Optimizing 2-Furylated Imidazole π-Bridges for NIR Lipid Droplet Imaging

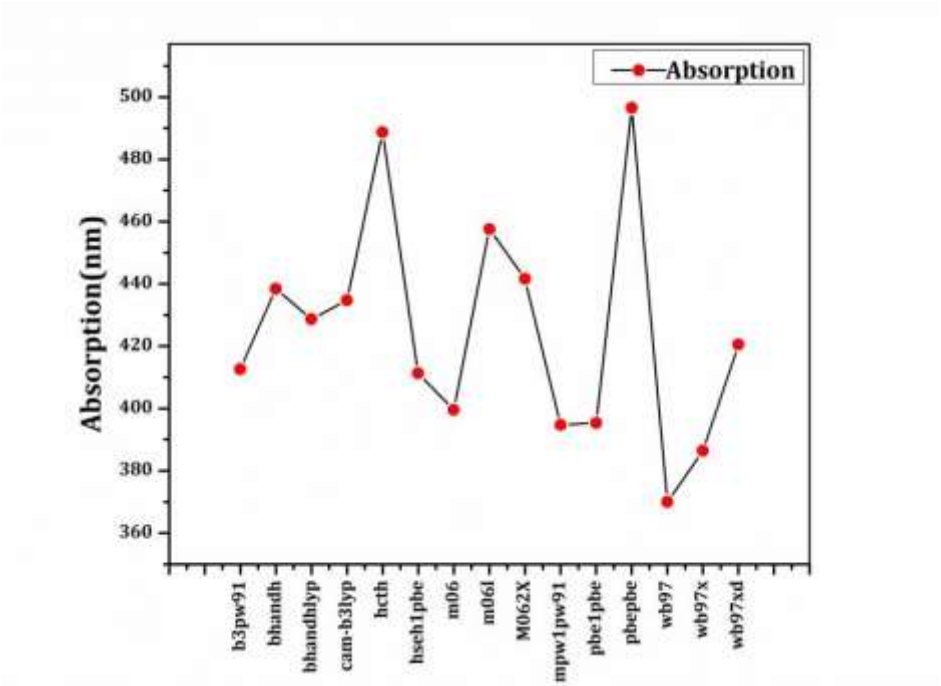
Anamika Suresh[a], Rohith Ramasamy[b], Deepa Kallumpurath[a], Rajadurai Vijay Solomon[b]*

[a]Department of Chemistry, R.S.M. SNDP Yogam College,

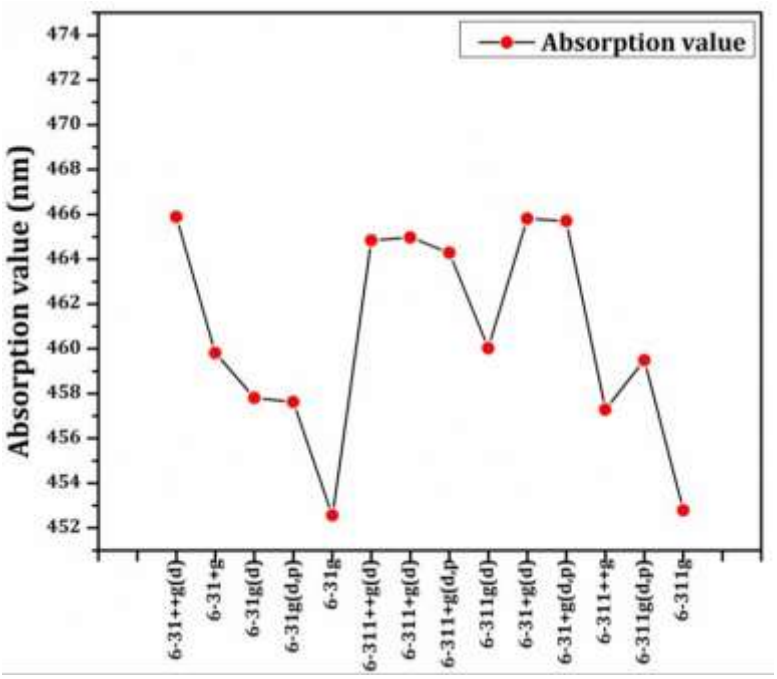
[Affiliated to the University of Calicut], Kozhikode – 673 305, Kerala, India

[b]Department of Chemistry, Madras Christian College (Autonomous), [Affiliated to the University of Madras], Chennai – 600 059, Tamil Nadu, India

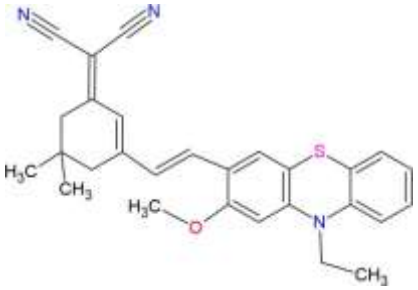
*corresponding author: vjsolo@gmail.com



SIF1. Functional benchmarking at M06L/6-31+g(d)



SIF2. Basis set bench marking M06L/6-31+g(d)



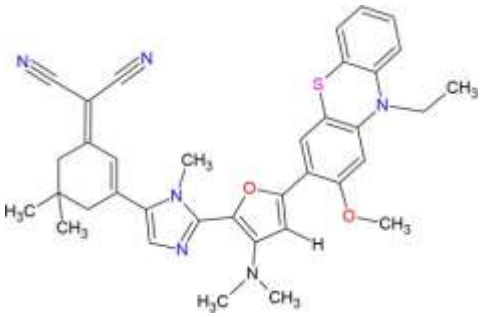
LD

LDP

LDP1

LDP2

LDP3



LDP4

LDP5

LDP6

LDP7

LDP8

SIF3. 2D structural representation of LD and LDPs

SIT1. Computed bond parameters of LD and LDPs at B3LYP/6-31+g(d) level of theory where length are in (Å) and bond angles given in ˚

Molecules	**Bond parameters**					
	Bond length (Å)		**Bond angle(˚)**		**Bond dihedral angle(˚)**	
LD	C41-C36	1.443	C3-C1-C25	124.16	C3-C1-C25-C26	-170.89
	C35-C29	1.427	C2-C1-C25	116.04	C2-C1-C25-C27	-168.74
	C1-C25	1.446	C36-C41-C42	117.39	C27-C29-C35-C39	-178.22
	C27-C31	1.359	C36-C41-C43	126.71	C30-C29-C35-C40	-178.82
LDP	C41-C36	1.451	C3-C1-C25	123.68	C3-C1-C25-C26	-154.17
	C35-C29	1.443	C2-C1-C25	116.50	C2-C1-C25-C27	-159.02
	C1-C25	1.432	C36-C41-C42	120.45	C27-C29-C35-C39	167.54
	C27-C31	1.460	C36-C41-C43	122.84	C30-C29-C35-C40	165.58
			C27-C29-C35	127.08	C42-C41-C36-C37	176.18
					C40-C36-C41-C43	176.69
LDP1	C41-C36	1.452	C3-C1-C25	124.53	C3-C1-C25-C26	159.69
	C35-C29	1.422	C2-C1-C25	116.29	C2-C1-C25-C27	169.58
	C1-C25	1.433	C36-C41-C42	116.29	C27-C29-C35-C39	-174.76
	C27-C31	1.371	C36-C41-C43	122.81	C30-C29-C35-C40	-170.77
			C27-C29-C35	121.90	C42-C41-C36-C37	-170.77
					C40-C36-C41-C43	-174.76

LDP2	C41-C36	1.452	C3-C1-C25	123.57	C3-C1-C25-C26	-154.00
	C35-C29	1.431	C2-C1-C25	116.61	C2-C1-C25-C27	-159.37
	C1-C25	1.432	C36-C41-C42	120.34	C27-C29-C35-C39	177.50
	C27-C31	1.464	C36-C41-C43	122.95	C30-C29-C35-C40	177.94
			C27-C29-C35	126.25	C42-C41-C36-C37	163.36
					C40-C36-C41-C43	160.56
LDP3	C41-C36	1.463	C3-C1-C25	124.41	C3-C1-C25-C26	158.15
	C35-C29	1.441	C2-C1-C25	116.06	C2-C1-C25-C27	167.67
	C1-C25	1.432	C36-C41-C42	119.98	C27-C29-C35-C39	135.84
	C27-C31	1.462	C36-C41-C43	122.96	C30-C29-C35-C40	137.57
			C27-C29-C35	127.11	C42-C41-C36-C37	165.85
					C40-C36-C41-C43	-169.26
LDP4	C41-C36	1.452	C3-C1-C25	123.55	C3-C1-C25-C26	152.76
	C35-C29	1.440	C2-C1-C25	116.51	C2-C1-C25-C27	-157.72
	C1-C25	1.431	C36-C41-C42	119.29	C27-C29-C35-C39	137.74
	C27-C31	1.462	C36-C41-C43	124.38	C30-C29-C35-C40	141.39
			C27-C29-C35	120.38	C42-C41-C36-C37	168.86
					C40-C36-C41-C43	169.72
LDP5	C41-C36	1.451	C3-C1-C25	116.70	C3-C1-C25-C26	-155.65

	C35-C29	1.412	C2-C1-C25	123.84	C2-C1-C25-C27	-161.65
	C1-C25	1.433	C36-C41-C42	123.13	C27-C29-C35-C39	-178.08
	C27-C31	1.363	C36-C41-C43	120.15	C30-C29-C35-C40	-177.86
			C27-C29-C35	120.36	C42-C41-C36-C37	176.91
					C40-C36-C41-C43	172.40
LDP6	C41-C36	1.451	C3-C1-C25	124.37	C3-C1-C25-C26	157.50
	C35-C29	1.432	C2-C1-C25	116.12	C2-C1-C25-C27	167.43
	C1-C25	1.431	C36-C41-C42	119.60	C27-C29-C35-C39	143.69
	C27-C31	1.462	C36-C41-C43	124.12	C30-C29-C35-C40	148.84
			C27-C29-C35	127.19	C42-C41-C36-C37	-171.11
					C40-C36-C41-C43	-167.02
LDP7	C41-C36	1.452	C3-C1-C25	123.55	C3-C1-C25-C26	-153.73
	C35-C29	1.432	C2-C1-C25	116.71	C2-C1-C25-C27	-160.16
	C1-C25	1.431	C36-C41-C42	116.16	C27-C29-C35-C39	175.48
	C27-C31	1.463	C36-C41-C43	134.87	C30-C29-C35-C40	177.61
			C27-C29-C35	125.27	C42-C41-C36-C37	158.42
					C40-C36-C41-C43	162.07
LDP8	C41-C36	1.461	C3-C1-C25	124.43	C3-C1-C25-C26	157.93
	C35-C29	1.443	C2-C1-C25	116.04	C2-C1-C25-C27	167.46

	C1-C25	1.432	C36-C41-C42	119.97	C27-C29-C35-C39	126.83
	C27-C31	1.460	C36-C41-C43	112.62	C30-C29-C35-C40	128.98
			C27-C29-C35	127.25	C42-C41-C36-C37	-170.06
					C40-C36-C41-C43	-166.76

SIT2. Weak interactions present in the LD and LDPs, where bond length are given in Å and bond angle given in degrees

Molecule	**Interaction**	**Distance (Å)**	**Angle (˚)**
LD	C29-H31---- O45	2.22	117.202
LDP	C31-H34---- O40	2.34	108.777
	C37-H38---- O61	2.35	106.398
LDP1	C34-H37---- O39	2.35	106.265
	C38-H40---- N44	3.09	74.383
	C32-H33---- O63	2.36	106.123
LDP2	C37-H40---- O35	2.34	106.398
	N41-H43-----N30	2.21	126.754
	C33-H34---- O71	2.34	106.652
LDP3	C30-H33---- O40	2.35	110.160
	N41-H42-----N39	2.19	127.918
	C36-H37---- O65	2.35	108.906
LDP4	C37-H40---- O35	2.36	101.086
	C46-H49---- N36	2.23	137.930
	C32-H33---- O68	2.35	106.881
LDP5	C30-H33---- O39	2.36	106.906
	C36-C41 ----O63	2.89	81.390
LDP6	C36-H39---- O34	2.33	107.924
	C40-H42---- O62	2.11	122.389
LDP7	C36-H39---- O34	2.38	105.427
	N40-H41-----O64	1.99	140.144
LDP8	C-36-H39---- O34	2.34	109.127
	C36-C41 ----O63	2.89	81.390

SIT3. Calculated emission of LD and LDPs at M06L/6-31+g(d) level

Molecule	**$\lambda_{(max)}$ in nm**	f_0	E **(eV)**	**Assignment**
LD	497.3	0.0031	2.493	HOMO-1→LUMO
LDP	592.9	0.364	2.091	HOMO-1→LUMO
LDP1	604.49	0.348	2.051	HOMO-1→LUMO
LDP2	634.86	0.555	1.953	HOMO-1→LUMO
LDP3	652.67	0.566	1.900	HOMO-1→LUMO
LDP4	696.4	0.327	1.780	HOMO-1→LUMO
LDP5	605.48	0.349	2.048	HOMO-1→LUMO
LDP6	699.73	0.207	1.772	HOMO-1→LUMO
LDP7	772.02	0.150	1.606	HOMO-1→LUMO
LDP8	581.36	0.356	2.133	HOMO-1→LUMO

SIT4. Stokes shift values of LD and LDPs

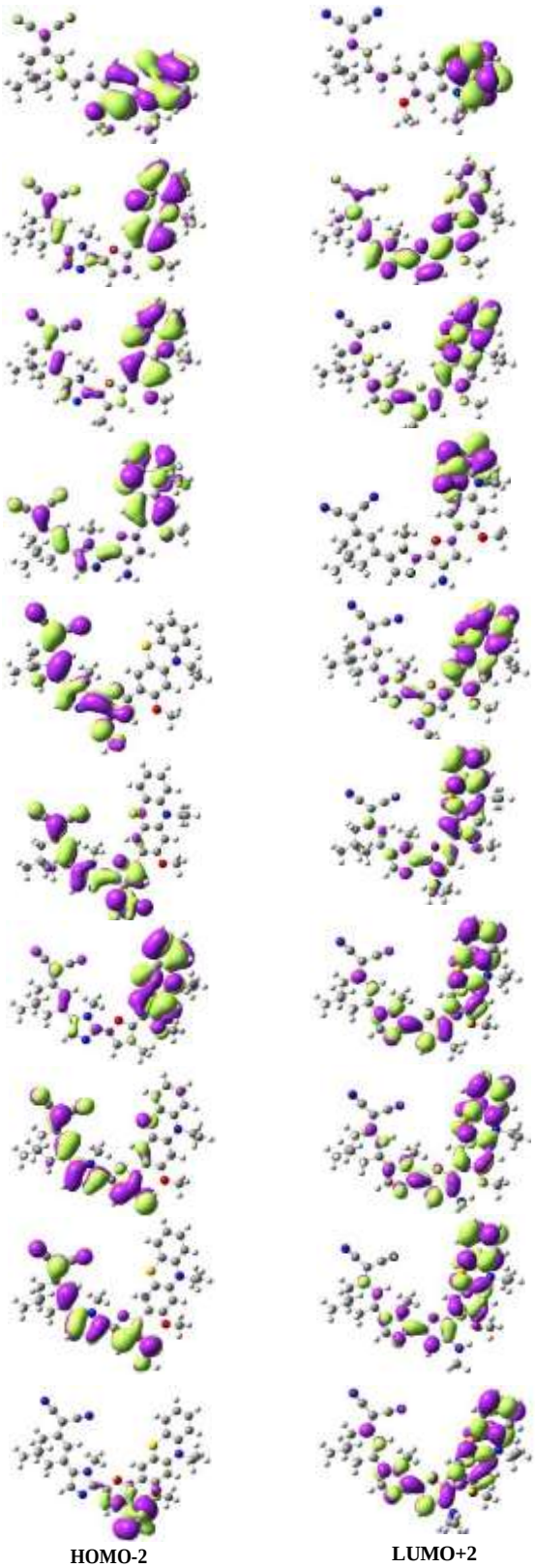
$\lambda_{(emis)}$ in nm	**$\lambda_{(abs)}$ in nm**	**$\lambda_{(abs)} - \lambda_{(emis)}$**
497.30	465.81	1359.39
592.90	548.50	1365.29
604.49	553.82	1513.54
634.86	574.82	1645.25
652.67	599.29	1364.73
696.40	610.44	2022.06
605.48	556.73	1446.21
699.73	617.83	1894.46
772.02	651.99	2384.63
581.36	549.30	1003.94

SIT5. Calculated absorption and emission of LD and LDPs at B3LYP/6-31+g(d) level

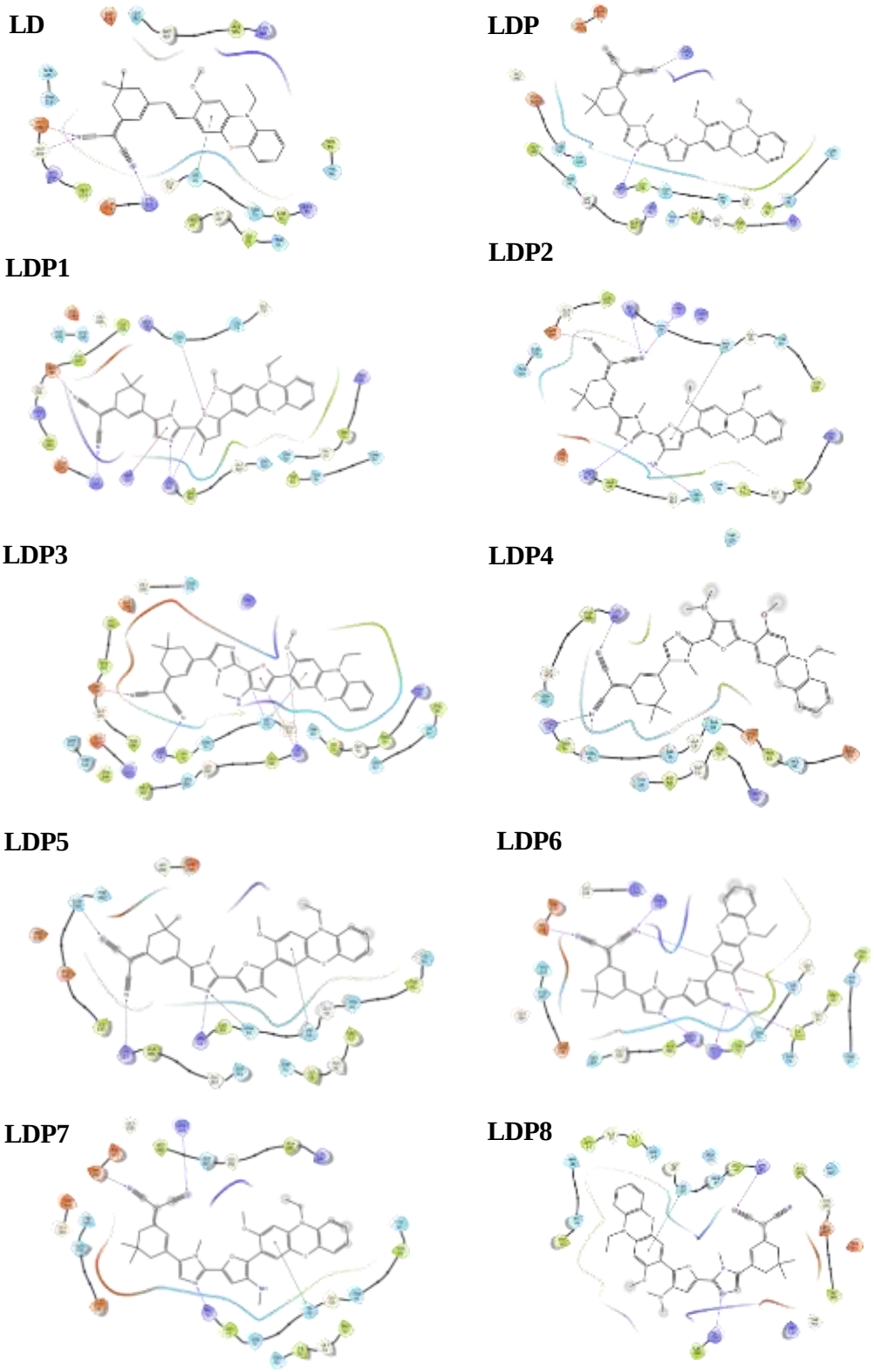
Molecule	**$\lambda_{(abs)}$ in nm**	**$\lambda_{(emis)}$ in nm**
LD	597.50	454.38
LDP	479.45	525.58
LDP1	610.60	453.80
LDP2	484.61	532.61
LDP3	488.09	530
LDP4	503	588.12
LDP5	638.74	783.34
LDP6	702.64	677.71
LDP7	653.84	601.79
LDP8	487.09	520.64

SIT6. Topological parameters of the weak interactions of LD and LDPs.

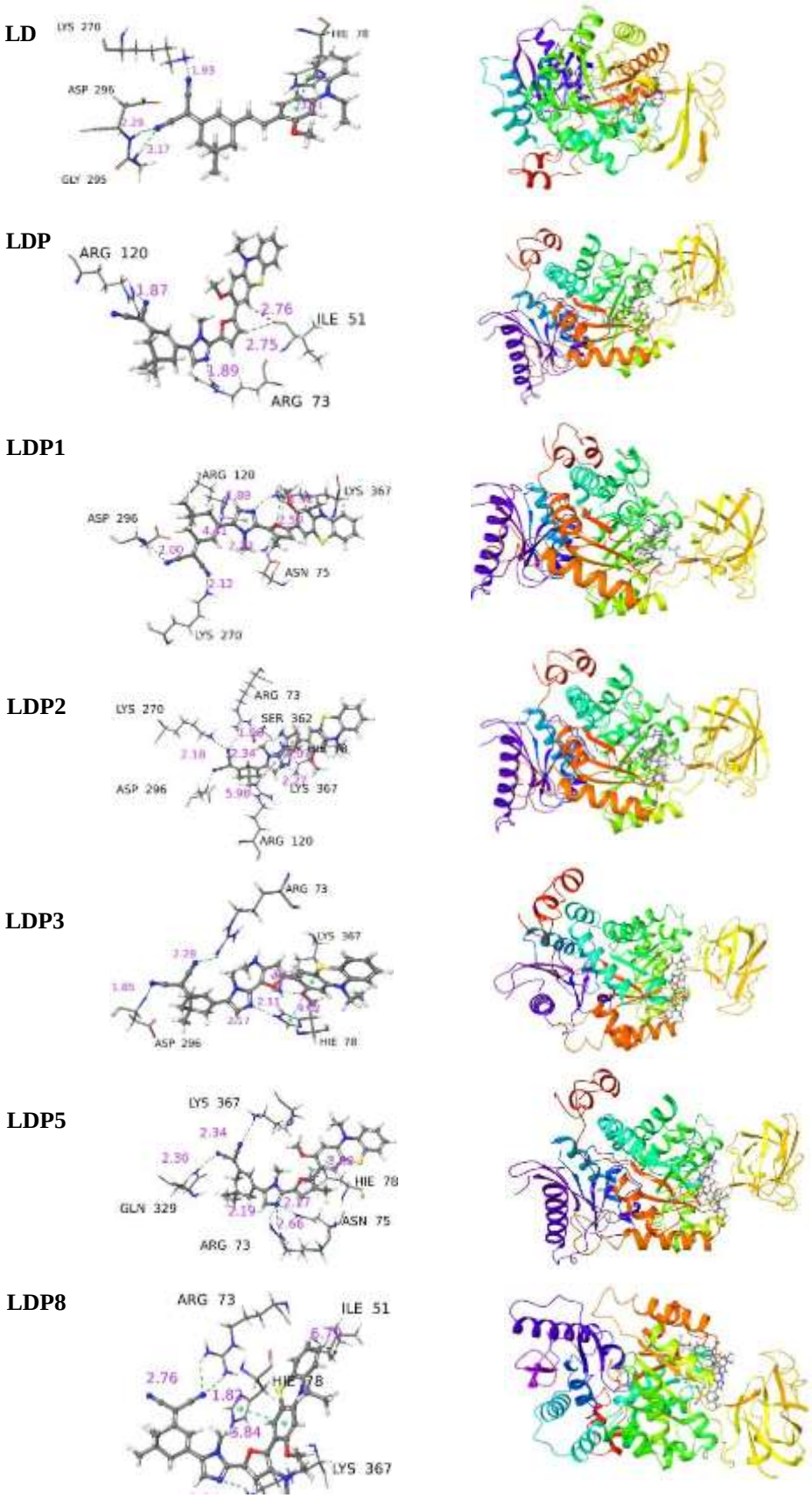
Molecules	**Interactions**	**ρ**	**$\nabla^2\rho$**	**V**	**G**	**Elipticity**
LD	C29-H31---O45	0.0171	0.0646	-0.0209	0.0149	0.0456
LDP	C31-H34---O40	0.0140	0.0554	-0.0105	0.0122	0.3314
	C37--H38---O61	0.0138	0.0559	-0.0104	0.0122	0.2771
LDP1	C32-H33 -----063	0.0136	0.0549	-0.0102	0.012	0.2928
	C34-H37---O39	0.0139	0.056	-0.0104	0.0122	0.6633
	C38-H40---N44	0.0084	0.031	-0.0052	0.0065	0.6633
LDP2	C37-H40---O35	0.0134	0.0531	-0.0100	0.011	0.2902
	C33-H34---O71	0.0141	0.0569	-0.0107	0.0125	0.2477
LDP3	C30-H33---O40	0.0131	0.0524	-0.0099	0.0115	0.3045
	C36-H37---O65	0.0139	0.056	-0.0105	0.0122	0.2411
LDP4	C37-H40---O35	0.1477	0.0607	-0.0111	0.0132	0.6893
	C32-H33---O68	0.0138	0.0557	-0.0104	0.0122	0.2461
	C46-H49---N36	0.0182	0.0588	-0.0126	0.0137	0.0652
LDP5	C36-H41---O63	0.0115	0.0457	-0.0087	0.0101	0.6949
	C30-H33---O39	0.1342	0.0539	-0.0100	0.0118	0.6949
LDP6	C40-H42---O34	0.2000	0.0734	-0.0173	0.0178	0.2334
	C36-H39---O34	0.0141	0.0562	-0.0106	0.0123	0.3814
LDP7	C36-O34---H39	0.0242	0.0537	-0.0099	0.0117	0.4496
	N40-H41---O64	0.0124	0.0536	-0.0076	0.0105	1.1428
LDP8	C36-H39---O34	0.0136	0.0543	-0.0102	0.0119	0.3164
	C45-H48---O68	0.0136	0.0543	-0.0102	0.0119	0.3164



SIF4. The Frontier molecular orbitals (HOMO -2 and LUMO+2) of the LD and LDPs obtained from the optimized geometries at M06L/6-31+g(d) level of theory.



SIF5. 2D interaction plot of LD and LDPs with the human pyruvate kinase (PDB ID: 3GR4)



SIF6. 3D docked view of LD, LDP, LDP1, LDP2, LDP3, LDP5 and LDP8 with the human pyruvate kinase (PDB ID: 3GR4)