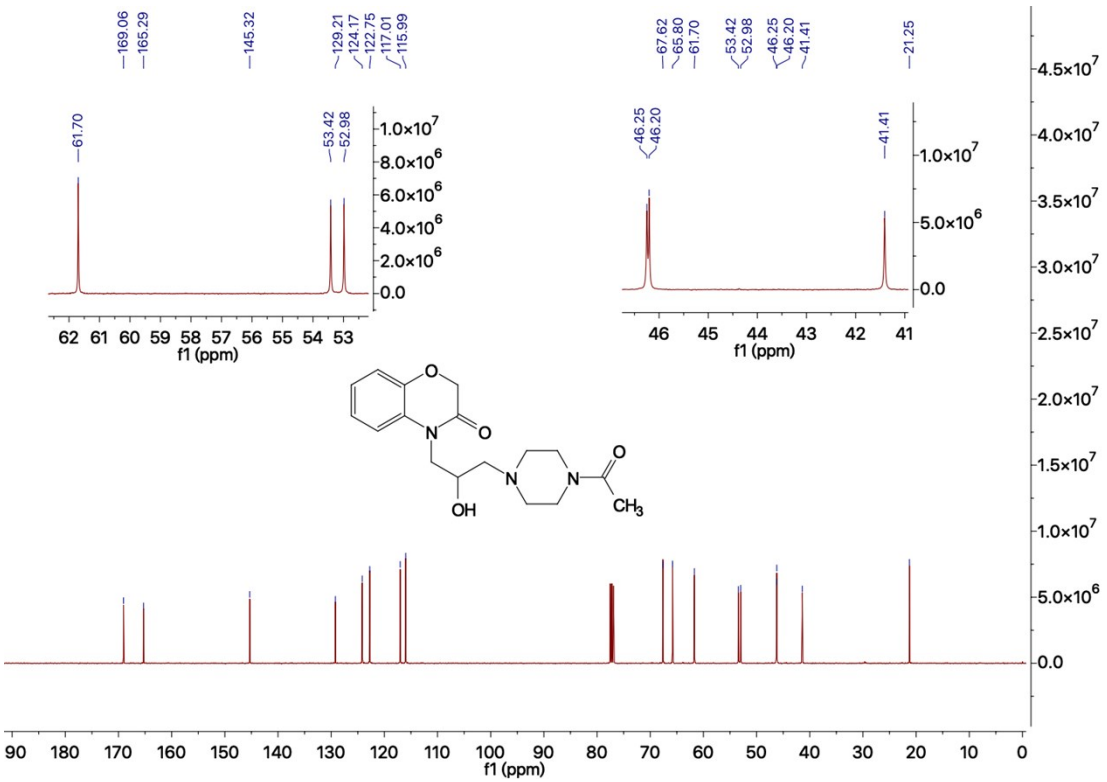

165.17
145.30
129.29
124.08
122.73
116.94
116.14
67.66
65.60
61.53
55.16
53.15
46.29
45.97
f1 (ppm)
O
N
O
OH
N
N—CH3

2018120746 #183 RT: 1.80 AV: 1 NL: 7.92E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

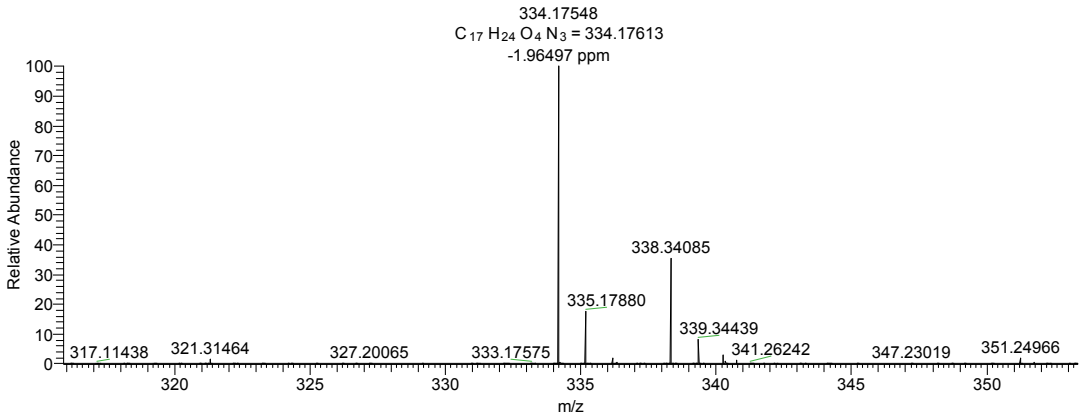


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4h

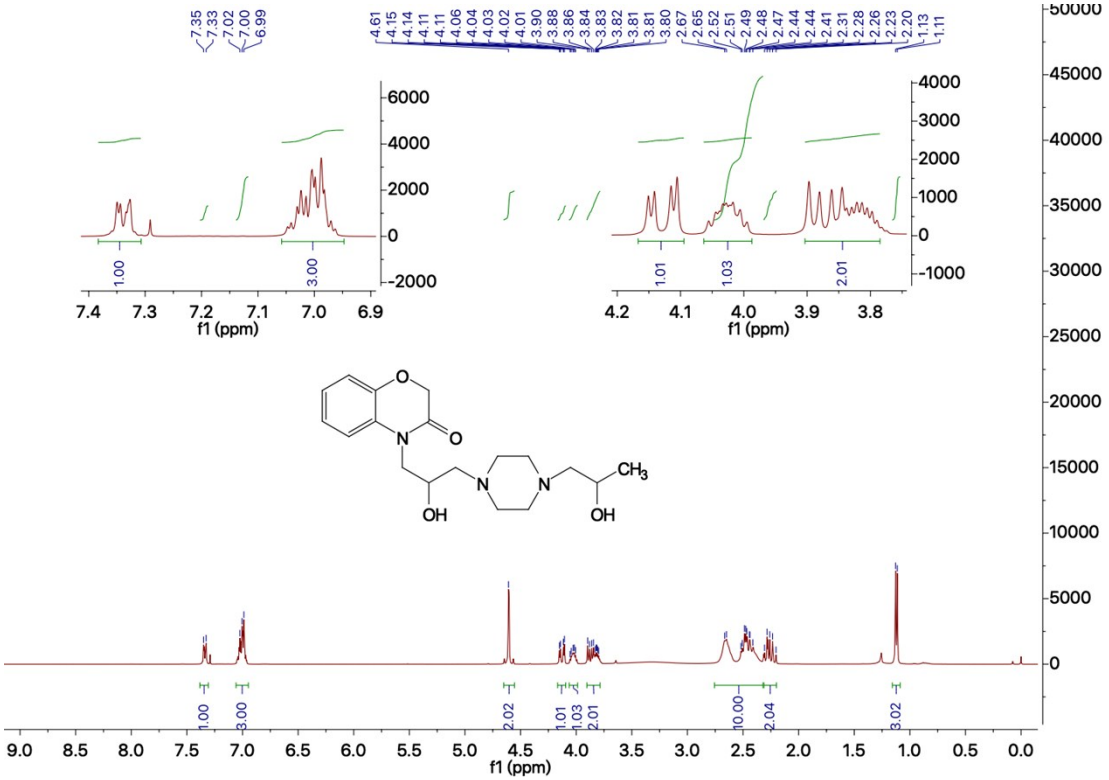


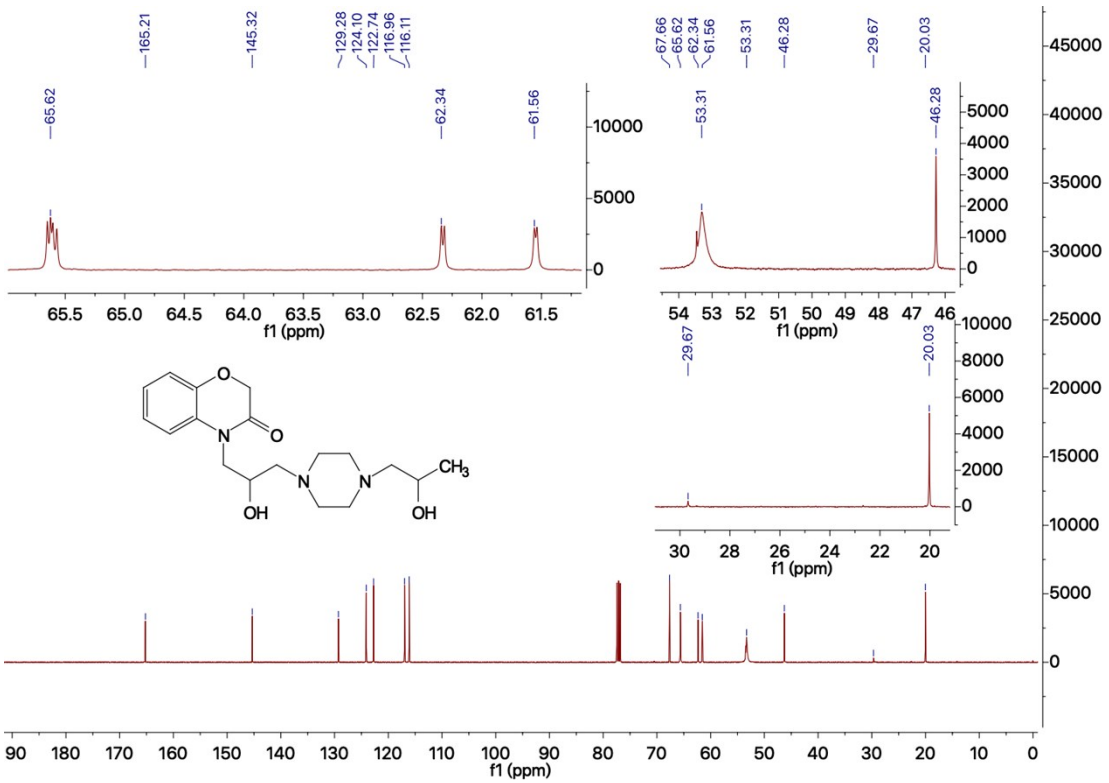


2018120747 #91 RT: 0.89 AV: 1 NL: 2.64E8
T: FTMS + p ESI Full ms [100.0000-1000.0000]

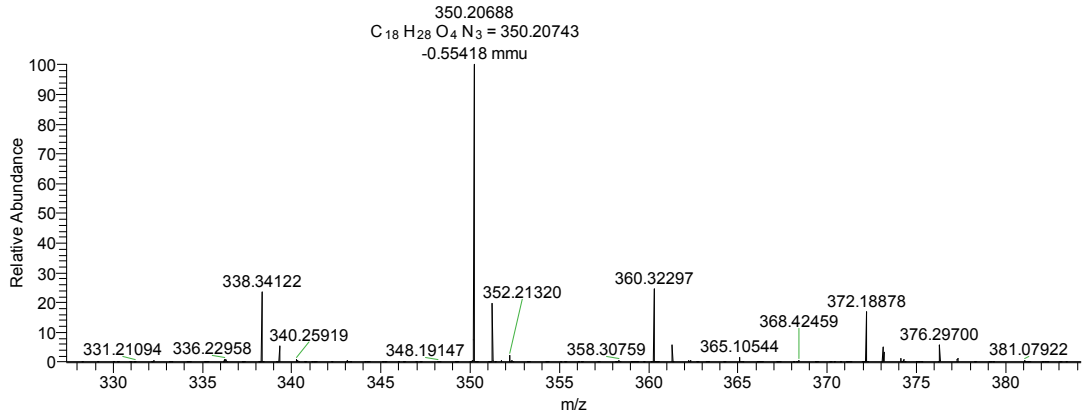


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4i

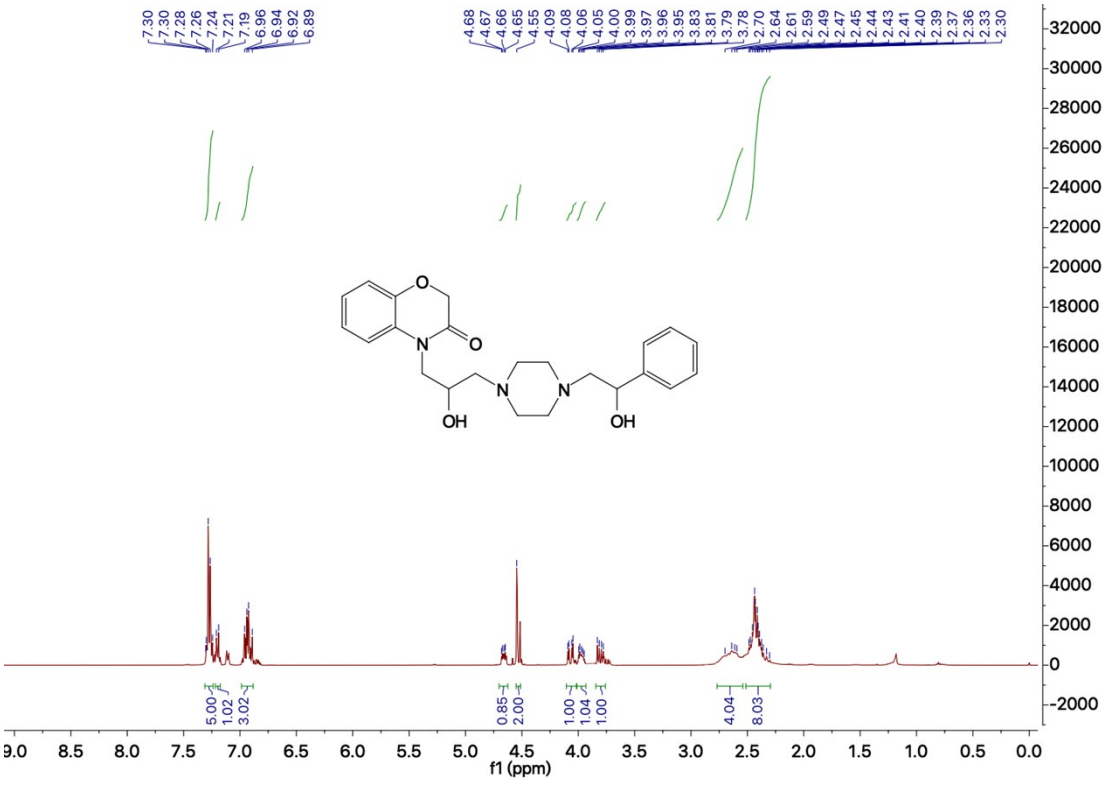

7.35
7.33
7.02
7.00
6.99
4.61
4.15
4.14
4.11
4.11
4.06
4.04
4.03
4.02
4.01
3.90
3.88
3.86
3.84
3.83
3.82
3.81
3.81
3.80
2.67
2.65
2.52
2.51
2.49
2.48
2.47
2.44
2.44
2.41
2.31
2.28
2.26
2.23
2.20
1.13
1.11
1.00
3.00
1.01
1.03
2.01
f1 (ppm)
OH
OH
CH3
1.00
3.00
2.02
1.01
1.03
2.01
10.00
2.04
3.02
f1 (ppm)

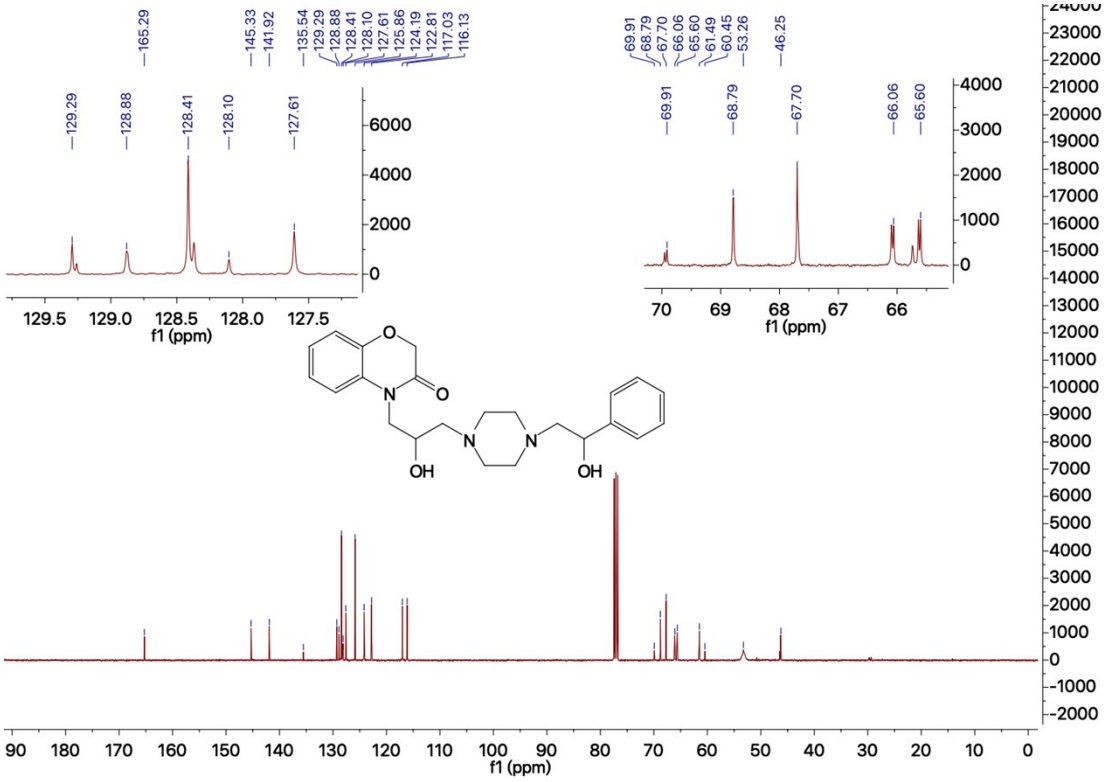

165.21
145.32
129.28
124.10
122.74
116.96
116.11
67.66
65.62
62.34
61.56
53.31
46.28
29.67
20.03
65.62
62.34
61.56
53.31
46.28
29.67
20.03
f1 (ppm)
OH
OH
CH3
f1 (ppm)

2018120754 #131 RT: 1.29 AV: 1 NL: 1.66E8
T: FTMS + p ESI Full ms [100.0000-1000.0000]

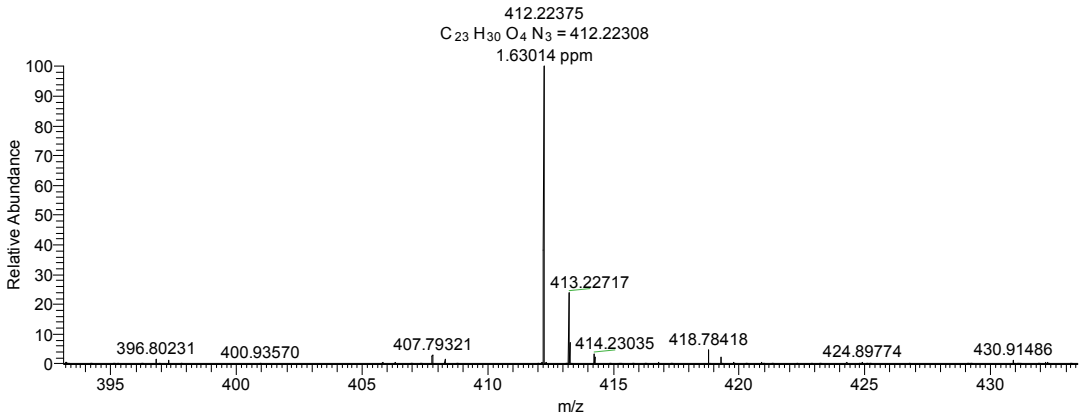


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4j

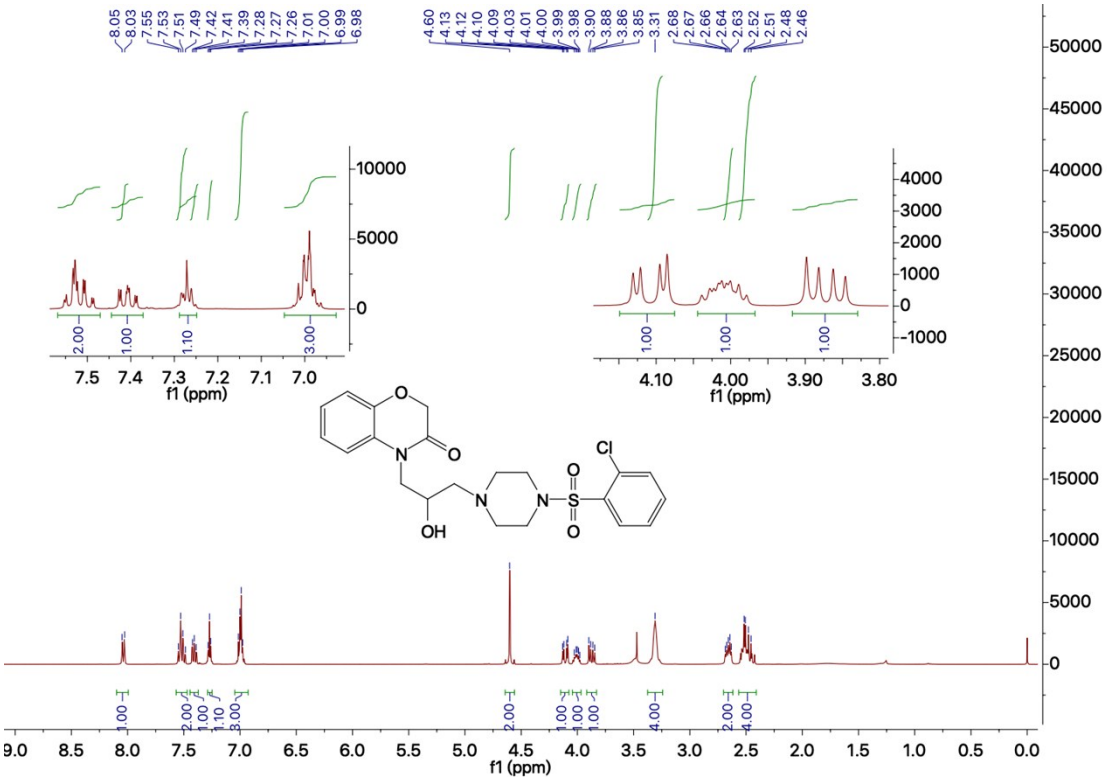


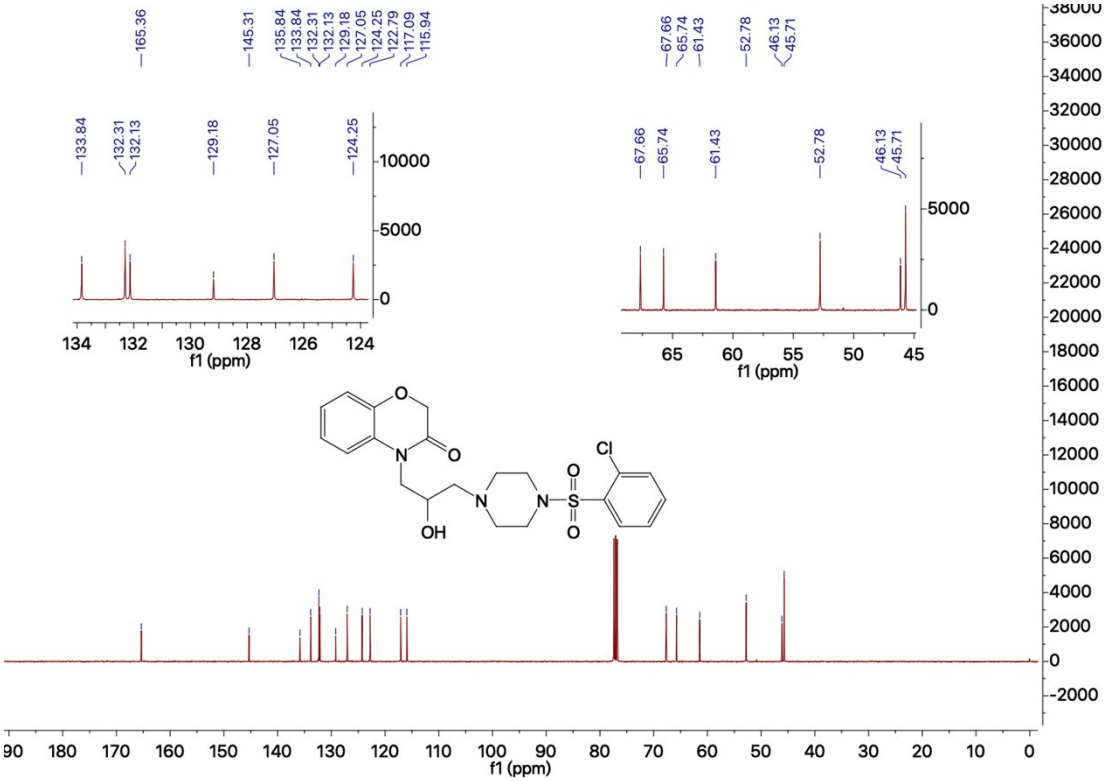


2019062804 #37 RT: 0.36 AV: 1 NL: 9.96E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

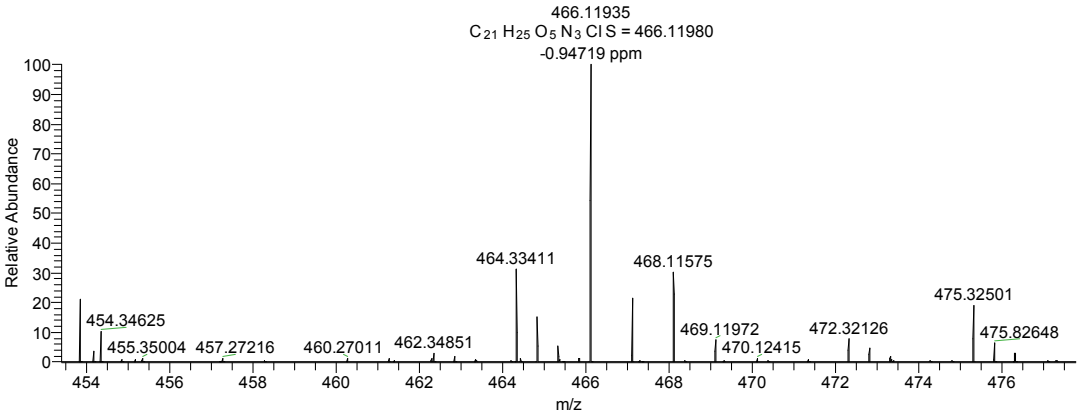


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4k

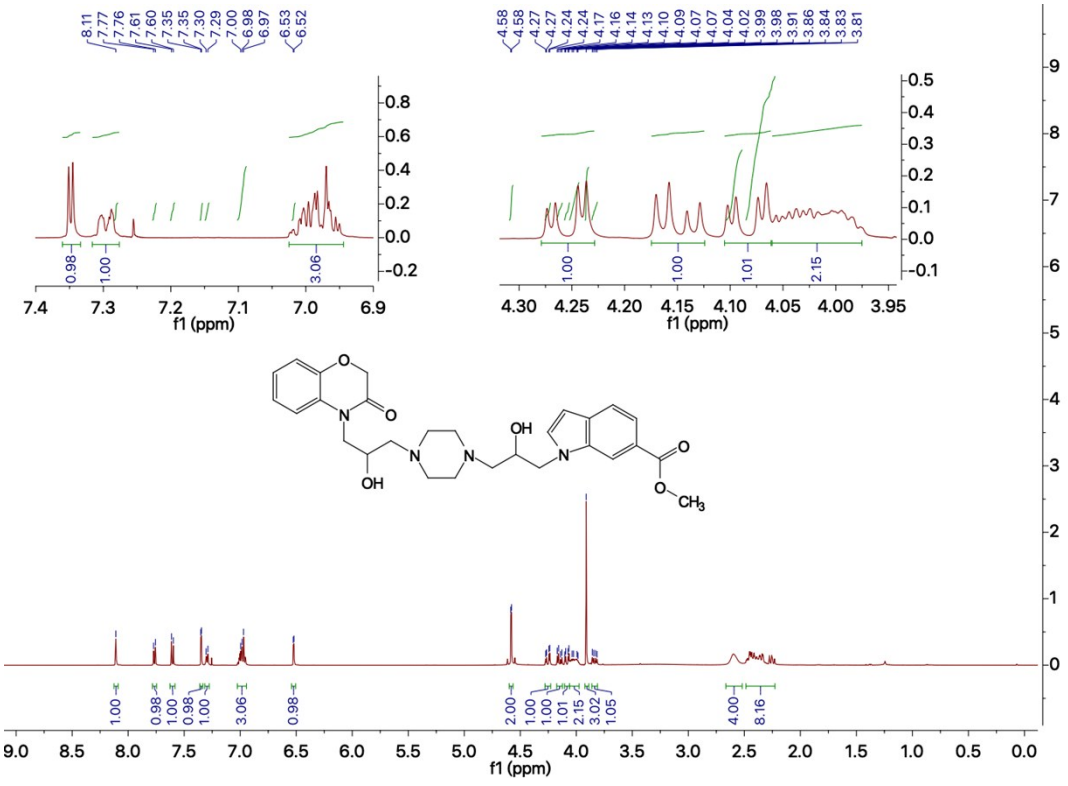

8.05
8.03
7.55
7.53
7.51
7.49
7.42
7.41
7.39
7.28
7.27
7.26
7.01
7.00
6.99
6.98
4.60
4.13
4.12
4.10
4.09
4.03
4.01
4.00
3.99
3.98
3.90
3.88
3.86
3.85
3.31
2.68
2.67
2.66
2.64
2.63
2.52
2.51
2.48
2.46
f1 (ppm)
Cl
OH

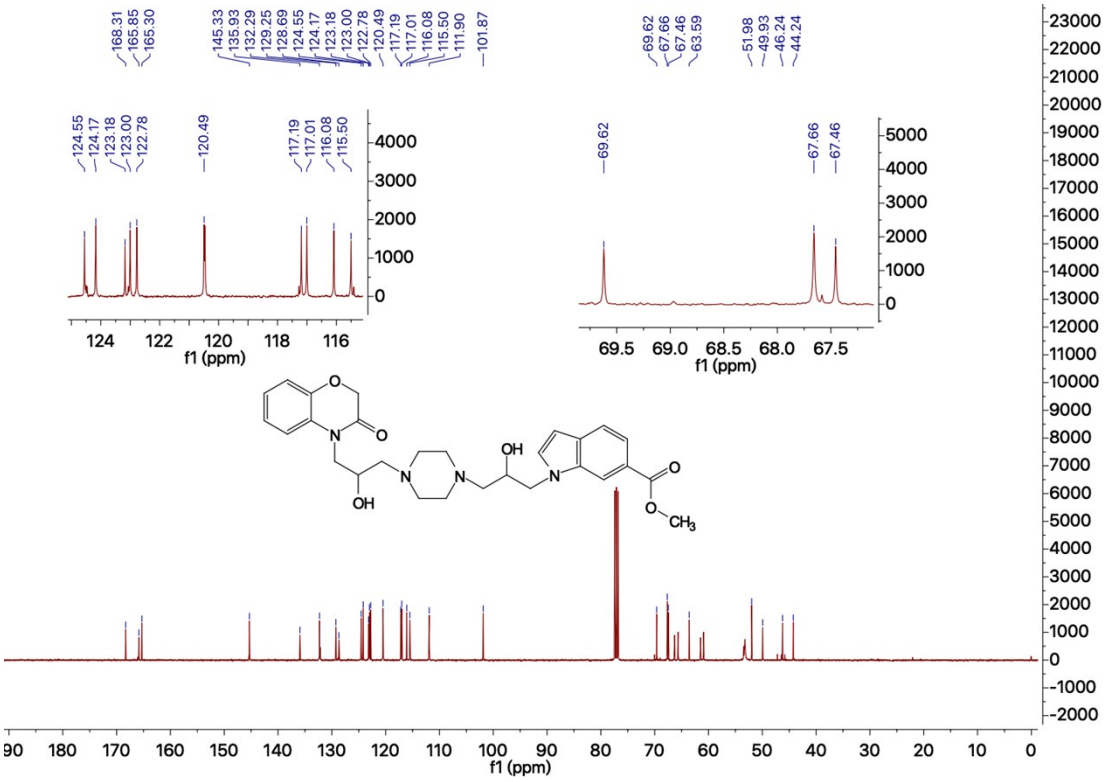

165.36
145.31
135.84
133.84
132.31
132.13
129.18
127.05
124.25
122.79
117.09
115.94
67.66
65.74
61.43
52.78
46.13
45.71
f1 (ppm)
Cl
OH

2018120762 #117 RT: 1.15 AV: 1 NL: 6.77E6
T: FTMS + p ESI Full ms [100.0000-1000.0000]

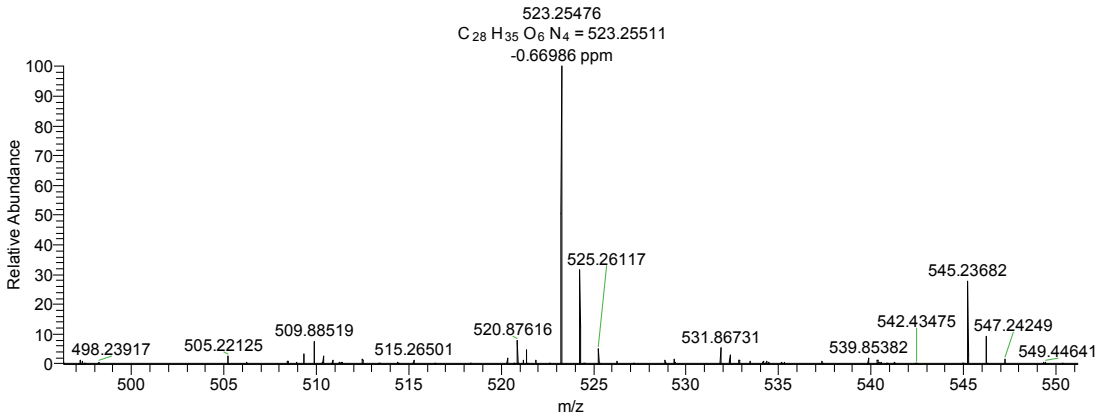


^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4l

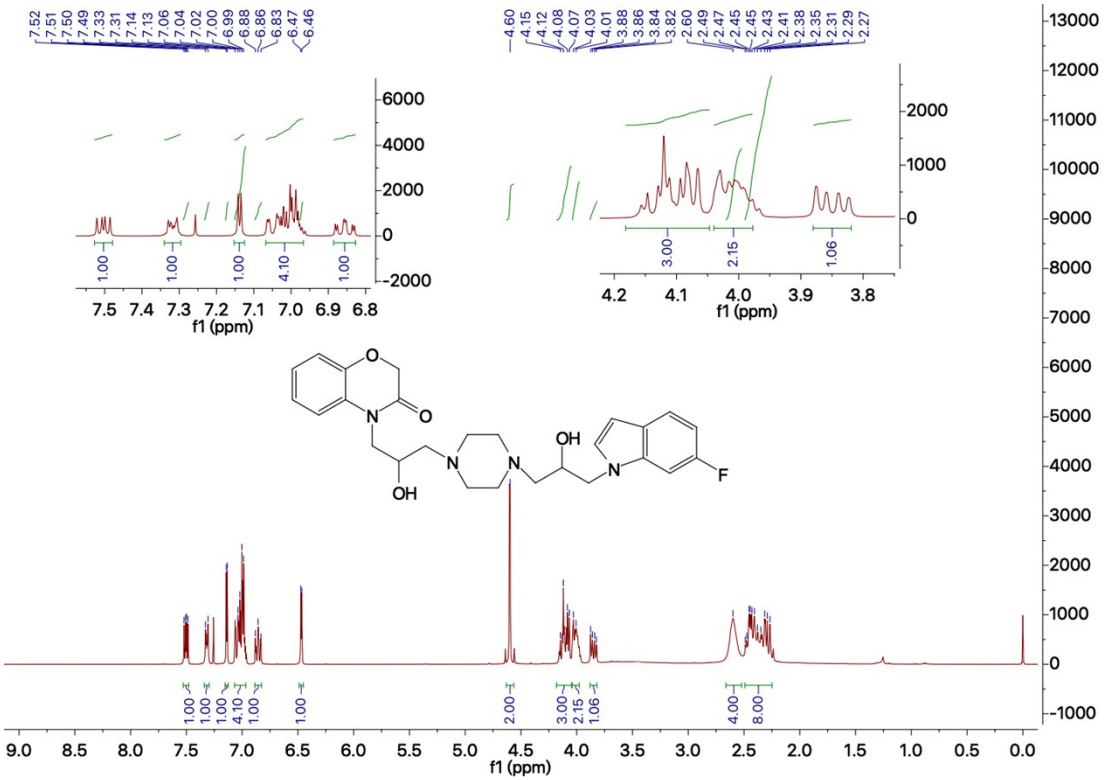


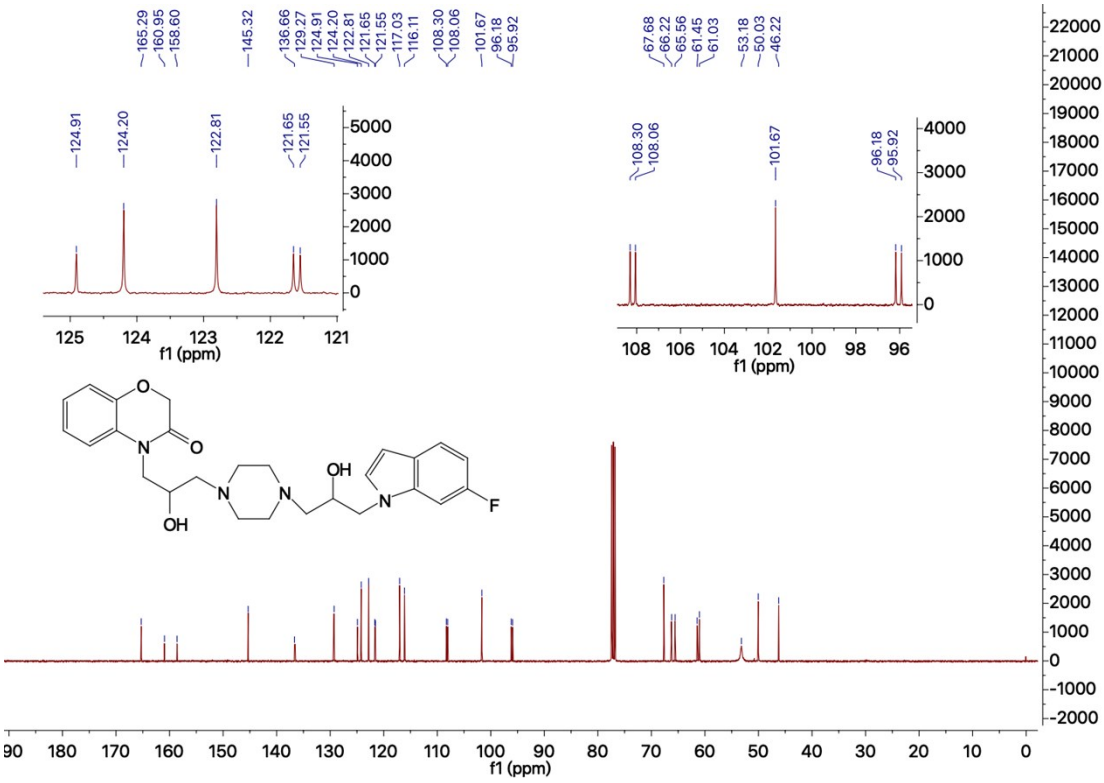


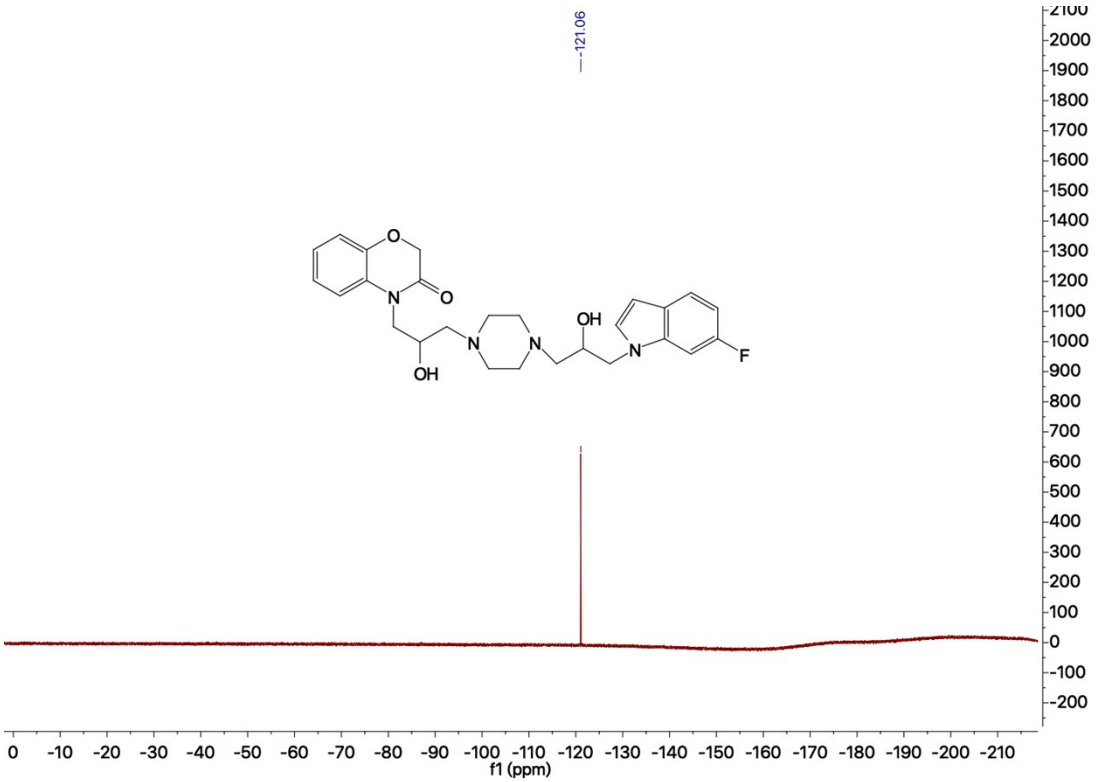
2018120758 #131 RT: 1.29 AV: 1 NL: 8.89E6
T: FTMS + p ESI Full ms [100.0000-1000.0000]



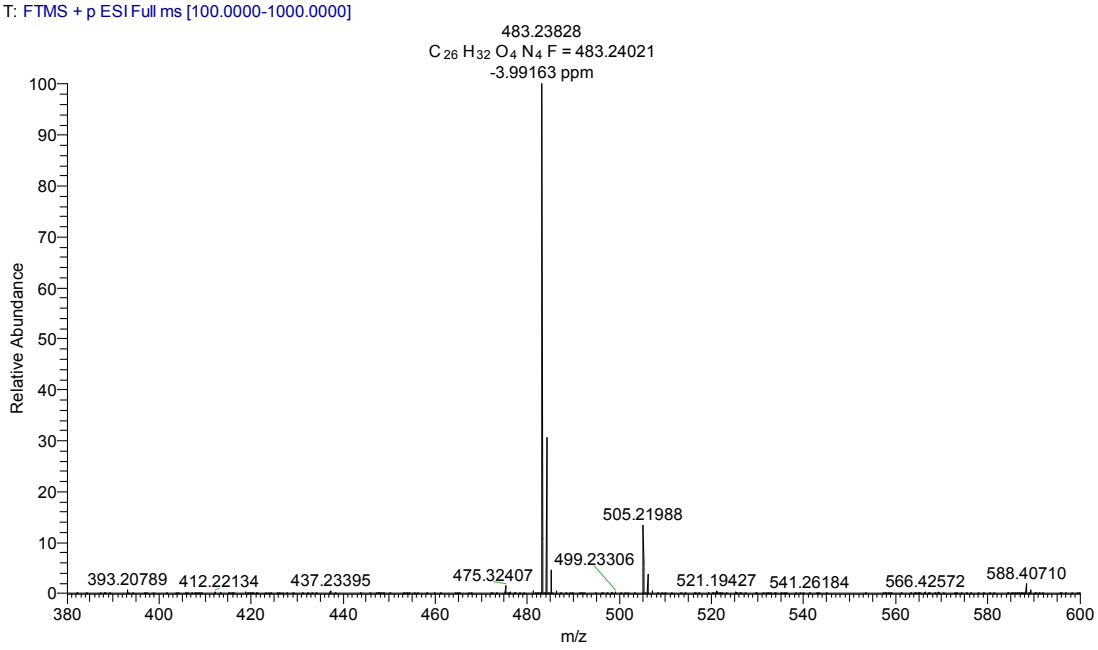
^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS spectra of the compound 4m


7.52 7.51 7.50 7.49 7.33 7.31 7.14 7.13 7.06 7.04 7.02 7.00 6.99 6.88 6.86 6.83 6.47 6.46
4.60 4.15 4.12 4.08 4.07 4.03 4.01 3.88 3.86 3.84 3.82 2.60 2.49 2.47 2.45 2.45 2.43 2.41 2.38 2.35 2.31 2.29 2.27
1.00 1.00 1.00 4.10 1.00
3.00 2.15 1.06
f1 (ppm)
O
N
O
OH
N
N
OH
N
F
OH
1.00 1.00 1.00 4.10 1.00 1.00 2.00 3.00 2.15 1.06 4.00 8.00
f1 (ppm)

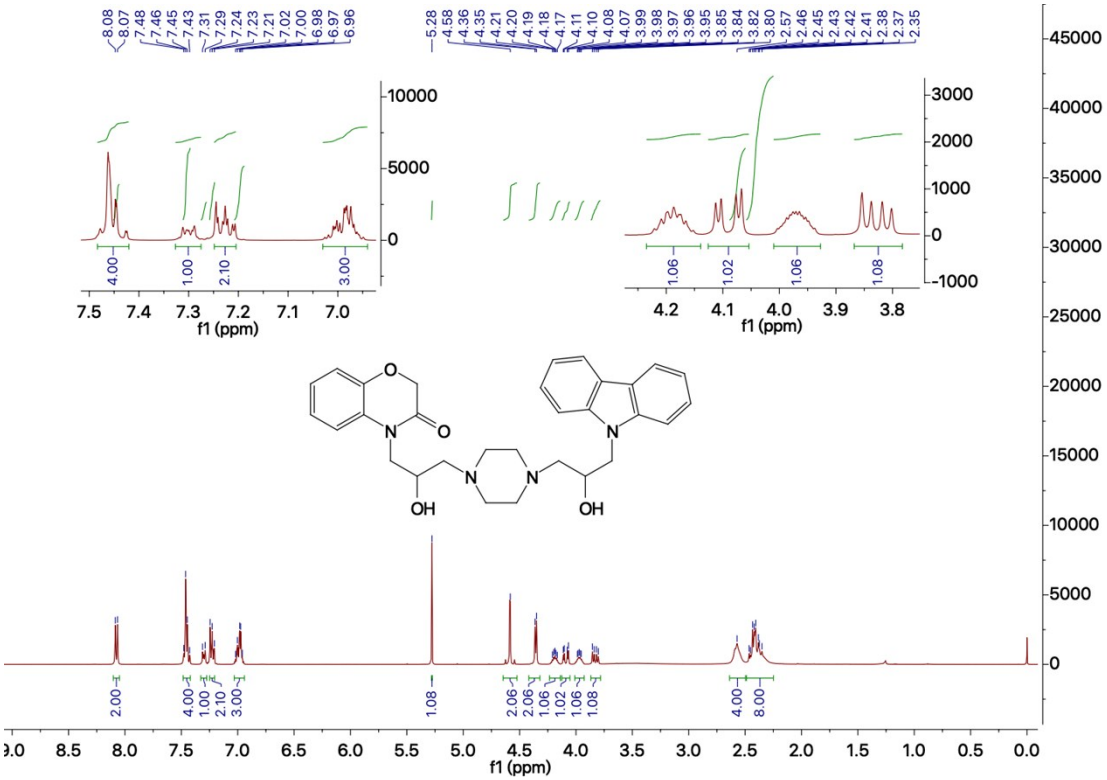

165.29 160.95 158.60 145.32 136.66 129.27 124.91 124.20 122.81 121.65 121.55 117.03 116.11 108.30 108.06 101.67 96.18 95.92
67.68 66.22 65.56 61.45 61.03 53.18 50.03 46.22
124.91 124.20 122.81 121.65 121.55
108.30 108.06 101.67 96.18 95.92
f1 (ppm)
f1 (ppm)
O
N
O
OH
N
N
OH
N
F
OH
f1 (ppm)

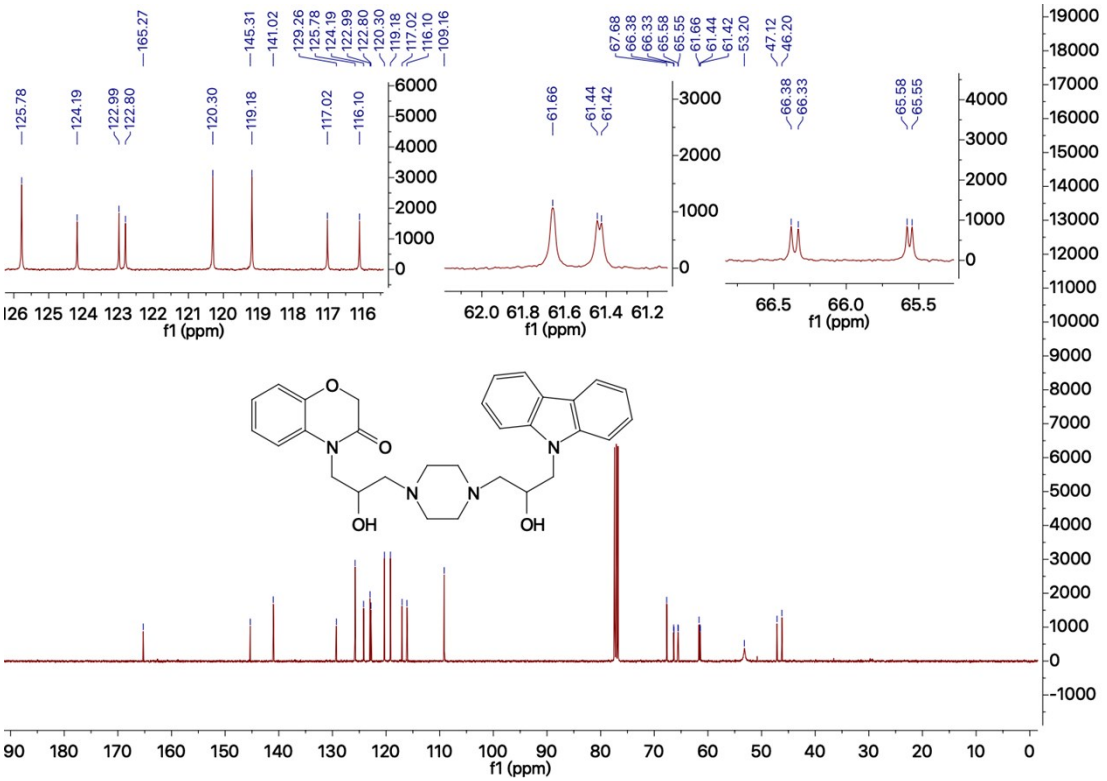


2019071707 #59 RT: 0.57 AV: 1 NL: 3.04E9
T: FTMS + p ESI Full ms [100.0000-1000.0000]



^{1}H NMR, ^{13}C NMR and HRMS spectra of the compound 4n


8.08
8.07
7.48
7.46
7.45
7.43
7.31
7.29
7.24
7.23
7.21
7.02
7.00
6.98
6.97
6.96
5.28
4.58
4.36
4.35
4.21
4.20
4.19
4.18
4.17
4.11
4.10
4.08
4.07
3.99
3.98
3.97
3.96
3.95
3.85
3.84
3.82
3.80
2.57
2.46
2.45
2.43
2.42
2.41
2.38
2.37
2.35
4.00
1.00
2.10
3.00
1.06
1.02
1.06
1.08
f1 (ppm)
O
N
O
N
N
N
OH
OH
2.00
4.00
1.00
2.10
3.00
1.08
2.06
2.06
1.06
1.02
1.06
1.08
4.00
8.00
f1 (ppm)


165.27
145.31
141.02
129.26
125.78
124.19
122.99
122.80
120.30
119.18
117.02
116.10
109.16
67.68
66.38
66.33
65.58
65.55
61.66
61.44
61.42
53.20
47.12
46.20
125.78
124.19
122.99
122.80
120.30
119.18
117.02
116.10
61.66
61.44
61.42
66.38
66.33
65.58
65.55
f1 (ppm)
O
N
O
N
N
N
OH
OH
f1 (ppm)

2018120753 #155 RT: 1.53 AV: 1 NL: 2.04E8
T: FTMS + p ESI Full ms [100.0000-1000.0000]