SUPPLEMENTARY DATA

Pyrrolo[3,4-*d*]pyridazinone derivatives bearing 1,3,4-oxadiazole moiety can serve as new class of selective COX-2 inhibitors. Design, synthesis, molecular docking, comprehensive spectroscopic and *in vitro* investigations

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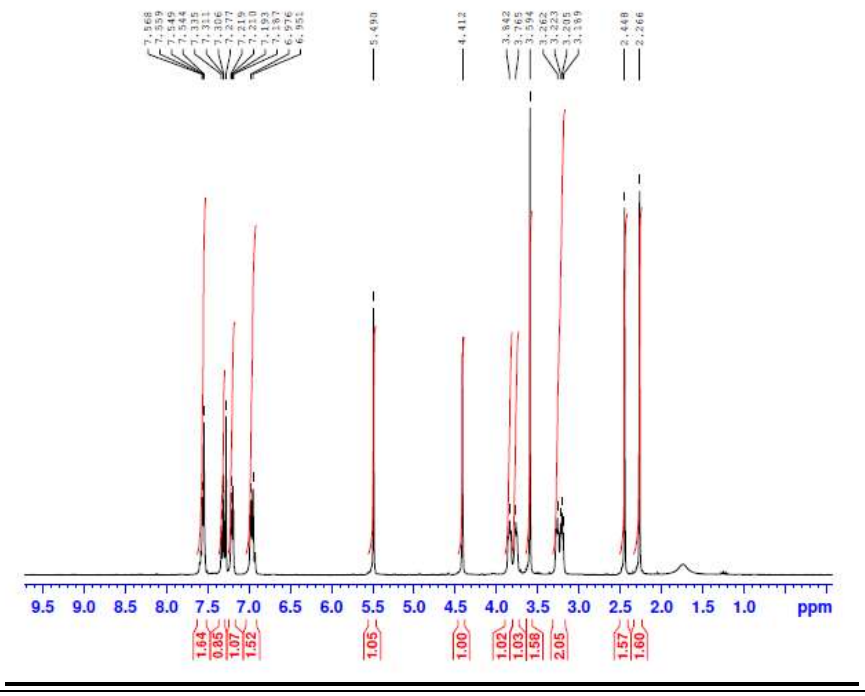
1. NMR spectra of new compounds



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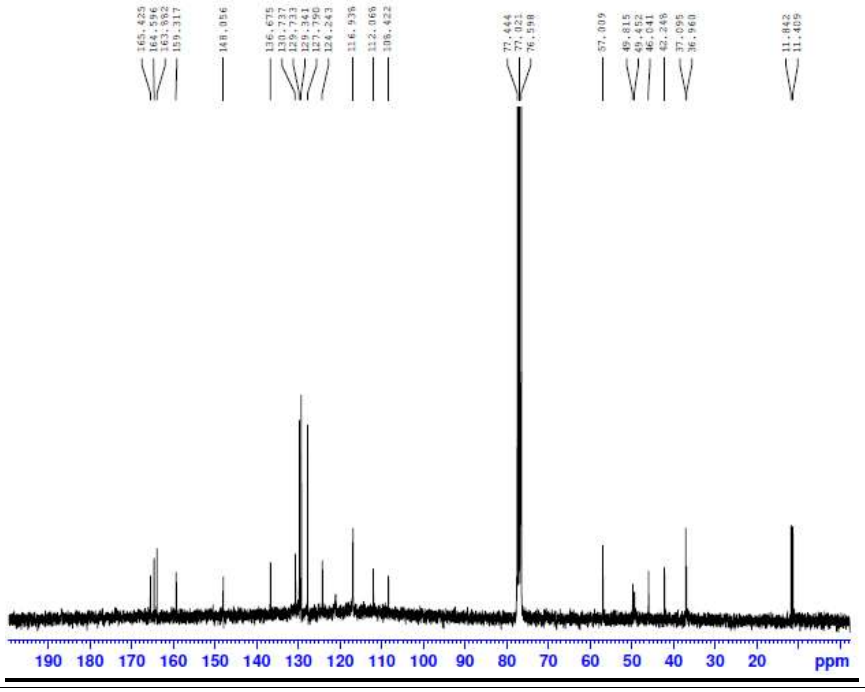

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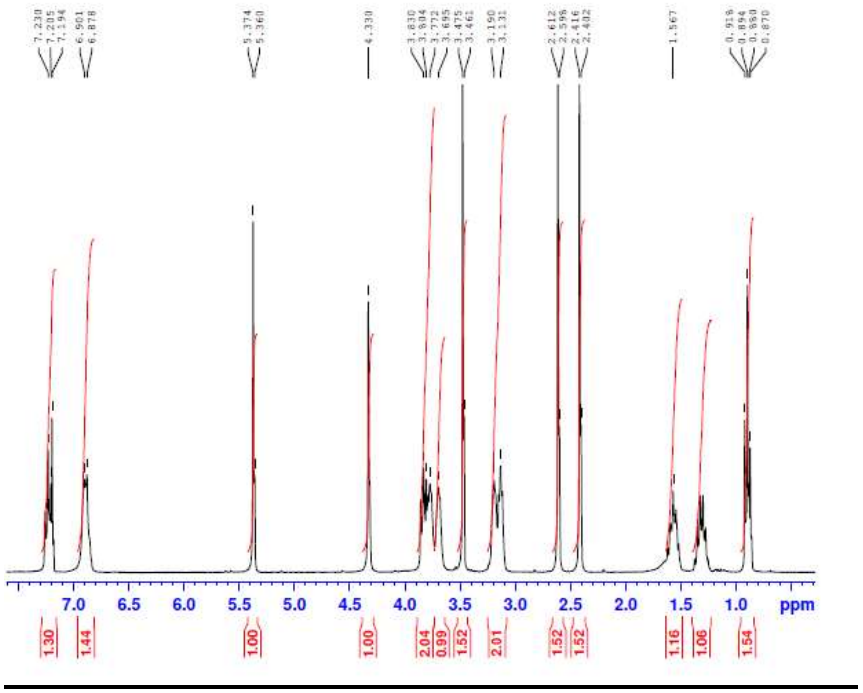
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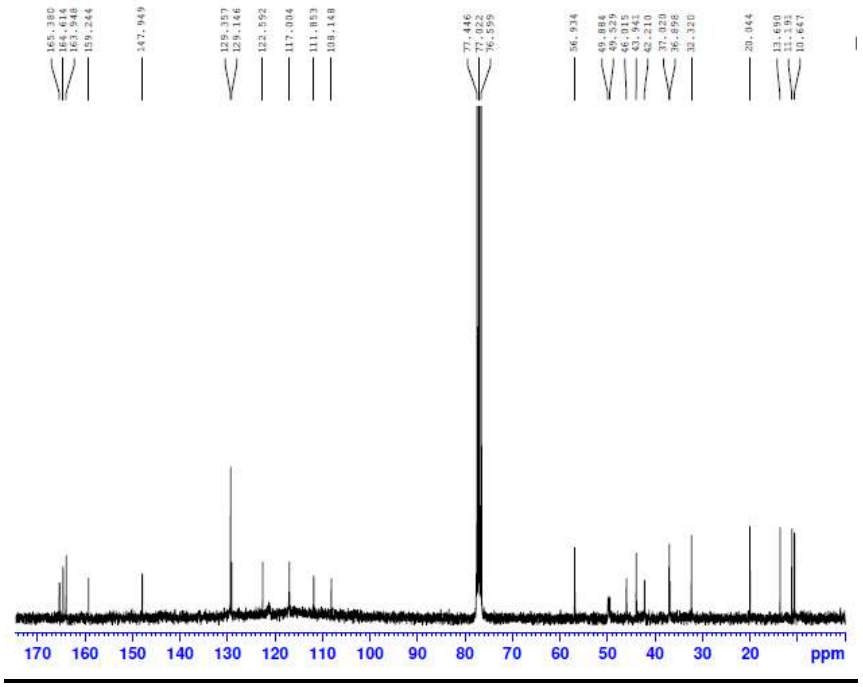
3.475
3.461
3.190
3.131
2.612
2.596
2.416
2.402
1.567
0.919
0.894
0.860
0.870
7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.30 1.44 1.00 1.00 2.04 0.99 1.52 2.01 1.52 1.52 1.16 1.06 1.54

5b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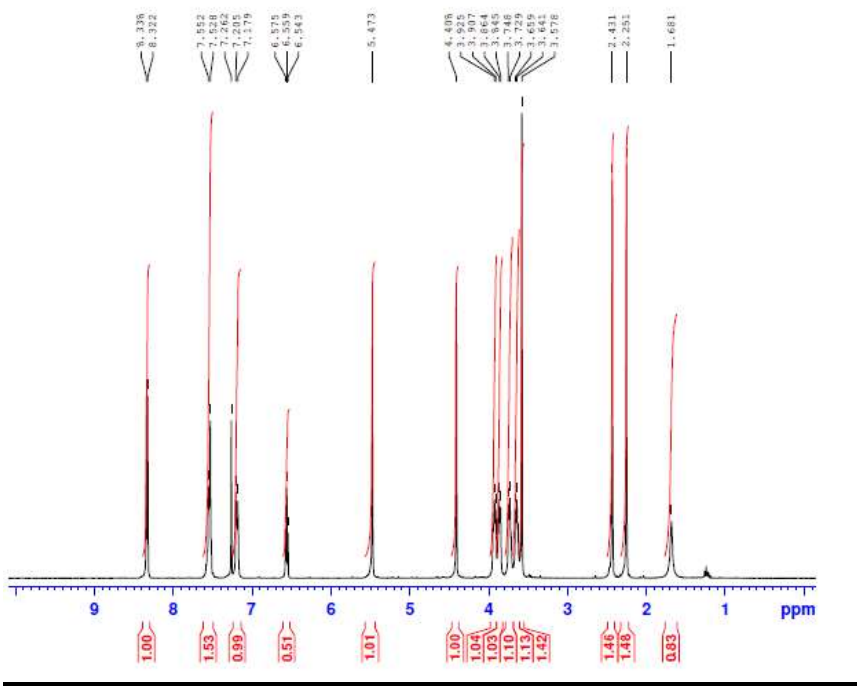
164.614
163.948
159.244
147.949
129.357
129.146
122.592
117.004
111.853
109.148
77.446
77.022
76.599
56.934
49.884
49.529
46.815
45.945
42.210
37.020
36.898
32.320
20.044
13.699
11.191
10.647
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

5b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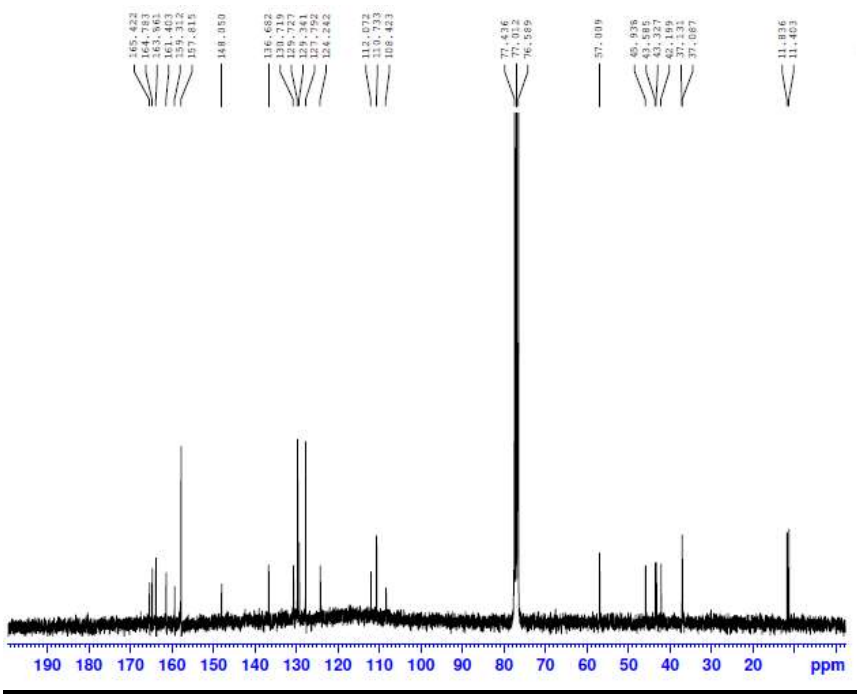
3.925
3.907
3.864
3.846
3.748
3.729
3.659
3.641
3.578
2.431
2.251
1.681
9
8
7
6
5
4
3
2
1
ppm
1.00
1.53
0.99
0.51
1.01
1.00
1.04
1.03
1.10
1.13
1.42
1.46
1.48
0.83

6a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127.792
124.242
112.072
110.733
108.423
77.436
77.012
76.589
57.009
45.938
43.585
43.327
42.199
37.231
37.087
11.836
11.463
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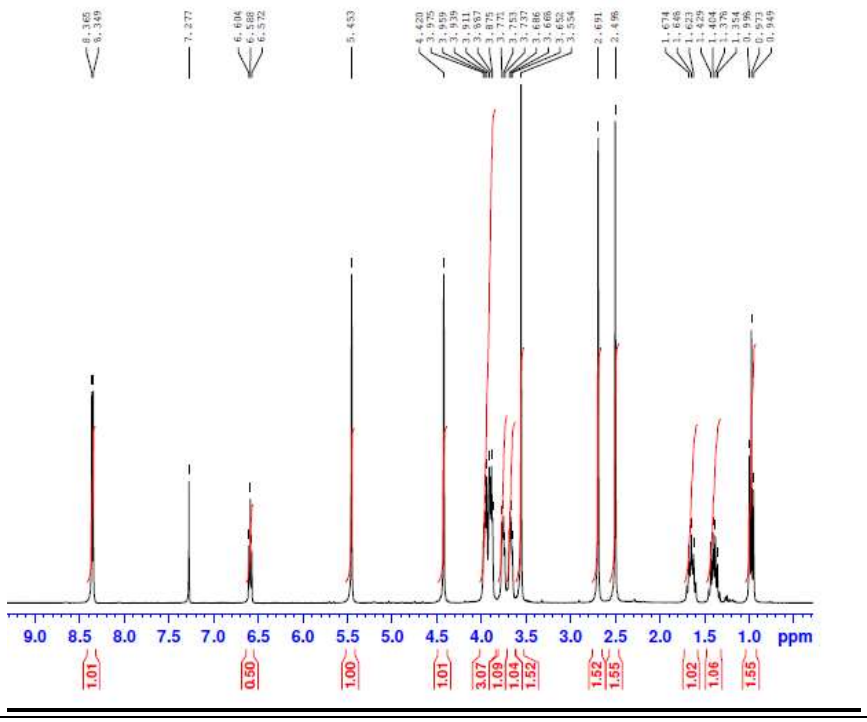
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

6a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8.349
7.277
6.604
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3.939
3.911
3.897
3.875
3.771
3.753
3.737
3.686
3.668
3.652
3.554
2.691
2.496
1.674
1.646
1.623
1.429
1.404
1.376
1.354
0.996
0.973
0.949
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.01
0.50
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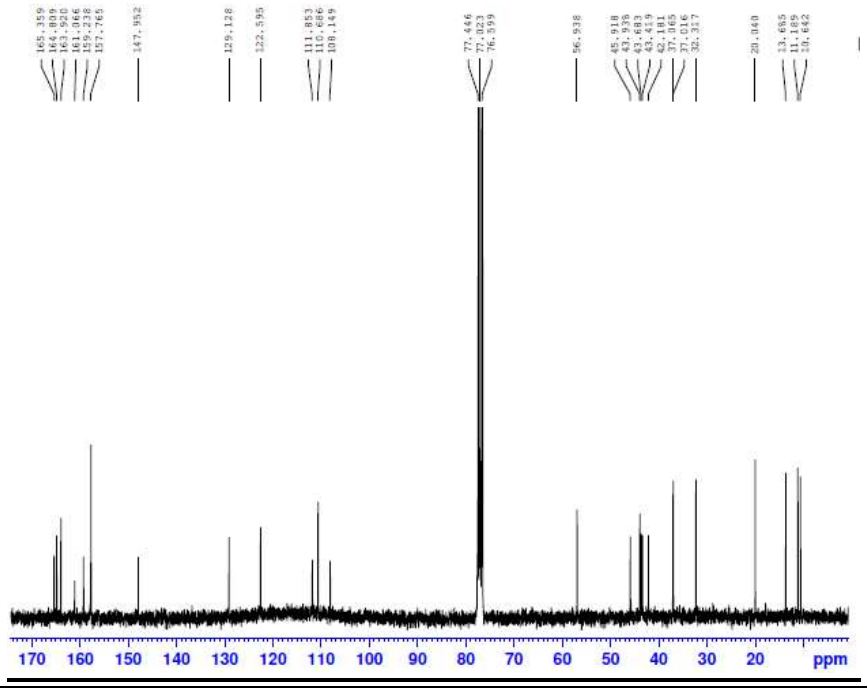
3.07
1.09
1.04
1.52
1.52
1.55
1.02
1.06
1.55

6b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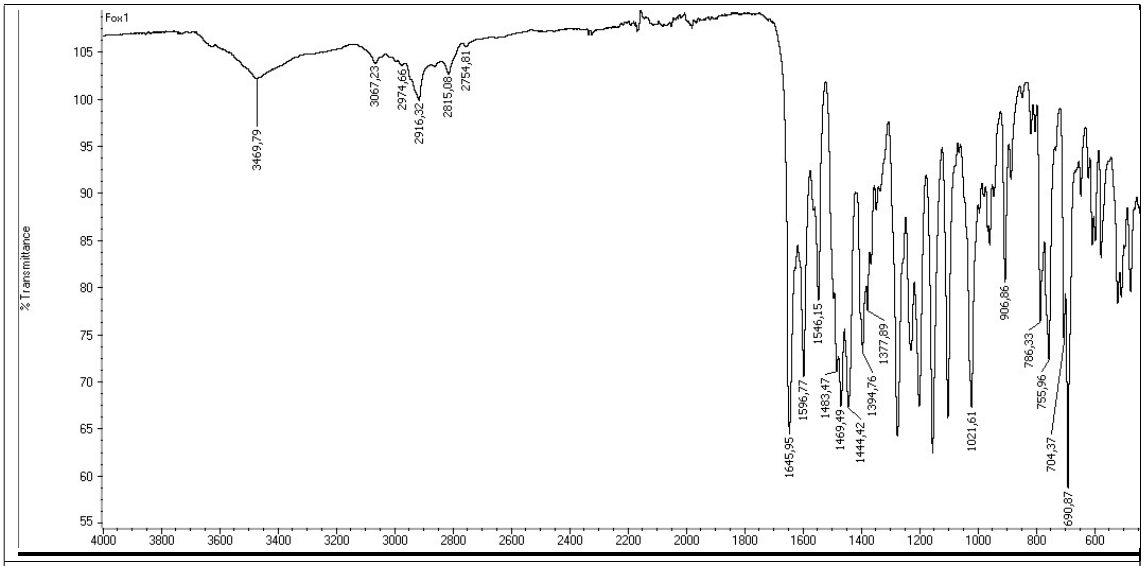
77.446
77.023
76.599
56.938
45.918
43.898
43.683
43.419
42.101
37.065
37.016
30.357
20.040
13.665
11.195
10.662
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

6b

2. IR spectra of new compounds



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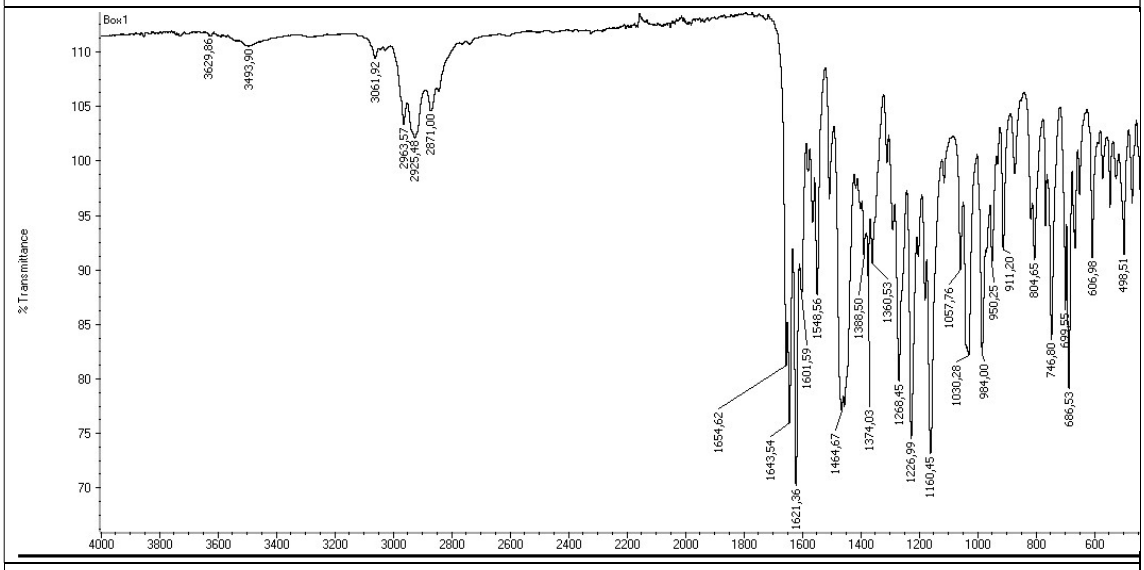

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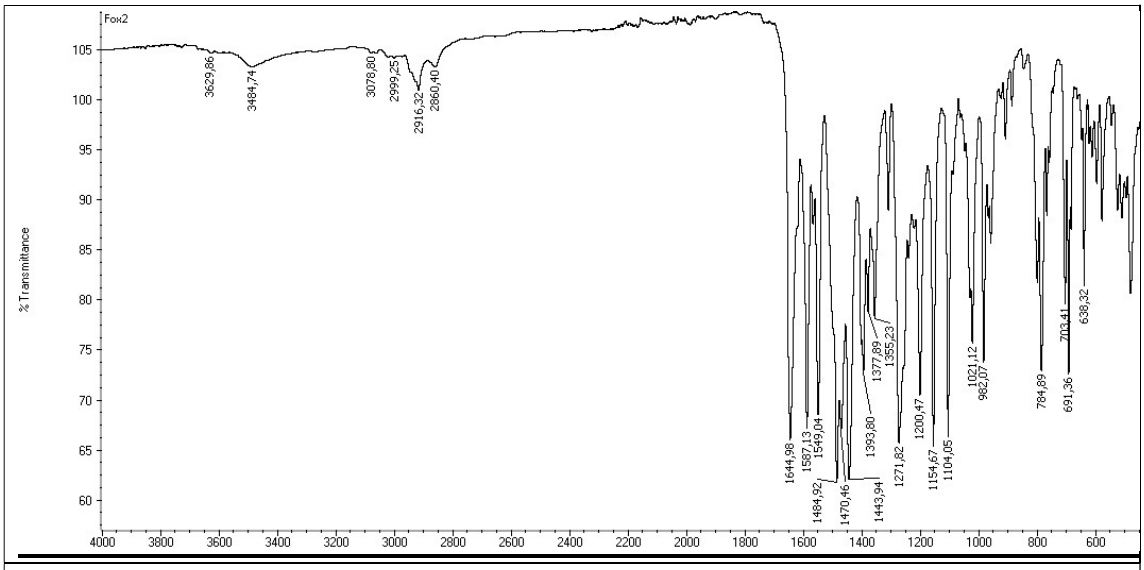
Fox2
% Transmittance
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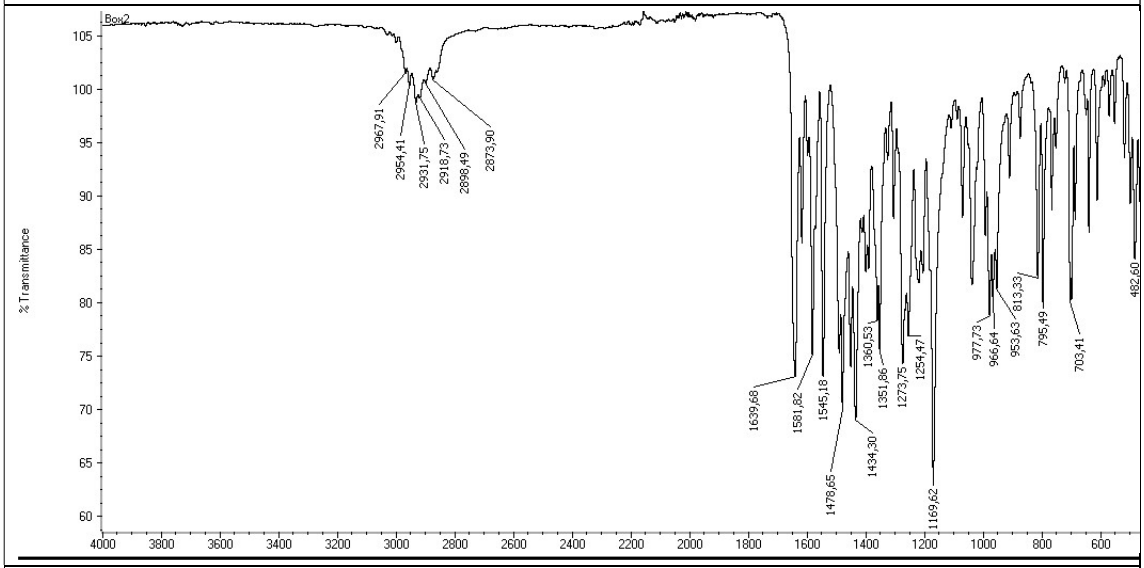
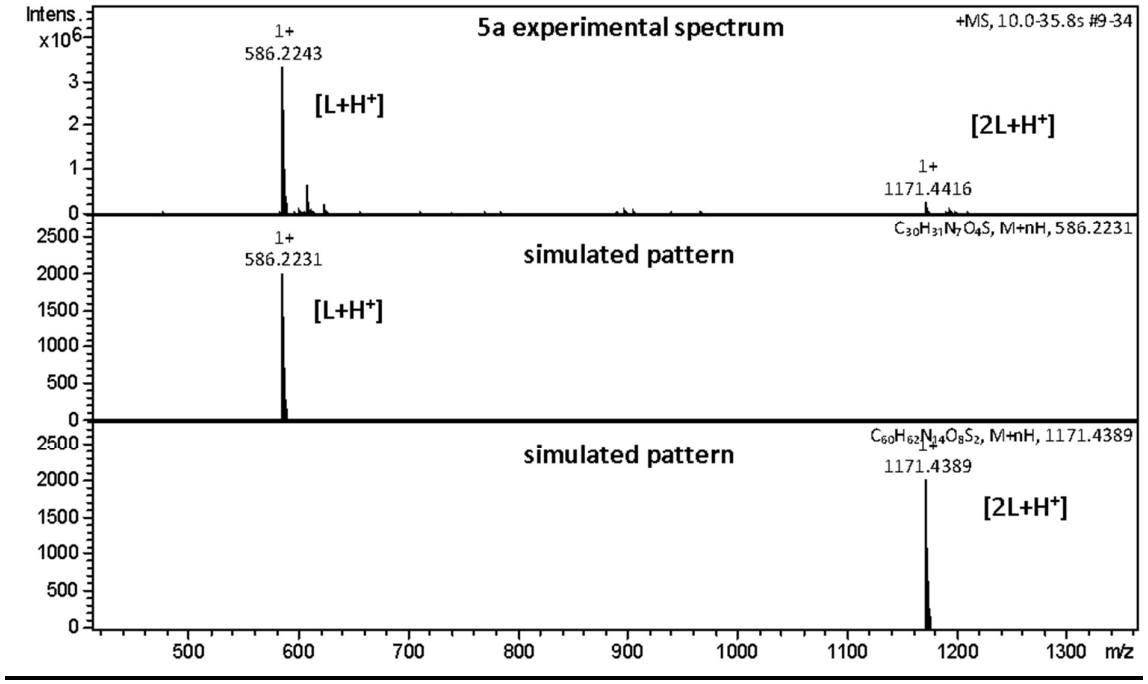
3484,74
3078,80
2999,25
2916,32
2860,40
1644,98
1587,13
1549,04
1484,92
1470,46
1443,94
1393,80
1377,89
1355,23
1271,82
1200,47
1154,67
1104,05
1021,12
982,07
784,89
703,41
691,36
638,32

6a


Box2
% Transmittance
2967,91
2954,41
2931,75
2918,73
2898,49
2873,90
1639,68
1581,82
1545,18
1478,65
1434,30
1360,53
1351,86
1273,75
1254,47
1169,62
977,73
966,64
953,63
813,33
795,49
703,41
482,60

6b

3. Mass spectra of new compounds



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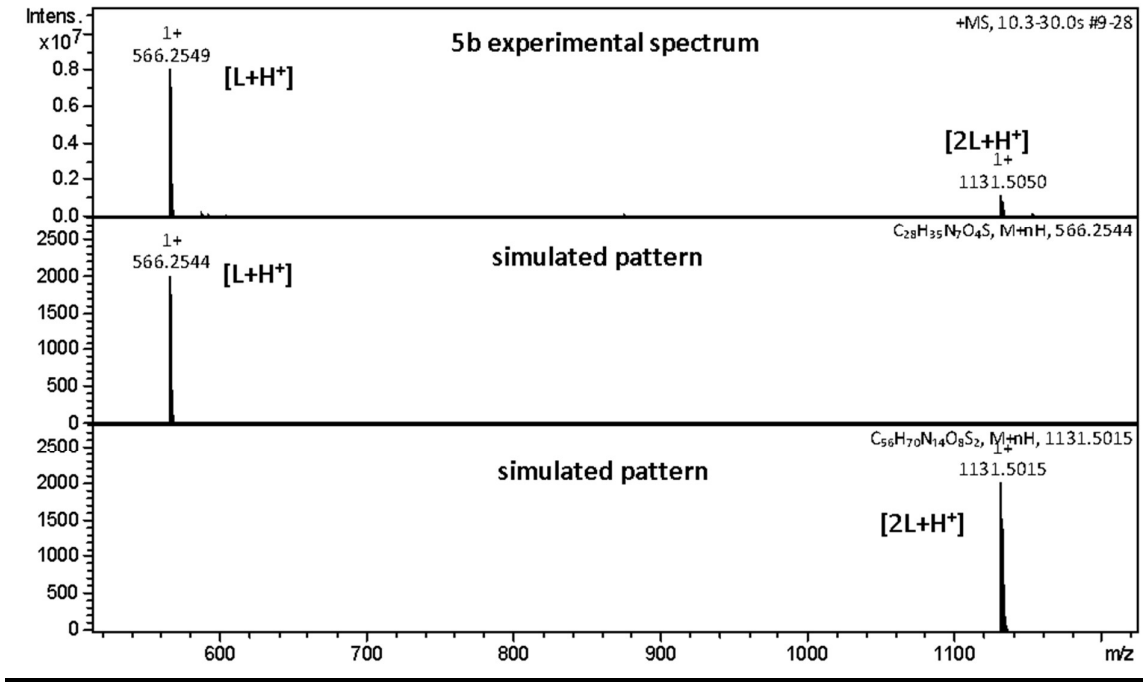

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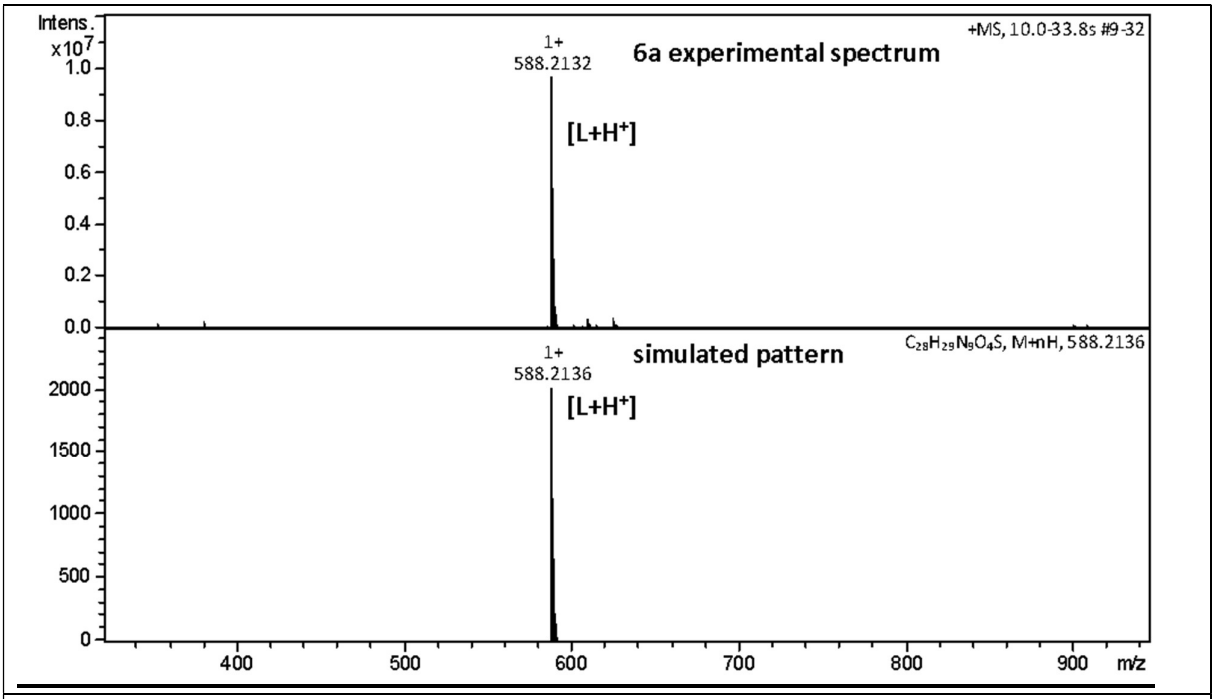
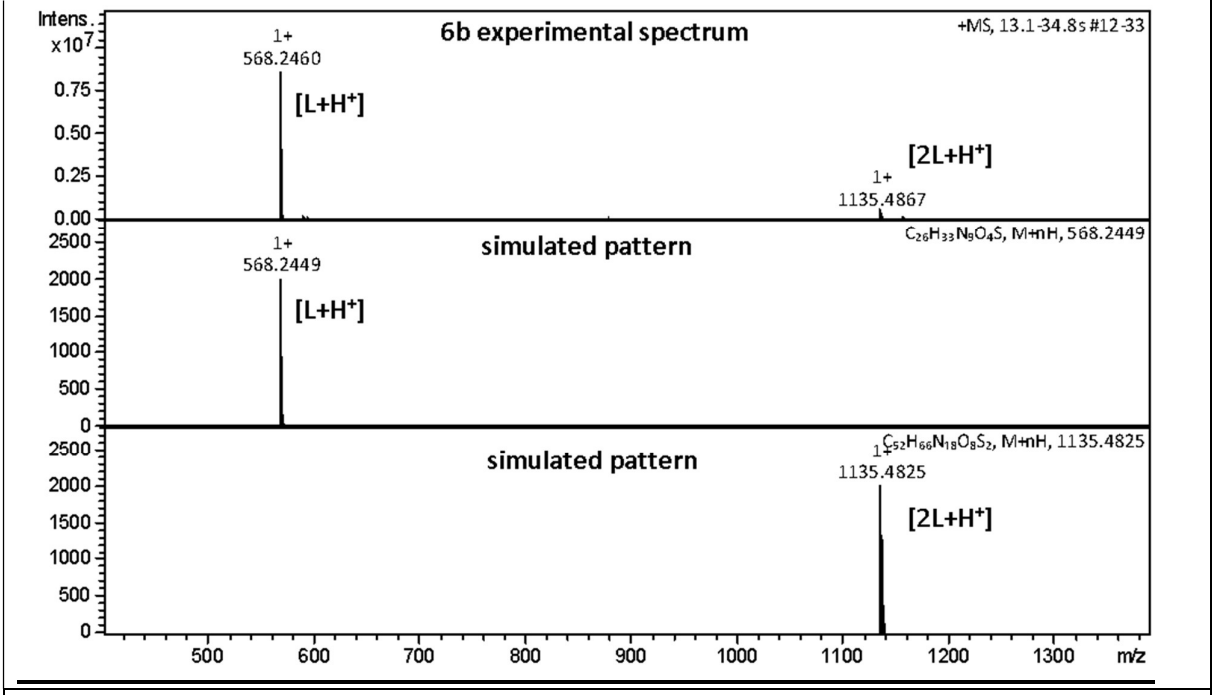

Intens.
x10^7
1.0
0.8
0.6
0.4
0.2
0.0
+MS, 10.0-33.8s #9-32
1+
588.2132
6a experimental spectrum
[L+H+]
2000
1500
1000
500
0
C28H29N9O4S, M+nH, 588.2136
1+
588.2136
simulated pattern
[L+H+]
400
500
600
700
800
900
m/z

6a


Intens.
x10^7
0.75
0.50
0.25
0.00
6b experimental spectrum
+MS, 13.1-34.8s #12-33
1+
568.2460
[L+H+]
[2L+H+]
1+
1135.4867
2500
2000
1500
1000
500
0
C26H33N9O4S, M+nH, 568.2449
1+
568.2449
simulated pattern
[L+H+]
C52H66N18O8S2, M+nH, 1135.4825
simulated pattern
1+
1135.4825
[2L+H+]
500
600
700
800
900
1000
1100
1200
1300
m/z

6b

4. Figures and tables

Fig. S1. Equtions used spectroscopic studies.

$$F_{corr} = F_{obs} 10^{\frac{(A_{ex}+A_{em})}{2}} (1)$$
Eq.1 where, F_{corr} and F_{obs} are the corrected and observed fluorescence intensities, respectively. A_{ex} and A_{em} are the absorbance values at excitation and emission wavelengths, respectively.
$$\frac{F_O}{F} = 1 + k_q \tau [Q] = 1 + K_{SV} (2)$$
Eq.2 where F_0 and F are the steady-state fluorescence intensities at the maximum wavelength in the absence and presence of quencher, respectively, k_q the quenching rate constant of the biomolecule, τ_0 the average lifetime of the biomolecule, [Q] is the quencher concentration, and K_{sv} is the Stern–Volmer constant
$$log \frac{F_0 - F}{F} = log K_b + n log[Q] (3)$$
Eq.3 where F_0 and F are the steady-state fluorescence intensities at the maximum wavelength in the absence and presence of quencher, respectively, [Q] is the quencher concentration
$$log K_b = -\frac{\Delta H^\circ}{RT} + \frac{\Delta S^\circ}{R} (4)$$ $$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ = -RT ln K_b (5)$$
Eq.4 and eq. 5 where K_b is the binding constant, R is the universal gas constant, entropic change (ΔS°), free energy change (ΔG°), enthalpy change (ΔH°)