Supplementary Materials

DFT-Assisted Spectroscopic Characterization, Reactivity Analysis, and Biological Interaction Study of 3-Bromo-N-tert-butylbenzene-1-sulfonamide (BTBS)

I.Optimized Geometrical Parameters

ST 1: Selected optimized geometrical parameters of BTBS (bond lengths in Å, bond angles and dihedral angles in °).

No.	Bond Atoms	Bond Length	Angle Atoms	Bond Angle	Dihedral Atoms	Dihedral Angle
1	Br1–C13	1.916	Br1–C13–C11	119.225	Br1–C13–C11–C15	179.865
2	S2–O3	1.464	Br1–C13–C15	119.368	S2–C10–C11–C12	176.685
3	S2–O4	1.463	O3–S2–O4	120.701	C10–C11–C13–H26	179.694
4	S2–N5	1.680	O3–S2–N5	112.235	C10–C12–C14–H27	180.063
5	S2–C10	1.807	O3–S2–C10	106.386	C12–C14–C15–H28	180.001
6	N5–C6	1.499	O4–S2–N5	104.443	C13–C15–C14–H29	180.064
7	N5–H16	1.016	O4–S2–C10	108.171	Br1–C13–C11–C10	179.459
8	C6–C7	1.537	N5–S2–C10	103.618	Br1–C13–C11–H26	359.765
9	C6–C8	1.534	S2–N5–C6	125.244	Br1–C13–C15–C14	180.140
10	C6–C9	1.539	S2–N5–H16	106.622	Br1–C13–C15–H29	0.204
11	C7–H17	1.092	S2–C10–C11	119.189	O3–S2–N5–C6	340.012
12	C7–H18	1.093	S2–C10–C12	118.859	O3–S2–N5–H16	115.433
13	C7–H19	1.095	C6–N5–H16	113.100	O3–S2–C10–C11	172.142
14	C8–H20	1.091	N5–C6–C7	104.545	O3–S2–C10–C12	348.928
15	C8–H21	1.092	N5–C6–C8	109.973	O4–S2–N5–C6	207.569
16	C8–H22	1.093	N5–C6–C9	111.625	O4–S2–N5–H16	342.990
17	C9–H23	1.094	C7–C6–C8	109.622	O4–S2–C10–C11	303.184
18	C9–H24	1.094	C7–C6–C9	110.052	O4–S2–C10–C12	119.970
19	C9–H25	1.090	C6–C7–H17	110.954	C10–S2–N5–C6	94.381

No.	Bond Atoms	Bond Length	Angle Atoms	Bond Angle	Dihedral Atoms	Dihedral Angle
20	C10–C11	1.394	C6–C7–H18	109.924	C10–S2–N5–H16	229.802
21	C10–C12	1.390	C6–C7–H19	111.156	N5–S2–C10–C11	53.648
22	C11–C13	1.389	C8–C6–C9	110.837	N5–S2–C10–C12	230.434
23	C11–H26	1.081	C6–C8–H20	111.659	S2–N5–C6–C7	186.588
24	C12–C14	1.394	C6–C8–H21	111.030	S2–N5–C6–C8	304.197
25	C12–H27	1.082	C6–C8–H22	109.197	S2–N5–C6–C9	67.647
26	C13–C15	1.395	C6–C9–H23	110.662	S2–C10–C11–C13	177.283
27	C14–C15	1.392	C6–C9–H24	110.093	S2–C10–C11–H26	356.978
28	C14–H28	1.084	C6–C9–H25	111.072	S2–C10–C12–C14	182.928
29	C15–H29	1.082	H17–C7–H18	108.667	S2–C10–C12–H27	2.990
30	–	–	H17–C7–H19	108.450	H16–N5–C6–C7	53.574
31	–	–	H18–C7–H19	107.591	H16–N5–C6–C8	171.183
32	–	–	H20–C8–H21	108.942	H16–N5–C6–C9	294.633
33	–	–	H20–C8–H22	107.684	N5–C6–C7–H17	60.531
34	–	–	H21–C8–H22	108.211	N5–C6–C7–H18	180.753
35	–	–	H23–C9–H24	107.870	N5–C6–C7–H19	299.763
36	–	–	H23–C9–H25	108.388	N5–C6–C8–H20	66.811
37	–	–	H24–C9–H25	108.665	N5–C6–C8–H21	305.016
38	–	–	C11–C10–C12	121.871	N5–C6–C8–H22	185.781
39	–	–	C10–C11–C13	118.121	N5–C6–C9–H23	57.049
40	–	–	C10–C11–H26	120.783	N5–C6–C9–H24	176.203
41	–	–	C10–C12–C14	118.767	N5–C6–C9–H25	296.611
42	–	–	C10–C12–H27	119.802	C8–C6–C7–H17	302.682
43	–	–	C13–C11–H26	121.095	C8–C6–C7–H18	62.904
44	–	–	C11–C13–C15	121.407	C8–C6–C7–H19	181.914
45	–	–	C14–C12–H27	121.432	C7–C6–C8–H20	181.220
46	–	–	C12–C14–C15	120.627	C7–C6–C8–H21	59.426
47	–	–	C12–C14–H28	119.831	C7–C6–C8–H22	300.191
48	–	–	C13–C15–C14	119.204	C9–C6–C7–H17	180.531
49	–	–	C13–C15–H29	120.164	C9–C6–C7–H18	300.753
50	–	–	C15–C14–H28	119.542	C9–C6–C7–H19	59.763
51	–	–	C14–C15–H29	120.632	C7–C6–C9–H23	301.436
52	–	–	–	–	C7–C6–C9–H24	60.590
53	–	–	–	–	C7–C6–C9–H25	180.998
54	–	–	–	–	C9–C6–C8–H20	302.901
55	–	–	–	–	C9–C6–C8–H21	181.107
56	–	–	–	–	C9–C6–C8–H22	61.871
57	–	–	–	–	C8–C6–C9–H23	180.008
58	–	–	–	–	C8–C6–C9–H24	299.162
59	–	–	–	–	C8–C6–C9–H25	59.570

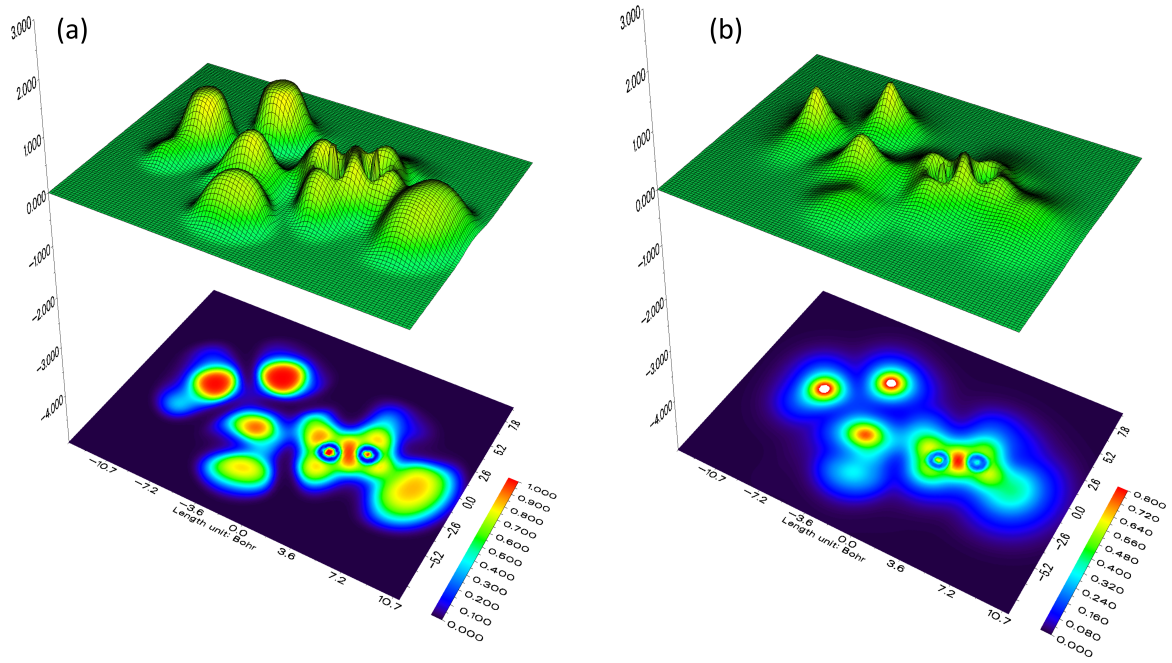
No.	Bond Atoms	Bond Length	Angle Atoms	Bond Angle	Dihedral Atoms	Dihedral Angle
60	–	–	–	–	C12–C10–C11–C13	0.598
61	–	–	–	–	C12–C10–C11–H26	180.293
62	–	–	–	–	C11–C10–C12–C14	359.623
63	–	–	–	–	C11–C10–C12–H27	179.685
64	–	–	–	–	C10–C11–C13–C15	359.593
65	–	–	–	–	C10–C12–C14–C15	359.955
66	–	–	–	–	C10–C12–C14–H28	179.956
67	–	–	–	–	H26–C11–C13–C15	179.899
68	–	–	–	–	C11–C13–C15–C14	0.005
69	–	–	–	–	C11–C13–C15–H29	180.069
70	–	–	–	–	H27–C12–C14–C15	179.892
71	–	–	–	–	H27–C12–C14–H28	359.893
72	–	–	–	–	C12–C14–C15–C13	0.226
73	–	–	–	–	C12–C14–C15–H29	180.163
74	–	–	–	–	C13–C15–C14–H28	180.226
75	–	–	–	–	H28–C14–C15–H29	0.162

II.Fukui Functions and Dual-Descriptors Analysis

ST 2: Fukui function and dual descriptor (Δf) values derived from DFT–NPA, indicating electrophilic and nucleophilic reactive sites within the title molecule.

Atoms	**N+1 (Anion)**	**N (Neutral)**	**N–1 (Cation)**	$f^+(\vec{r})$	$f^-(\vec{r})$	$f^0(\vec{r})$	Δf
Br1	-0.00435	0.07825	0.30876	-0.08260	-0.23051	-0.15655	0.14791
S2	2.20010	2.21050	2.18621	-0.01040	0.02429	0.00694	-0.03469
O3	-0.96030	-0.92099	-0.84204	-0.03931	-0.07895	-0.05913	0.03964
O4	-0.95239	-0.91048	-0.82940	-0.04191	-0.08108	-0.06149	0.03917
N5	-0.90838	-0.89710	-0.74488	-0.01128	-0.15222	-0.08175	0.14094
C6	0.10651	0.11775	0.11839	-0.01124	-0.00064	-0.00594	-0.01060
C7	-0.58244	-0.57277	-0.57775	-0.00967	0.00498	-0.00234	-0.01465
C8	-0.59311	-0.59102	-0.59550	-0.00209	0.00448	0.00120	-0.00657
C9	-0.59541	-0.59174	-0.57878	-0.00367	-0.01296	-0.00832	0.00929
C10	-0.36995	-0.24804	-0.21336	-0.12191	-0.03468	-0.07830	-0.08723
C11	-0.27890	-0.20852	-0.21216	-0.07038	0.00364	-0.03337	-0.07402
C12	-0.22747	-0.19441	-0.08920	-0.03306	-0.10521	-0.06914	0.07215
C13	-0.09519	-0.10020	-0.07326	0.00501	-0.02694	-0.01096	0.03195
C14	-0.23110	-0.17902	-0.18280	-0.05208	0.00378	-0.02415	-0.05586
C15	-0.37257	-0.20622	-0.11025	-0.16635	-0.09597	-0.13116	-0.07038
H16	0.37495	0.40265	0.42193	-0.02770	-0.01928	-0.02349	-0.00842
H17	0.19939	0.21067	0.21553	-0.01128	-0.00486	-0.00807	-0.00642
H18	0.12560	0.20899	0.23244	-0.08339	-0.02345	-0.05342	-0.05994
H19	0.15200	0.19913	0.21224	-0.04713	-0.01311	-0.03012	-0.03402
H20	0.22200	0.21761	0.21634	0.00439	0.00127	0.00283	0.00312
H21	0.21493	0.20938	0.20996	0.00555	-0.00058	0.00249	0.00613
H22	0.18579	0.20874	0.23407	-0.02295	-0.02533	-0.02414	0.00238
H23	0.17775	0.19923	0.21402	-0.02148	-0.01479	-0.01813	-0.00669
H24	0.16139	0.20168	0.23013	-0.04029	-0.02845	-0.03437	-0.01184
H25	0.22611	0.22992	0.23425	-0.00381	-0.00433	-0.00407	0.00052
H26	0.21997	0.24239	0.25791	-0.02242	-0.01552	-0.01897	-0.00690
H27	0.21887	0.24244	0.26108	-0.02357	-0.01864	-0.02110	-0.00493
H28	0.18773	0.21594	0.24650	-0.02821	-0.03056	-0.02938	0.00235
H29	0.19846	0.22522	0.24964	-0.02676	-0.02442	-0.02559	-0.00234

III.Electron Localization Analysis



SF 1: Three-dimensional ELF (a) and LOL (b) maps of BTBS highlighting electron localization features.

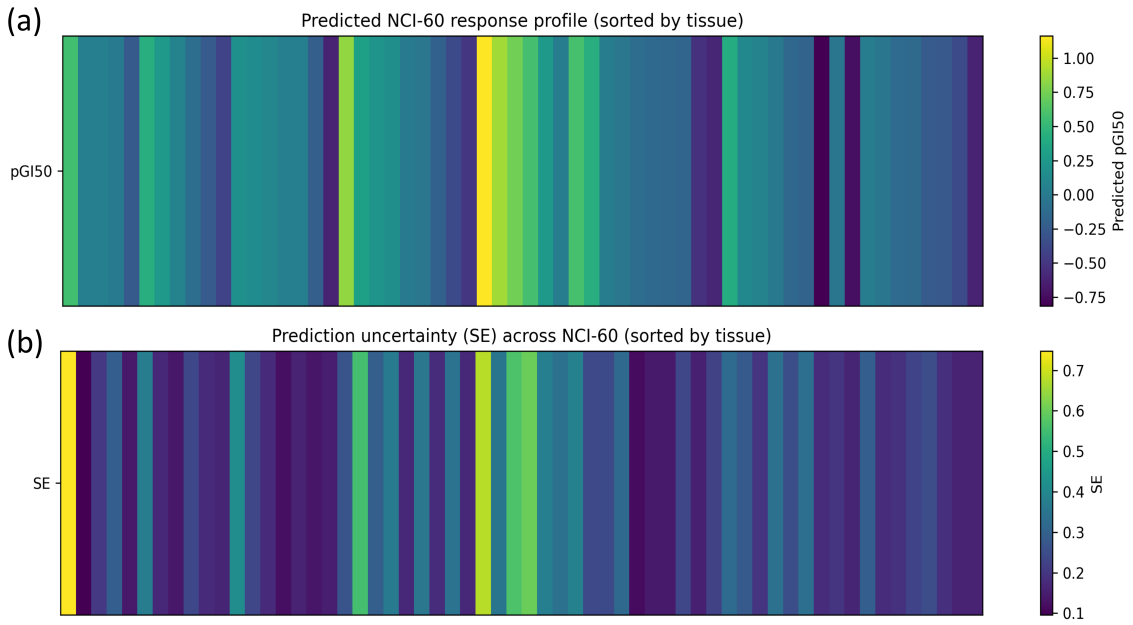
IV.Molecular Docking Interaction Summary

ST 3: Protein–ligand interaction profile of BTBS. Interaction types: Hydrophobic (Alkyl – β, Pi–Alkyl – α, Pi–Sulphur – γ), Pi–Sigma – δ, H-bond (Conventional – ζ_1, Carbon H-bond – ζ_2, π-donor H-bond – ζ_3), π–π stacked – ε, and π–cation – Θ.

Protein (PDB ID)	Bonded Residue	Interaction(s)	Bond Distance (Å)	Estimated K_i (mM)	Binding Energy (kcal/mol)	RMSD (Å)
1U9V	TYR67	δ, α	3.94, (4.72, 5.29)	1.98	-7.78	63.328
	ALA134	α	4.29			
	ALA163	α	5.29			
	LEU160	β	4.29			
	LEU209	β	4.78			
	GLY66	ζ_1	1.94			
	TRP26	ζ_2	3.77			
	CYS25	γ	5.94			

Protein (PDB ID)	Bonded Residue	Interaction(s)	Bond Distance (Å)	Estimated K_i (mM)	Binding Energy (kcal/mol)	RMSD (Å)
3KS3	HIS119	γ	5.94	2.12	-7.74	15.460
	HIS96	γ	5.45			
	HIS64	α	4.11			
	HIS94	ε, α	4.06, (3.97, 5.33, 4.70)			
	GLN92	ζ_3	3.24			
	ALA65	β	3.28			
	VAL143	β	3.40, 4.94			
	VAL121	β	4.20, 4.42			
	LEU198	β	4.72, 4.64			
	TRP209	α	5.30, 4.49			
	THR199	ζ_1	2.07			
	THR200	ζ_1	2.21			
5E2R	HIS94	ζ_1, ε, Θ, α	1.84, (3.87, 3.58, 4.70)	2.94	-7.55	15.248
	HIS96	ζ_1, γ, α	1.95, (5.01, 4.44)			
	HIS119	ζ_1, α	1.94, (4.33)			
	THR199	ζ_1	1.85, 2.59			
	THR200	ζ_1, δ	2.59, (3.74)			
	ALA65	β, α	3.46, (5.28)			
	VAL207	β	4.78			
	VAL121	β	3.59, 4.31			
	VAL143	β	3.29, 4.10			
	LEU141	β	5.07			
	LEU198	β	4.35, 4.76			
	TRP209	α	4.70, 4.79, 5.50			

V.NCI-60 Anticancer Activity Prediction



SF 2: Predicted NCI-60 response profile (a) and corresponding prediction uncertainty (b) for BTBS across the NCI-60 cancer cell line panel, ordered by tissue group. Lower standard error indicates higher prediction precision.

Data Source

NCI-60/DTP GI_{50}/pGI_{50} pharmacological data were obtained from the CellMiner and CellMinerCDB databases. Prediction uncertainty was evaluated using a similarity-weighted neighborhood approach, where lower standard error corresponds to higher prediction confidence.