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Chemical, Spectral, Biological, and Toxicological Studies of Some Benzene Derivatives Used in Pharmaceuticals: In Silico Approach

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Table S1 Bond Distances (Å) of benzene and its derivatives.

Name	Atom Number	Bond Distances (Å)	
		Calculated	Experimental
Benzene	C1-C2	1.3965	1.3970
	C1-H7	1.0865	1.0840
1(a)	C1-C3	1.4012	1.3950
	C2-C5	1.3952	1.3950
	C2-H8	1.0875	1.0830
	C9-C14	1.0973	1.0930
1(b)	C2-C5	1.4004	1.4010
	C5-C7	1.3963	1.3970
	C1-H10	1.0980	1.0930
	C1-C3	1.5401	1.5400
1(c)	C1-C2	1.4119	1.4100
	C1-C5	1.5102	1.5400
	C3-H9	1.0874	1.0830
	C5-H12	1.0969	1.0830
1(d)	C1-C3	1.4002	1.4000
	C1-C7	1.5108	1.5400
	C3-H9	1.0876	1.0830
	C7-H13	1.0943	1.0940
1(e)	C2-C3	1.4013	1.4010
	C3-C6	1.3953	1.3990
	C1-H9	1.0966	1.0940
	C1-C5	1.5390	1.5400
1(f)	C1-C2	1.4072	1.4017
	C2-C4	1.3911	1.3901
	C2-H9	1.0856	1.0830
	C7-C8	1.3384	1.3245
	C7-H14	1.0897	1.0900
2(a)	C2-C3	1.4008	1.3990
	C8-O1	1.2162	1.1907
	C3-H9	1.0876	1.0755
	C8-H14	1.1135	1.0942
2(b)	C2-C3	1.4029	1.4000
	C3-C6	1.3946	1.3910
	C3-H10	1.0852	1.0830
	C5-O1	1.2218	1.2100
	C5-C9	1.5195	1.5400
	C9-H16	1.0955	1.0940
2(c)	C3-C4	1.4019	1.4000
	C3-C9	1.5030	1.5400
	C9-O1	1.2248	1.2100
	C9-N2	1.3754	1.4700
	N2-H15	1.0080	0.9900
	C4-H10	1.0861	1.0830
2(d)	C3-C4	1.4014	1.3901
	C4-C6	1.3919	1.3901
	C9-O1	1.3579	1.3560
	C9-O2	1.2152	1.2200
	O1-H15	0.9715	0.9520
	C4-H14	1.0846	-
2(e)	C3-C4	1.4013	1.4000
	C4-C6	1.3923	1.3910

	C9-O1	1.3541	1.4300
	C9-O2	1.2258	1.2100
	C4-H11	1.0846	1.0830
	C10-H16	1.0927	1.0940
3(a)	O1-H13	0.9661	0.9560
	C2-O1	1.3679	1.3640
	C2-C4	1.3994	1.3980
	C4-H9	1.0849	1.0820
3(b)	C2-C3	1.3996	1.3990
	C3-H9	1.0835	1.0820
	C8-O1	1.4181	1.4330
3(c)	C2-C3	1.4053	1.3920
	C2-N1	1.3981	1.4310
	N1-H13	1.0111	0.9900
	C3-H8	1.0875	1.0840
3(d)	C4-C5	1.3935	1.3990
	C5-H10	1.0825	1.0930
	C4-N3	1.4733	1.4860
	N3-O1	1.2305	1.2230
3(e)	C2-C3	1.4052	1.3970
	C3-C5	1.3915	1.3960
	C8-N1	1.1633	1.1580
	C3-H9	1.0847	1.0820
4(a)	F7-C4	1.3511	1.3540
	C4-C3	1.3900	1.3825
	C1-H8	1.0854	1.0812
4(b)	Cl1-C2	1.7600	1.7252
	C2-C7	1.3552	1.4025
	C3-H8	1.0700	1.0790
4(c)	Br1-C2	1.9100	1.8500
	C2-C3	1.3552	1.3750
	C6-H11	1.0700	1.0720
4(d)	I12-C4	2.1000	2.1400
	C1-C2	1.4014	1.3970
	C5-H10	1.0700	1.9100

Table S2 Bond Angles (°) of benzene and some of its derivatives.

Name	Atom Number	Bond Angles (°)	
		Calculated	Experimental
Benzene	C1-C2-C4	120.00	120.00
	C1-C3-H9	119.96	120.00
1(a)	C1-C2-C5	121.02	120.00
	H11-C8-H12	107.21	107.40
1(b)	C2-C5-C7	121.22	121.50
	C4-C1-C1	111.02	111.00
	H11-C3-H13	107.70	108.80
	H10-C1-C3	107.39	109.40
	H15-C4-C1	110.68	110.60
1(c)	C2-C1-C3	118.99	119.50
	C7-C8-C4	119.52	119.60
	C1-C2-C6	120.83	120.60
	C7-C3-H9	119.58	119.70
	H14-C6-H15	107.68	107.60
1(d)	C3-C1-C5	117.68	-
	C5-C6-C2	121.16	121.20
	C5-C1-C7	121.14	121.20
	C1-C3-H9	119.42	119.40
	H13-C7-H14	107.18	-
1(e)	C2-C3-C6	121.02	120.00
	C2-C1-C5	112.91	113.40
	H1-C1-H9	106.46	107.40
	C1-C5-H14	111.03	110.60
1(f)	C1-C2-C4	120.88	120.90
	C1-C7-C8	127.70	126.70
	H14-C7-C8	117.91	118.00
	H15-C8-H16	116.24	116.50
2(a)	C2-C4-C6	119.89	119.97
	C2-C8-O1	124.73	124.50
	H14-C8-O1	120.79	120.37
2(b)	C2-C3-C6	120.37	120.42
	H15-C9-H17	107.35	107.30
	O1-C5-C9	120.45	120.30
2(c)	C8-C6-C4	120.05	120.00
	C4-C3-C5	119.30	119.50
	C4-C3-C9	123.35	122.00
	C3-C9-N2	116.31	116.00
	C3-C9-O1	122.01	122.00
	C9-N2-H15	120.26	119.50
	C9-N2-H16	115.06	118.50
	H15-N2-H16	116.76	116.60
	N2-C9-O1	121.67	121.40
	C8-C6-H12	120.13	120.00
	C6-C4-H10	119.35	119.60
2(d)	C3-C4-C5	120.03	119.91
	O1-C9-O2	121.91	121.24
	C3-C9-O1	113.13	113.80
	C3-C9-O2	124.97	125.30
	C9-O1-H15	105.61	105.80
2(e)	C3-C4-C6	120.08	120.00
	O1-C9-O2	122.92	122.90

	C9-O1-C10	115.13	115.10
	C3-C9-O1	112.52	112.50
	C3-C9-O2	124.56	125.20
	H16-C10-H17	108.72	-
	O1-C10-H16	110.65	-
3(a)	C2-O1-H13	109.00	109.00
	C4-C2-C3	120.06	120.00
	C3-C5-H10	119.28	119.10
3(b)	C2-O1-C8	118.22	118.60
	C2-C4-C6	120.00	119.80
	H14-C8-H15	109.13	109.70
3(c)	C2-C3-C5	120.48	120.40
	H13-N1-H14	111.49	113.90
	C2-N1-H14	114.84	114.90
3(d)	C4-C5-C7	118.46	117.70
	O2-N3-O1	124.63	125.30
	C4-N3-O1	117.69	117.30
3(e)	C2-C3-C5	119.69	119.90
	C2-C8-N1	179.98	180.00
4(a)	F7-C4-C3	118.84	119.02
	H11-C5-C6	121.99	121.83
	H11-C5-C4	119.53	119.40
	C5-C4-C3	122.30	121.89
4(b)	Cl1-C2-C3	120.00	119.00
	C3-C2-H8	120.00	120.00
	C3-C2-C7	119.99	119.90
4(c)	C4-C2-C3	120.00	120.40
	Br1-C2-C4	119.99	119.80
	C6-C7-H12	120.00	120.20
4(d)	I12-C4-C3	120.00	120.00
	C1-C2-C3	120.00	120.00
	C4-C5-H10	120.00	120.00

Table S3 Molecular formula (MF), molecular weight (MW), energies (Hartree), and dipole moment (Debye) of benzene and its remaining studied analogs.

Name	MF	MW	Internal Energy	Enthalpy	Gibbs Free Energy	Dipole Moment
Benzene	C_6H_6	78.110	-232.153	-232.152	-232.183	0.000
1(c)	C_8H_{10}	106.160	-310.736	-310.735	-310.779	0.080
1(e)	C_8H_{10}	106.167	-310.731	-310.729	-310.771	0.297
2(b)	C_8H_8O	120.151	-384.762	-384.761	-384.803	2.983
2(c)	C_7H_7NO	121.140	-400.830	-400.829	-400.870	3.498
2(d)	$C_7H_6O_2$	122.123	-420.712	-420.711	-420.752	1.915
3(a)	C_6H_5OH	94.110	-307.374	-307.367	-307.374	1.335
3(b)	C_7H_8O	108.140	-346.643	-346.642	-346.681	1.315
3(e)	C_7H_5N	103.120	-324.395	-324.394	-324.431	4.546
4(b)	C_6H_5Cl	112.560	60.610	61.202	38.473	1.920
4(d)	C_6H_5I	204.010	60.579	61.172	37.389	1.770

Table S4 Energy (eV) of HOMO-LUMO, gap, hardness (η), softness (S), chemical potential (μ), electronegativity (χ), and electrophilicity (ω) of benzene and remaining studied derivatives.

Name	εHOMO	εLUMO	Gap	η	S	μ	χ	ω
Benzene	-6.721	0.082	6.803	3.402	0.147	-3.320	3.320	1.620
1(c)	-6.259	0.190	6.449	3.225	0.155	-3.035	3.035	1.428
1(e)	-6.426	0.118	6.544	3.272	0.306	-3.154	3.154	1.520
2(b)	-6.667	-1.578	5.089	2.545	0.393	-4.123	2.062	3.340
2(c)	-5.552	-0.603	4.949	2.474	0.202	-3.077	3.077	11.716
2(d)	-7.075	-1.605	5.470	2.735	0.366	-4.331	2.166	3.429
3(a)	-5.959	-0.136	5.823	2.912	0.172	-3.048	3.048	1.595
3(b)	-5.865	0.084	5.949	2.975	0.336	-2.891	2.891	1.404
3(e)	-7.265	-1.424	5.841	2.921	0.342	-4.345	4.345	3.231
4(b)	-6.630	-0.259	6.371	3.185	0.157	-3.445	3.445	18.899
4(d)	-6.591	-0.368	6.223	3.111	0.161	-3.479	3.479	18.831

Table S5 Molecular electrostatic potential values of benzene and some selected derivatives.

Name	Positive Value	Negative Value
Benzene	2.574e-2	-2.574e-2
1(a)	2.717e-2	-2.717e-2
1(b)	2.654e-2	-2.654e-2
1(c)	2.803e-2	-2.803e-2
1(d)	2.825e-2	-2.825e-2
1(e)	2.681e-2	-2.681e-2
1(f)	2.384e-2	-2.384e-2
2(a)	5.081e-2	-5.081e-2
2(b)	5.326e-2	-5.326e-2
2(c)	5.863e-2	-5.863e-2
2(d)	5.879e-2	-5.879e-2
2(e)	5.284e-2	-5.284e-2
3(a)	6.255e-2	-6.255e-2
3(b)	3.190e-2	-3.190e-2
3(c)	4.161e-2	-4.161e-2
3(d)	4.723e-2	-4.723e-2
3(e)	5.454e-2	-5.454e-2
4(a)	2.252e-2	-2.252e-2
4(b)	2.102e-2	-2.102e-2
4(c)	2.084e-2	-2.084e-2
4(d)	3.827e1	-3.827e1

Table S6 Selected vibrational frequencies (cm-1) of benzene and its remaining studied analogs. Calculated in the gas phase (scaled).

Name	Assignments	Vibrational Frequencies (cm^{-1}) (Initial)	Vibrational Frequencies (cm^{-1}) (Scaled)
1. Benzene	νC-C stretch	1525	1468
	νC-H stretch	3207	3087
1(a)	νC-C[a] stretch	1665	1603
	νC-H[a] stretch	3205	3085
	νC-H[b] stretch	3037	2924
1(b)	νC-C[b] stretch	1127	1085
	νC-C[a] stretch	1662	1600
	νC-H[b] stretch	3042	2929
	νC-H[a] stretch	3204	3084
1(c)	νC-H[a] stretch	1630	1569
	νC=C[a] stretch	1675	1613
	νC-H[b] stretch	3184	3065
1(d)	νC-H[a] stretch	1665	1603
	νC=C[a] stretch	1634	1573
	νC-H[b] stretch	3032	2919
1(e)	νC-C[a] stretch	1641	1580
	νC-H[a] stretch	3204	3084
	νC-C[b] stretch	1087	1046
	νC-H[b] stretch	3043	2929
1(f)	νC-C[a] stretch	1660	1598
	νC-H[a] stretch	3208	3088
	νC=C[b] stretch	1710	1646
2(a)	νC-H[a] stretch	3206	3086
	νC=C[a] stretch	1659	1597
	νC=O stretch	1799	1732
	νC-H stretch	2898	2790
	νC-C stretch	1232	1186
2(b).	νC-H[a] stretch	3210	3090
	νC=C[a] stretch	1489	1433
	νC=O stretch	1778	1712
	νC-H stretch	3049	2935
	νC-C stretch	1288	1240
2(c)	νN-H stretch	3593	3459
	νC-H stretch	3207	3087
	νC=O stretch	1785	1718
	νC=N stretch	1624	1563
2(d)	νC-H[a] stretch	3200	3081
	νC=C[a] stretch	1496	1440
	νC-O[b]stretch	1392	1340
	νC=O[b]stretch	1819	1751
	νO-H stretch	3766	3626
	νC-C stretch	1216	1171
2(e)	νC-H[a] stretch	3206	3084
	νC=C[a] stretch	1491	1435
	νC-O[b] stretch	1309	1260
	νC=O[b]stretch	1800	1733
	νC-H stretch	3066	2952
	νC-C stretch	1144	1101
3(a)	νC-H[a] stretch	3214	3094

	νO-H[b] stretch	3823	3680
	νC=O[b] stretch	1667	1605
3(b)	νC-H[a] stretch	3204	3084
	νC-H stretch	3014	2902
	νC=C stretch	1663	1601
	νC-O stretch	1294	1246
3(c)	νC-C[a] stretch	1643	1582
	νC-N stretch	1315	1266
	νN-H stretch	3567	3434
	νC-H stretch	3185	3066
3(d)	νC-H[a] stretch	3193	3074
	νC-H[a] stretch	1645	1584
	νN-O stretch	1676	1613
	νC-N stretch	863	831
	νC=O stretch	1630	1569
	νC-N stretch	1245	1199
3(e)	νC-H[a] stretch	3209	3089
	νC-N stretch	2349	2261
	νC=C stretch	1630	1569
4(a)	νC-C stretch	1657	1595
	νC-H stretch	3209	3089
	νC-F stretch	1277	1229
4(b)	νC-C stretch	1647	1586
	νC-H stretch	3367	3241
	νC-Cl stretch	1004	967
	νC-C stretch	1641	1580
	νC-H stretch	3366	3240
	νC-Br stretch	989	952
4(d)	νC-C stretch	1641	1580
	νC-H stretch	3366	3240
	νC-I stretch	989	952

[a] = aliphatic, [b] = benzene

Table S7 Electronic absorption spectra of Benzene and its remaining derivatives. Calculated at TD-DFT/ B3LYP/ 6-311g (d,p).

Name	Excited state	Wavelength (nm)	Excitation energy (eV)	Configurations Composition	Oscillator strength
1. Benzene	$S_0 \rightarrow S_1$	229.60	5.400	0.500(H-1→L), 0.500(H→L+1))	0.000
	$S_0 \rightarrow S_2$	202.76	6.115	-0.498(H-1→L+1), 0.498(H→L)	0.000
1(a)	$S_0 \rightarrow S_1$	233.35	5.313	0.443(H-1→L+1), 0.549(H→L)	0.003
	$S_0 \rightarrow S_2$	206.24	6.012	-0.452(H-1→L), 0.537(H→L+1)	0.011
1(b)	$S_0 \rightarrow S_1$	234.11	5.296	-0.433(H-1→L+1), 0.543(H→L),	0.003
	$S_0 \rightarrow S_2$	207.61	5.972	0.429(H-1→L), -0.103(H→L), 0.542(H→L+1),	0.021
1(c)	$S_0 \rightarrow S_1$	235.45	5.266	0.472(H-1 → L+1), 0.526(H→L)	0.001
	$S_0 \rightarrow S_2$	209.09	5.930	-0.475(H-1→L), 0.519(H→L+1)	0.006
1(d)	$S_0 \rightarrow S_1$	238.24	5.204	-0.394(H-1 → L+1), 0.587(H→L)	0.042
	$S_0 \rightarrow S_2$	209.75	5.911	-0.414(H-1→L), 0.569(H→L+1)	0.042
1(e)	$S_0 \rightarrow S_1$	233.76	5.304	0.442(H-1→L+1), 0.547(H→L)	0.003
	$S_0 \rightarrow S_2$	207.16	5.985	-0.431(H-1→L), 0.552(H→L+1)	0.024
1(f)	$S_0 \rightarrow S_1$	257.20	4.821	0.471(H-1→L), -0.271(H→L), 0.444(H→L+1)	0.035
	$S_0 \rightarrow S_2$	250.18	4.956	0.223(H-1→L), 0.641(H→L), 0.165(H→L+1)	0.233
2(a)	$S_0 \rightarrow S_1$	351.52	3.527	0.694(H→L), -0.133(H → L+3)	0.000
	$S_0 \rightarrow S_2$	273.15	4.539	0.248(H-2→L), -0.178(H-2→L+1), 0.630(H-1→L)	0.023
2(b)	$S_0 \rightarrow S_1$	349.71	3.545	0.694(H→L), -0.131(H→L+2)	0.000
	$S_0 \rightarrow S_2$	265.89	4.663	0.269(H-2→L), -0.200(H-2→L+1), 0.611(H-1→L), 0.118(H-1→L+1)	0.024
2(c)	$S_0 \rightarrow S_1$	288.94	4.291	0.69426(H → L), 0.13170(H → L+3)	0.0002
	$S_0 \rightarrow S_2$	241.81	5.127	-0.144(H-3→L), -0.111(H-3→L+1), 0.426(H-2→L), 0.245(H-2→L+1), 0.387(H-1→L), -0.273(H-1→L+1)	0.007
2(d)	$S_0 \rightarrow S_1$	285.50	4.343	0.693(H-2→L), 0.132(H-2→L+2)	0.000
	$S_0 \rightarrow S_2$	262.15	4.730	0.157(H-1→L), 0.253(H-1→L+1), 0.638(H→L)	0.022

2(e)	$S_0 \rightarrow S_1$	305.61	4.057	0.672(H-2→L), -0.124(H-2→L+2), 0.138(H-1→L)	0.000
	$S_0 \rightarrow S_2$	268.08	4.625	-0.214(H-1→L), -0.221(H-1→L+1), 0.620(H→L)	0.021
3(a)	$S_0 \rightarrow S_1$	242.93	5.104	-0.322(H-1→L+1), 0.629(H→L)	0.026
	$S_0 \rightarrow S_2$	209.87	5.908	0.202(H-1→L), 0.594(H→L+1)	0.036
3(b)	$S_0 \rightarrow S_1$	243.28	5.096	-0.323(H-1→L+1), 0.628(H→L)	0.021
	$S_0 \rightarrow S_2$	214.01	5.793	0.311(H-1→L), 0.626(H→L+1)	0.065
3(c)	$S_0 \rightarrow S_1$	242.75	5.108	-0.330(H-1→L+1), 0.618(H→L)	0.009
	$S_0 \rightarrow S_2$	224.28	5.528	0.212(H-2→L+1), 0.181(H-1→L), 0.636(H→L+1)	0.070
3(d)	$S_0 \rightarrow S_1$	409.39	3.029	0.698(H→L), -0.108(H→L+2)	0.000
	$S_0 \rightarrow S_2$	309.82	4.002	0.697(H-4→L), -0.112(H-4→L+2)	0.000
3(e)	$S_0 \rightarrow S_1$	241.03	5.144	0.535(H-1→L), -0.125(H-1→L+1), -0.205(H→L), -0.393(H→L+1)	0.009
	$S_0 \rightarrow S_2$	216.74	5.720	0.186(H-1→L), 0.253(H-1→L+1), 0.609(H→L), -0.145(H→L+1)	0.135
4(a)	$S_0 \rightarrow S_1$	233.66	5.306	0.398(H-1→L +1), 0.583(H →L)	0.013
	$S_0 \rightarrow S_2$	204.04	6.077	-0.469(H-1→L), 0.523(H→L+1)	0.002
4(b)	$S_0 \rightarrow S_1$	237.65	5.217	-0.201(H-1→L), 0.373(H-1→L+1), 0.49534(H→L), 0.273(H →L +1)	0.003
	$S_0 \rightarrow S_2$	211.68	5.857	-0.286(H-1→L), -0.176(H-1→L+1), -0.285(H→L), 0.548(H →L +1)	0.068
4(c)	$S_0 \rightarrow S_1$	240.44	5.157	-0.384(H-1→L), 0.111(H-1→L+1), 0.158(H→L), 0.561(H→L+1)	0.003
	$S_0 \rightarrow S_2$	223.86	5.538	0.702(H→L+2)	0.0002
4(d)	$S_0 \rightarrow S_1$	255.10	4.860	0.706(H→L+2)	0.0003
	$S_0 \rightarrow S_2$	247.59	5.007	-0.349(H-1→L), 0.613(H→L+1)	0.004

Table S8 Average binding affinities and nonbonding interactions of some selected benzene derivatives with three receptor proteins [2(c) and 3(a-e) with 1A06, 4(a-d) with 1G9G, and 2(a, b, d, e) with 6KBP].

Name	Binding Affinity (Kcal/mol)	Residue in Contact	Interaction Type	Bond Distance (Å)
2(a)	-5.8	TYR228	H	2.47797
		TYR229	H	1.86144
		TYR230	PPS	3.98237
		TYR231	PPTSh	4.99644
2(b)	-6.3	TYR228	H	2.56600
		ARG283	H	2.58336
		ARG283	H	1.92828
		TYR224	PPS	4.00509
		TYR228	PPTSh	5.01098
2(c)	-5.8	SER287	H	2.69548
		SER287	H	2.55553
		ARG257	H	2.03740
		ARG257	H	2.39112
		LEU238	PA	4.17441
		ALA291	PA	4.97693
2(d)	-6.3	TYR228	H	2.41855
		ARG283	H	1.85949
		TYR224	PPS	3.98152
		TYR228	PPTSh	5.02573
2(e)	-6.4	TYR228	H	2.44934
		ARG283	H	2.01817
		ARG283	H	2.20044
		GLY313	CHy	2.74732
		TYR224	PPS	3.96017
		TYR228	PPTSh	4.98930
3(a)	-5.0	ARG410	PC	4.97461
		LEU407	PA	5.10374
		LEU430	PA	4.85679
		LEU453	PA	4.52167
3(b)	-5.0	ARG257	H	2.24597
		ARG257	H	2.17863
		HIS242	CHy	2.96245
		LEU238	PA	5.13502
		LEU260	PA	5.15454
		ALA291	PA	4.38925
3(c)	-5.1	LEU407	PA	5.25629
		LEU430	PA	4.81274
		VAL433	PA	5.48736
		LEU453	PA	4.31638
3(d)	-6.0	ARG410	H	2.35701
		ARG485	CHy	2.98633
		ARG410	PC	4.61472
		LEU407	PA	5.05419
		LEU430	PA	4.74330
		VAL433	PA	5.36191
		LEU453	PA	4.41903
3(e)	-5.1	ARG410	PC	4.96185
		LEU407	PA	5.16833
		LEU430	PA	4.95594
		LEU453	PA	4.50768

4(a)	-5.5	ALA228	X	2.87347
		ASN227	X	3.05933
		TRP154	PPS	3.91610
		TRP154	PPS	3.73566
		TRP298	PPTSh	4.89408
		ALA228	PA	5.43087
4(b)	-5.4	TRP154	PPS	3.73960
		TRP154	PPS	3.90401
		TRP154	PA	4.03595
		PHE180	PA	4.46132
		TYR403	PA	5.38404
		ALA228	PA	5.10639
4(c)	-5.4	TRP154	PPS	3.77609
		TRP154	PPS	3.85991
		TRP298	PPTSh	4.90171
		ALA228	PA	5.14410
4(d)	-5.5	TRP154	PPS	3.88113
		TRP154	PPS	3.76166
		TRP298	PPTSh	4.87585
		TRP154	PA	4.55617
		TRP154	PA	5.13027
		ALA228	PA	5.08567

H = Conventional Hydrogen Bond, A = alkyl, PA = Pi-alkyl, PC = Pi-cation, Pa = Pi-anion, X = Halogen bond, CHy = Carbon Hydrogen Bond, Pd = Pi-donor, PS = Pi-sigma, PSu = Pi-sulfur, PPS = Pi-Pi stacked, PPTSh = Pi-Pi T-shaped

Table S9 Pharmacokinetic parameters of remaining studied benzene derivatives.

Name	Absorption				Distribution	Metabolism	Toxicity				
	HIA	HOB	C2P	P-GpI	BBB	CYP4502C9	hERG	Carcinogen	AOT	RAT LD_{50} (mol/kg)	Biodegradation
Benzene	+0.992	+0.55	+0.909	NI (0.988)	+1.000	NS (0.809)	WI (0.848)	NC (0.556)	III	1.796	B (0.925)
1(a)	+0.996	+0.55	+0.907	NI (0.990)	+0.973	NS (0.955)	WI (0.929)	NC (0.545)	III	1.600	B (0.532)
1(b)	+0.996	+0.55	+0.888	NI (0.991)	+0.971	NS (0.963)	WI (0.961)	C (0.500)	III	1.582	B (0.525)
1(c)	+0.601	+0.55	+0.909	NI (0.992)	+0.984	NS (0.915)	WI (0.945)	NC (0.566)	III	1.551	B (0.524)
1(d)	+0.995	+0.55	+0.910	NI (0.990)	+0.975	NS (0.953)	WI (0.944)	C (0.510)	III	1.447	B (0.524)
1(e)	+0.996	+0.55	+0.907	NI (0.990)	+0.973	NS (0.955)	WI (0.929)	NC (0.545)	III	1.601	B (0.502)
1(f)	+0.992	+0.55	+0.896	NI (0.984)	+0.969	NS (0.909)	WI (0.919)	NC (0.539)	III	1.732	B (0.710)
2(a)	+0.996	+0.55	+0.938	NI (0.990)	+0.980	NS (0.823)	WI (0.938)	NC (0.592)	III	1.943	B (0.747)
2(b)	+1.000	+0.55	+0.934	NI (0.976)	+0.979	NS (0.970)	WI (0.910)	NC (0.581)	III	2.024	B (0.804)
2(c)	+0.995	+0.55	+0.908	NI (0.996)	+0.996	NS (0.907)	WI (0.992)	NC (0.755)	III	1.988	B (0.767)
2(d)	+0.989	+0.85	+0.919	NI (0.994)	+0.956	NS (0.986)	WI (0.971)	NC (0.602)	III	1.790	B (0.898)
2(e)	+0.995	+0.55	+0.880	NI (0.970)	+0.971	NS (0.788)	WI (0.961)	NC (0.639)	III	1.954	B (0.865)
3(a)	+0.993	+0.55	+0.933	NI (0.992)	+0.908	NS (0.789)	WI (0.847)	NC (0.759)	II	2.504	B (0.749)
3(b)	+0.997	+0.55	+0.899	NI (0.973)	+0.904	NS (0.777)	WI (0.804)	NC (0.782)	III	1.915	B (0.673)
3(c)	+0.985	+0.55	+0.882	NI (0.986)	+0.955	NS (0.859)	WI (0.957)	NC (0.500)	II	2.539	B (0.592)
3(d)	+0.986	+0.55	+0.647	NI (0.977)	+0.942	NS (0.804)	WI (0.682)	C (0.600)	II	2.488	NB (0.781)
3(e)	+0.989	+0.55	+0.896	NI (0.989)	+0.947	NS (0.828)	WI (0.915)	NC (0.606)	III	1.771	B (0.756)
4(a)	+0.994	+0.55	+0.876	NI (0.989)	+0.989	NS (0.865)	WI (0.946)	NC (0.539)	III	1.630	NB (0.935)
4(b)	+0.994	+0.55	+0.879	NI (0.993)	+0.984	NS (0.837)	WI (0.916)	NC (0.511)	III	2.104	NB (0.834)
4(c)	+0.991	+0.55	+0.864	NI (0.988)	+0.982	NS (0.864)	WI (0.941)	NC (0.589)	III	2.057	NB (0.859)
4(d)	+0.968	+0.55	+0.863	NI (0.992)	+0.981	NS (0.849)	WI (0.930)	NC (0.613)	III	2.098	NB (0.936)

HIA = Human intestinal absorption, HOB = Human oral bioavailability, C2P = CACO-2 permeability, P-GpI = *p*-glyco protein inhibitor, BBB = Blood-brain barrier, hERG = human Ether-a-go-go Related Gene, C = Carcinogen, AOT = Acute oral toxicity, RAT = Rat acute toxicity, NI=Non-inhibitor, WI= Weak inhibitor, NC = Non-carcinogen, CYP3A4*I* = CYP3A4 Inhibition, B = Biodegradable, NB = non-biodegradable.

Table S10 Predicted biological activities of benzene and remaining studied benzene analogs.

Name	Analgesic	Antipyretic	Anti-inflammation	Gastrointestinal motility stimulant	Diabetic nephropathy treatment	Hematopoietic inhibitor	Antiviral	
							Activity	Virus
Benzene	0.356	0.326	0.261	0.282	0.472	0.608	0.676	Picornavirus
1(a)	0.322	0.352	0.392	0.246	0.284	0.524	0.604	Picornavirus
1(b)	0.294	0.542	0.650	0.215	0.295	0.457	0.549	Picornavirus
1(c)	0.322	0.375	0.375	0.246	0.267	0.524	0.604	Picornavirus
1(d)	0.323	0.334	0.456	0.255	0.287	0.537	0.603	Picornavirus
1(e)	0.322	0.352	0.392	0.246	0.284	0.524	0.604	Picornavirus
1(f)	0.278	0.294	0.474	0.226	0.254	0.394	0.427	Hepatitis B
2(a)	0.293	0.307	0.415	0.181	0.206	0.432	0.544	Picornavirus
2(b)	0.288	0.491	0.552	0.202	0.251	0.445	0.537	Rhinovirus
2(c)	0.344	0.424	0.431	0.267	0.219	0.524	0.194	Hepatitis B
2(d)	0.354	0.593	0.485	0.186	0.326	0.467	0.165	Hepatitis B
2(e)	0.310	0.488	0.406	0.243	0.320	0.422	0.189	Hepatitis B
3(a)	0.308	0.443	0.566	0.258	0.233	0.460	0.241	Hepatitis B
3(b)	0.303	0.402	0.597	0.316	0.253	0.507	0.603	Picornavirus
3(e)	0.291	0.241	0.662	0.197	0.243	0.429	0.185	Hepatitis B
3(c)	0.321	0.322	0.591	0.129	0.225	0.611	0.742	Picornavirus
3(d)	0.287	0.301	0.402	0.205	0.207	0.508	0.714	Picornavirus
4(b)	0.476	0.307	0.396	0.299	0.281	0.507	0.652	Picornavirus
4(c)	0.291	0.321	0.407	0.257	0.266	0.453	0.525	Influenza
4(d)	0.291	0.321	0.407	0.257	0.266	0.453	0.525	Influenza

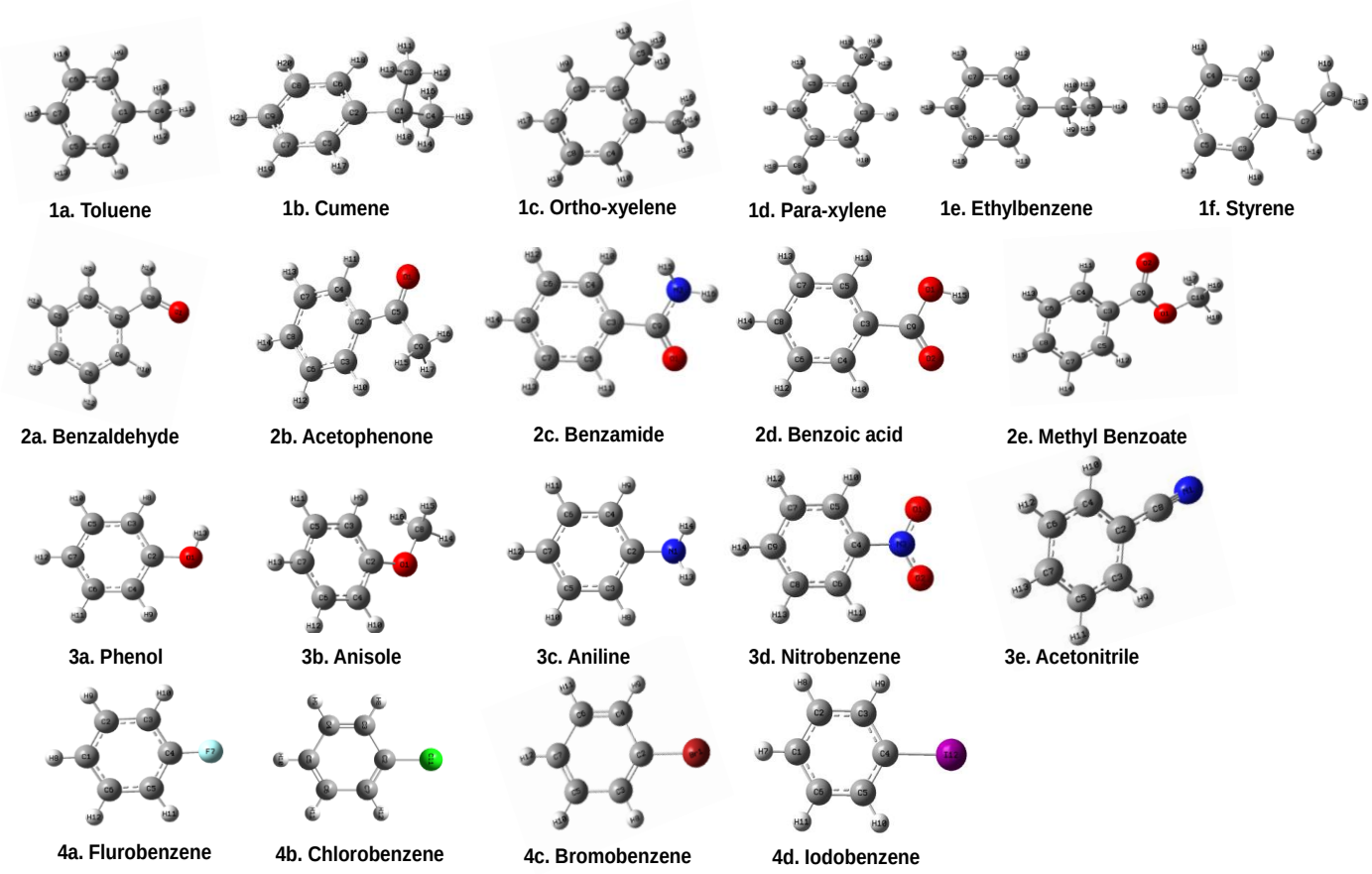

Figure S1 Optimized Structures of selected benzene derivatives.

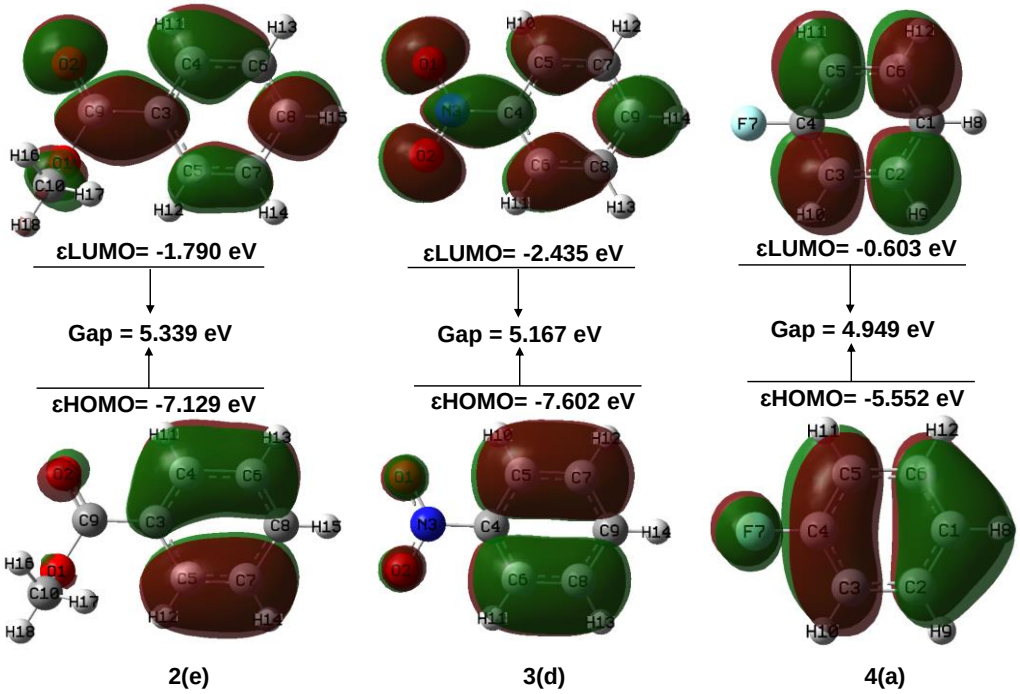

Figure S2 Molecular orbital map of some selected compounds

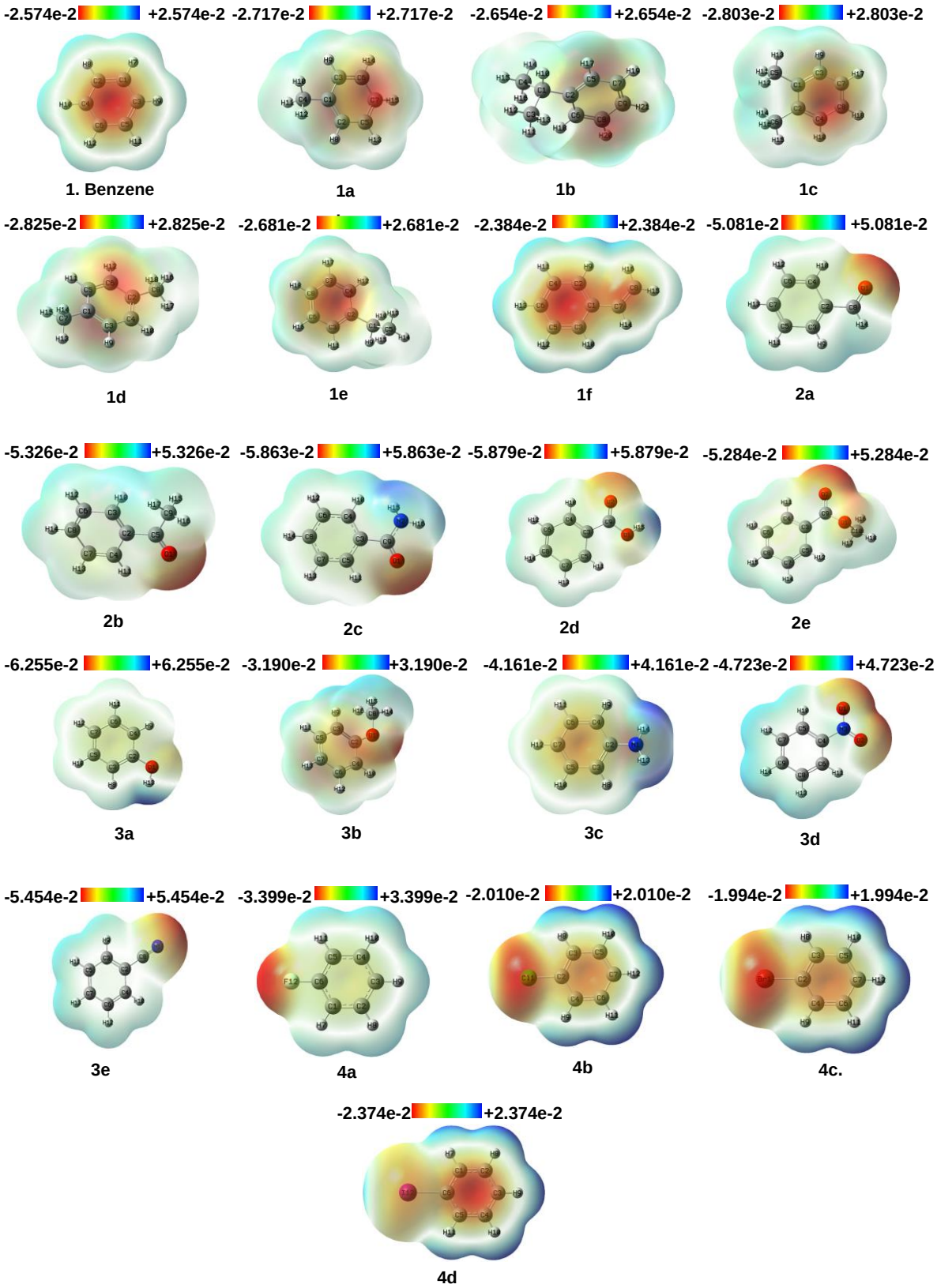

Figure S3 Electrostatic potential maps of benzene derivatives.

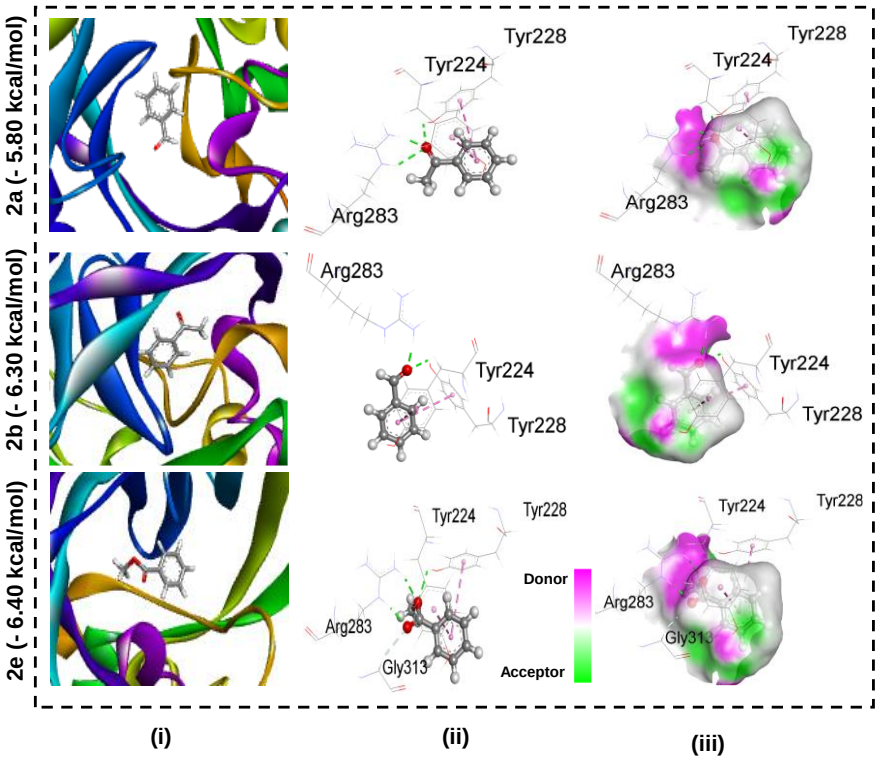

Figure S4 (i) Docked conformer, (ii) Non-bonding interactions and (iii) hydrogen bond surface for compounds 2a, 2b and 2e with receptor protein 6KBP.