Supplementary Information (SI) for RSC Advances.
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Supporting Information

Computational design, synthesis, *in vitro* and *in vivo* evaluation of a 3,4-methylenedioxyphenol (Sesamol) derivative as an NRF2/HO-1 pathway activator for protection against Drug-induced liver injury

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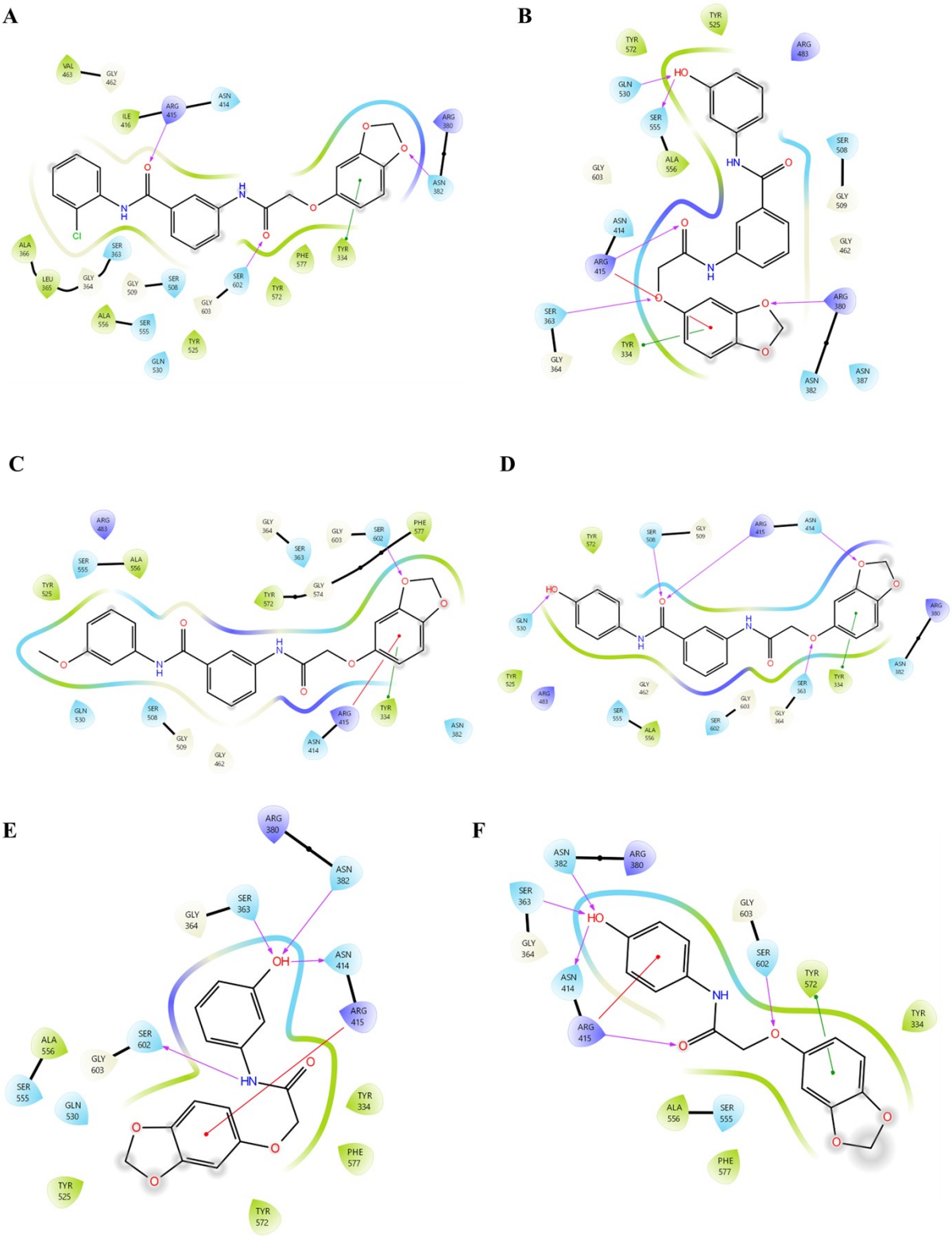


Fig S1 (1/2): 2D interaction image of A) 133699-2ClBen, B) 133699-3OMeBen, C) 133699-3HyBen, D) 133699-4HyBen, E) 133840-3HyBen, F) 133840-4HyBen. (Continued on the next page.)

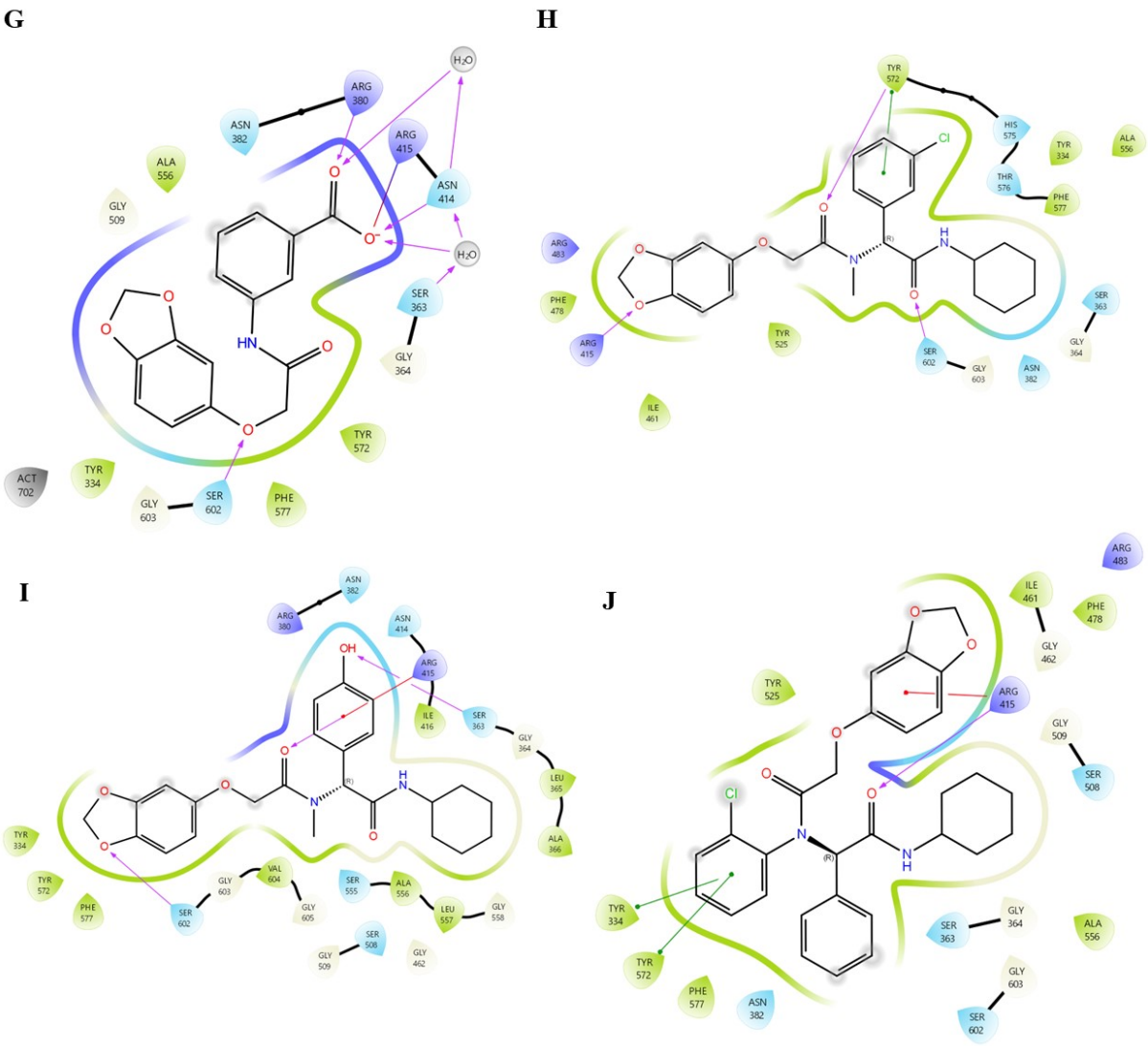


Fig S1 (2/2): 2D interaction image of G) 133840-3CaBen, H) 133861-3ClBen, I) 133861-4HyBen, and J) 133862-2ClBen.

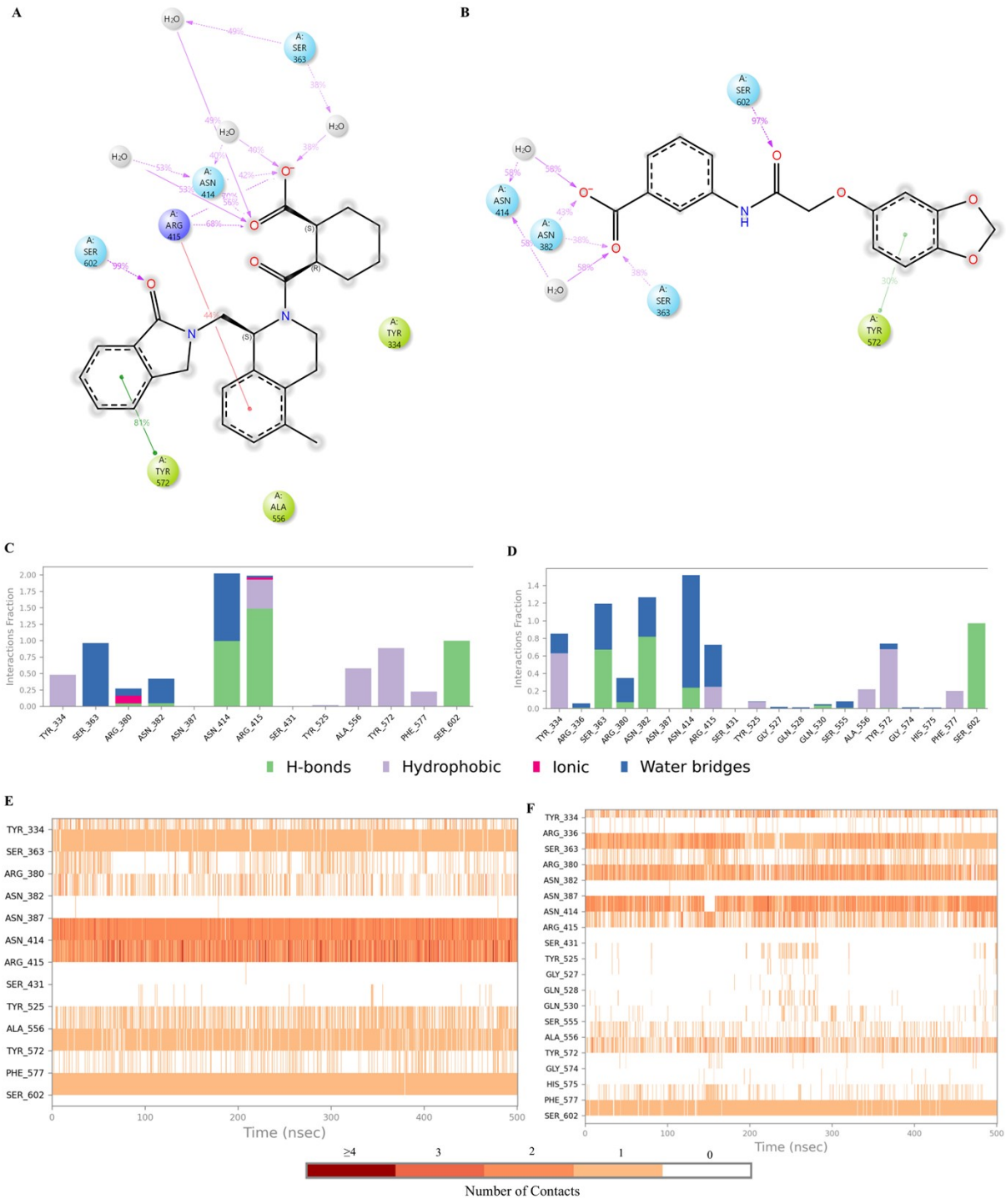


Fig S2: Protein–Ligand Contact Interaction of Complexes **A)** Ccomplex-1 and **B)** Complex-2; Protein–Ligand Contact Histograms of Complexes **C)** Complex-1 and **D)** Complex-2; Protein–Ligand Complex Timelines of Complexes **E)** Complex-1 and **F)** Complex-2.

Table S1: Predicted ADME profile of the top 10 compounds

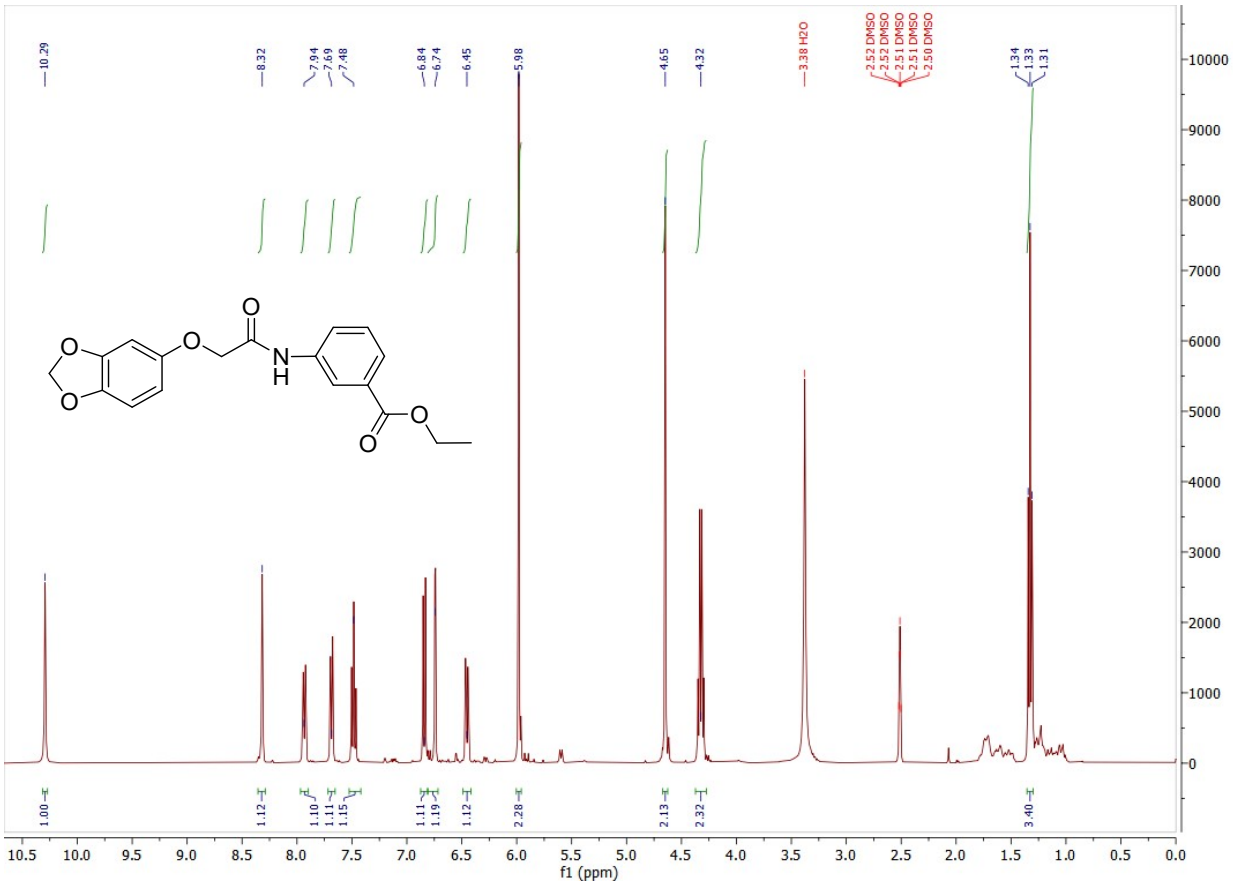
Title	mol MW	donor HB	accpt HB	QPlogS	QPlog BB	QPlog Khsa	%HumanOral Absorption	Rule of 5
133699-2ClBen	424.84	2	7.25	-4.209	-0.573	0.173	100	0
133699-3HyBen	406.39	3	8	-4.796	-1.332	0.003	91	0
133699-3OMeBen	420.42	2	8	-4.24	-0.673	0.123	100	0
133699-4HyBen	406.39	3	8	-4.618	-1.349	0.004	90	0
133840-3HyBen	287.27	2	5.5	-2.425	-0.566	-0.277	92	0
133840-4HyBen	287.27	2	5.5	-2.4	-0.6	-0.295	91	0
133840-3CaBen	315.28	2	6.75	-3.139	-1.237	-0.494	72	0
133861-3ClBen	458.94	1	7.75	-4.054	-0.255	-0.203	100	0
133861-4HyBen	440.49	2	8.5	-2.277	-0.748	-0.514	8	0
133862-2ClBen	521.01	1	7.75	-5.388	-0.313	0.392	100	1
Normal Range	130.0 to 725.0	0.0 to 6.0	2.0 to 20.0	-6.5 to 0.5	-3.0 to 1.2	-1.5 to 1.5	>80% High <25% low	maximum is 4

Synthesis, Characterization, and Spectra of Ethyl 3-(2-(benzo[d][1,3]dioxol-5-yloxy)acetamido)benzoate:

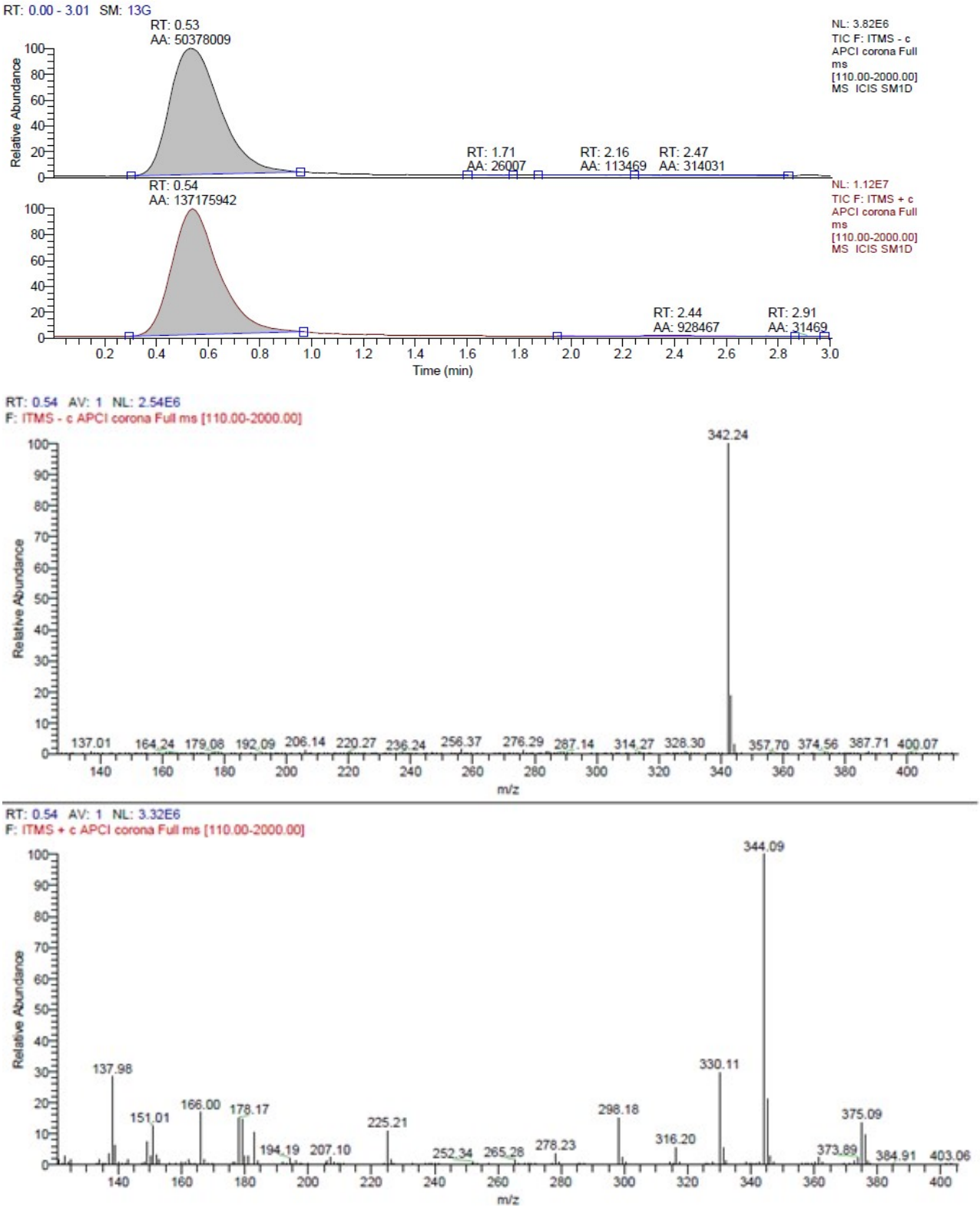
Synthesis: 2-(Benzo[d][1,3]dioxol-5-yloxy)acetic acid (1 eq), HOBt (1.5 eq), and DCC (3 eq) were added sequentially to a round-bottom flask containing ethyl acetate under ice-cold conditions (0 °C). After stirring for 45 minutes, the white precipitate formed was filtered off under vacuum. The filtrate was then treated with ethyl aminobenzoate (1 eq) and triethylamine (3 eq) and stirred for 6 hours at room temperature. The reaction mixture was washed with water, and the organic phase was dried under reduced pressure. The crude product was purified by successive washings with hexane and petroleum ether, yielding Ethyl 3-(2-(benzo[d][1,3]dioxol-5-yloxy)acetamido)benzoate.

Characterization: Light brown liquid (80% yield); BP: 450-455 ^{o}C ; ^{1}H NMR (400 MHz, DMSO) δ 10.29 (s, 1H), 8.32 (s, 1H), 7.94 (s, 1H), 7.69 (s, 1H), 7.48 (s, 1H), 6.84 (s, 1H), 6.74 (s, 1H), 6.45 (s, 1H), 5.98 (s, 2H), 4.65 (s, 2H), 4.32 (s, 2H), 1.33 (t, J = 7.1 Hz, 3H).

Spectra:

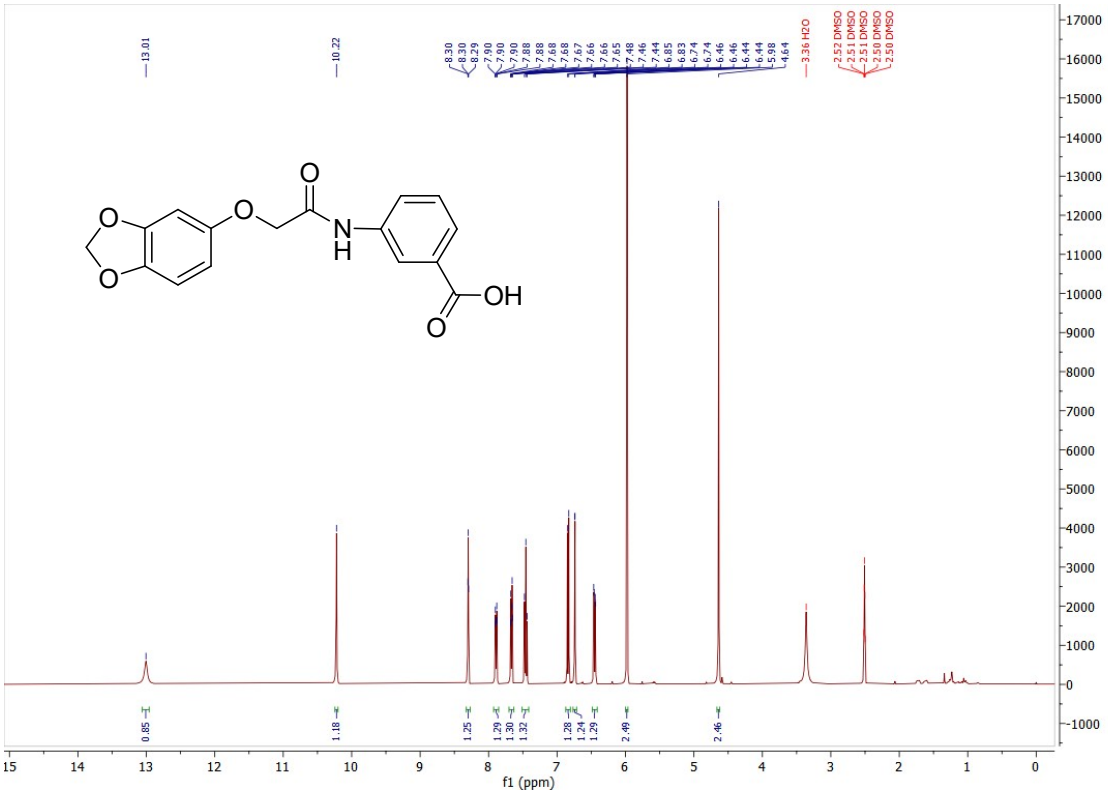


400 MHz ^{1}H NMR spectrum of Ethyl 3-(2-(benzo[d][1,3]dioxol-5-yloxy)acetamido)benzoate in DMSO

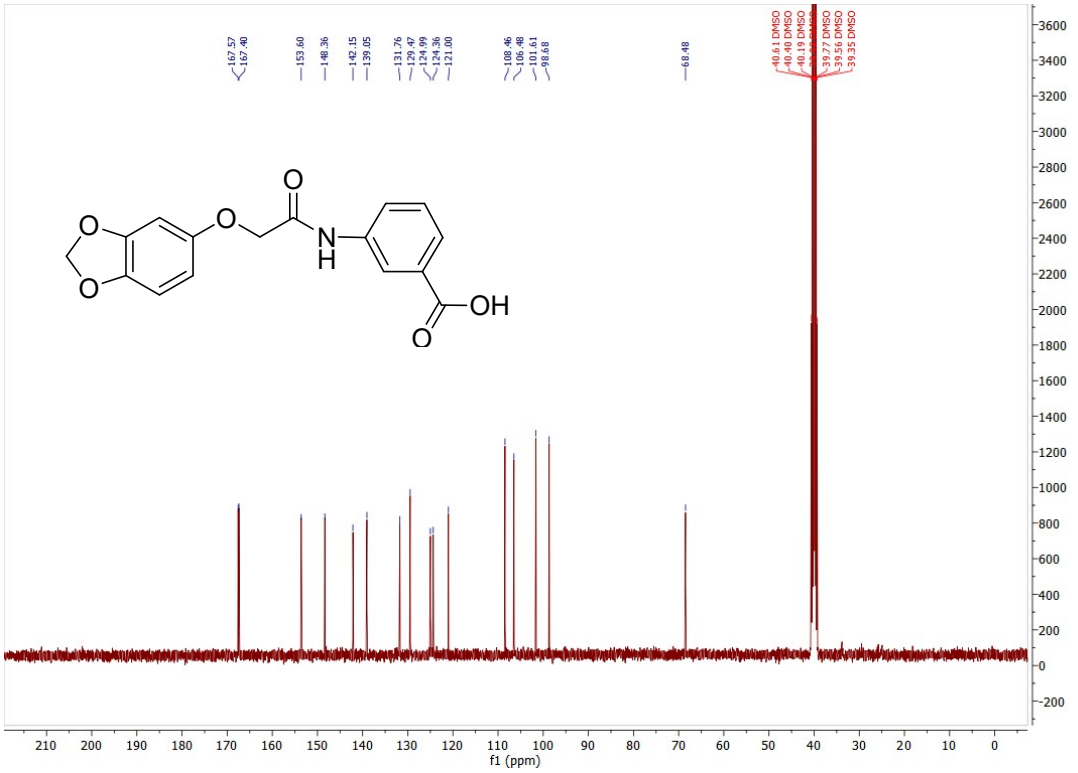


LCMS of Ethyl 3-(2-(benzo[d][1,3]dioxol-5-yloxy)acetamido)benzoate (Molecular Mass: 343 g/mol)

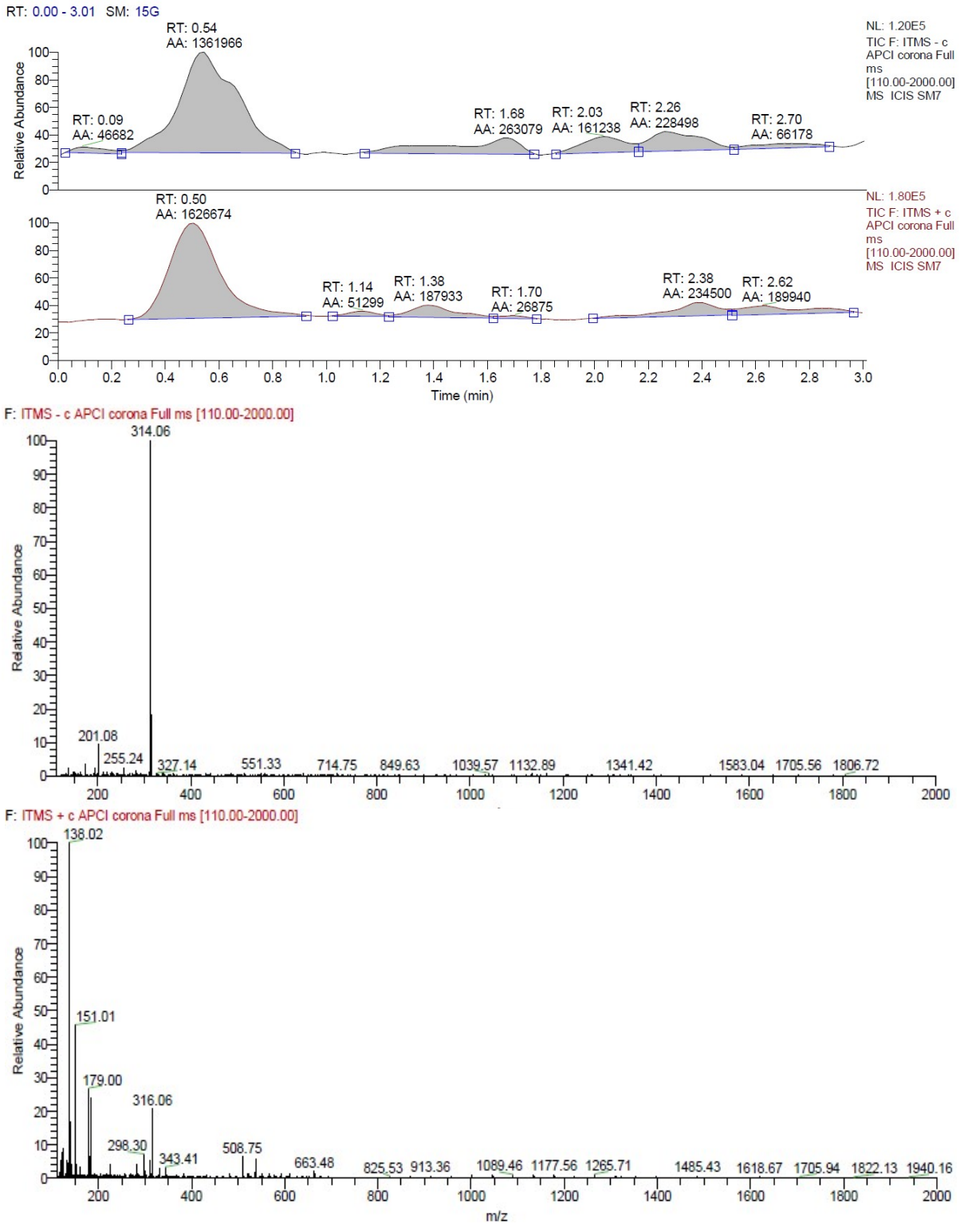
Spectra of 3-(2-(benzo[d][1,3]dioxol-5-yloxy)acetamido)benzoic acid (SMD):



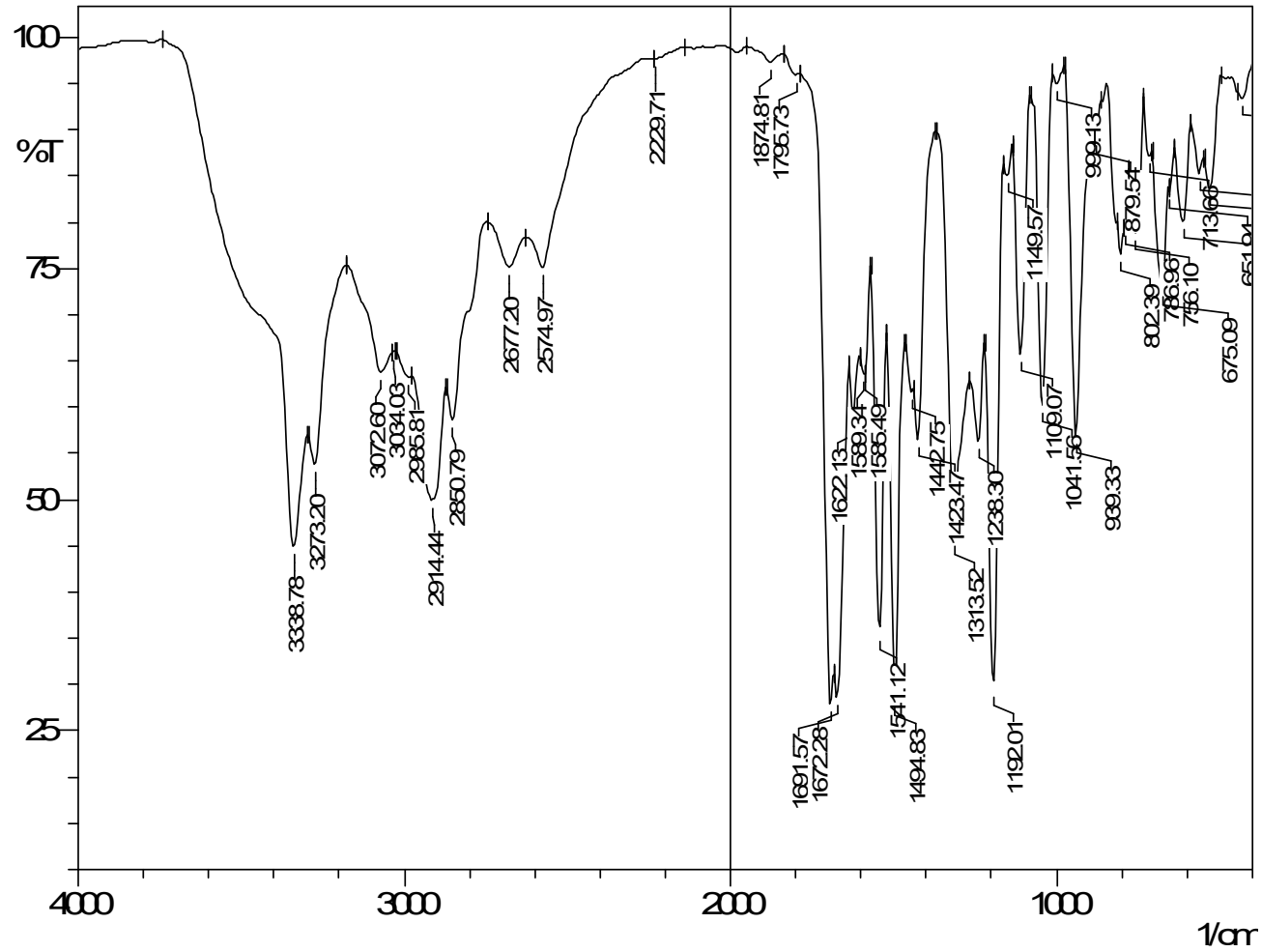
400 MHz ^{1}H NMR spectrum of compound SMD in DMSO



101 MHz ^{13}C NMR spectrum of compound SMD in DMSO



LCMS of SMD (Molecular Mass: 315.07 g/mol)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1000
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2914.44
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756.10
713.66
675.09

FT-IR of SMD