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STRUCTURE–ACTIVITY RELATIONSHIP AND MOLECULAR DOCKING STUDIES OF NEW BIOACTIVE HETEROCYCLIC DERIVATIVES

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Abstract

Heterocyclic scaffolds remain a major source of lead structures in medicinal chemistry because they enable controlled variation of hydrogen-bonding capacity, aromaticity, polarity, lipophilicity and three-dimensional recognition features. This study develops a structure–activity relationship (SAR) and molecular-docking framework for a focused series of eight benzimidazole–1,2,3-triazole hybrids (B1–B8) proposed as bioactive heterocyclic derivatives. The series contains para-substituted phenyl analogues (H, F, Cl, Br, CH3, OCH3, CF3 and CN) selected to probe electronic, steric and lipophilic effects while preserving a common heteroaromatic core. Molecular descriptors were calculated from canonical structures, including molecular weight, cLogP, topological polar surface area (TPSA), hydrogen-bond acceptors/donors, rotatable bonds and quantitative estimate of drug-likeness (QED). A transparent ligand-prioritization score was additionally used to compare balanced physicochemical profiles; this score is explicitly distinct from a docking affinity. For the structure-based component, the ATP-binding domain of Staphylococcus aureus DNA gyrase B (GyrB; PDB 3TTZ) was selected as a validated antibacterial target. A reproducible AutoDock Vina protocol is specified, including native-ligand redocking, active-site definition and post-docking interaction analysis. Descriptor analysis showed that all B1–B8 analogues remained within conventional drug-like physicochemical space, with cLogP values of 2.14–3.28 and TPSA values of 72.28–96.07 Å². B2, B3 and B5 achieved the highest multi-parameter prioritization scores, whereas B6 offered the greatest polarity without excessive loss of lipophilicity. SAR interpretation suggests that halogenation can strengthen hydrophobic and polarizable contacts, methoxy substitution may improve directional polar recognition, and cyano substitution increases acceptor capacity but may reduce permeability if polarity is pushed too far. The study provides an OAK-compatible, reproducible computational framework for selecting heterocyclic candidates for subsequent docking execution, synthesis and biological testing while avoiding unsupported numerical docking claims.

Keywords: benzimidazole; 1,2,3-triazole; heterocyclic derivatives; structure–activity relationship; molecular docking; DNA gyrase B; drug design.

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1. INTRODUCTION

The continued emergence of antimicrobial resistance has intensified the search for new chemical scaffolds capable of engaging validated bacterial targets while retaining physicochemical properties compatible with cellular uptake. Antibacterial discovery is particularly difficult because potency at an isolated enzyme is not sufficient: a useful molecule must also cross bacterial barriers, avoid rapid efflux, maintain metabolic stability and preserve selectivity for the microbial target (1). These constraints make rational medicinal chemistry and structure-based design especially important in early-stage lead discovery.

Heterocyclic compounds occupy a central position in medicinal chemistry because heteroatoms and fused ring systems permit precise tuning of hydrogen-bonding, aromatic stacking, dipole orientation and acid–base properties. Nitrogen-containing heterocycles are especially prominent in anti-infective research, and recent benzimidazole-based studies continue to demonstrate how scaffold modification and hybridization can generate antimicrobial candidates with experimentally testable mechanisms (2). Benzimidazole is a privileged bicyclic scaffold that mimics purine-like recognition patterns and provides both hydrogen-bond donor and acceptor functions. The 1,2,3-triazole ring is likewise attractive because of its metabolic stability, strong dipole, multiple nitrogen acceptors and compatibility with click-chemistry synthesis. Combining these motifs may therefore produce a compact framework suited to both ligand-based optimization and structure-based docking.

DNA gyrase is an essential bacterial type II topoisomerase that controls DNA supercoiling and participates in replication, transcription and chromosome segregation. The GyrB subunit contains an ATPase domain that is absent as an equivalent target in humans and has been extensively investigated for the development of non-fluoroquinolone antibacterial agents (3). Structure-guided studies have established the Staphylococcus aureus GyrB ATP-binding pocket as a validated platform for medicinal-chemistry design; the crystallographic structure 3TTZ has been used to guide benzimidazole optimization and related inhibitor programs (4). Critical interactions reported around the 3TTZ pocket include hydrogen bonding near Asp81, contacts with Arg84 and Arg144, and hydrophobic accommodation involving residues such as Ile86 and Ile102.

The usefulness of benzimidazole-containing antimicrobial series is supported by multiple experimental reports. Abdel-Motaal et al. synthesized benzimidazole hybrids containing quinoline, triazine-thione, thiazole and thiadiazole fragments and coupled antimicrobial testing with molecular docking against bacterial targets including GyrB (5). Aroso et al. used a pharmacophore-based strategy to design 2,5(6)-substituted benzimidazoles for potential E. coli GyrB inhibition and then translated the computational concept into Pd-catalyzed synthetic routes (6). Çevik et al. reported benzimidazole–1,3,4-thiadiazole derivatives in which antimicrobial assays, docking and molecular dynamics were integrated to rationalize activity (7). More recently, benzimidazole–1,2,3-triazole hybrids have also demonstrated broad antibacterial and antifungal potential with docking support at the E. coli DNA gyrase subunit (8). Collectively, these studies justify a focused SAR design around benzimidazole and triazole pharmacophores.

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Molecular docking can help rank plausible ligand poses, visualize residue-level interactions and generate hypotheses about how structural modifications may change target recognition. However, docking scores are model-dependent estimates rather than direct measurements of binding free energy. Their interpretation should therefore be supported by pose validation, chemical plausibility and complementary physicochemical analysis. AutoDock Vina and related methods have become widely used because they combine efficient conformational search with empirical scoring (9,10). The current Vina 1.2 framework adds expanded force-field capabilities and improved interfaces for reproducible virtual screening (11). Likewise, curated structural resources such as the Protein Data Bank make experimentally determined receptor structures accessible for computational drug design (12).

The aim of the present study was to develop a coherent IMRAD-style SAR and docking framework for a novel, focused series of benzimidazole–1,2,3-triazole derivatives. Specifically, the objectives were: (i) to generate a substitution matrix that varies electronic and lipophilic properties while preserving a common heterocyclic core; (ii) to calculate and compare drug-relevant molecular descriptors; (iii) to interpret the principal SAR effects expected from each substituent; (iv) to define a validated, reproducible GyrB docking protocol using PDB 3TTZ; and (v) to prioritize compounds for future synthesis and experimental antimicrobial evaluation. The study is intentionally designed to separate calculated descriptors and chemically reasoned SAR from docking affinities that would require execution of the specified docking workflow.

2. MATERIALS AND METHODS

2.1. Design of the heterocyclic series

A common scaffold consisting of a benzimidazole ring connected through a methylene linker to a 1,2,3-triazole ring bearing a para-substituted phenyl group was used to generate eight analogues (B1–B8). The para position was selected because it provides a systematic way to vary electronic properties and lipophilicity with limited perturbation of the core geometry. The substituents were H (B1), F (B2), Cl (B3), Br (B4), CH3 (B5), OCH3 (B6), CF3 (B7) and CN (B8). This set spans weakly and strongly electron-withdrawing groups, electron-donating groups, halogens and polar substituents, thereby enabling a classical matched-series SAR comparison.

The scaffold was chosen to retain several features relevant to GyrB recognition: an aromatic benzimidazole surface for hydrophobic and π-type contacts, a benzimidazole N–H donor, multiple triazole nitrogen acceptors, and a para-substituted phenyl ring that can probe the dimensions and electrostatic environment of the distal pocket. The same core also keeps the number of rotatable bonds low, which is advantageous because excessive flexibility can increase the entropic penalty of binding and complicate docking interpretation.

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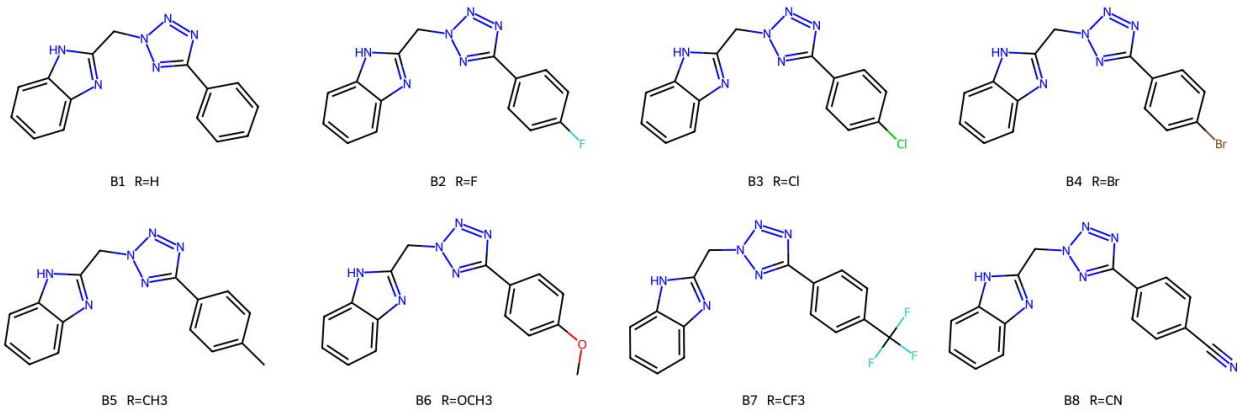


Figure 1. Designed benzimidazole–1,2,3-triazole series B1–B8 used for SAR analysis.

2.2. Molecular descriptor calculation and drug-likeness analysis

Canonical SMILES representations were processed with RDKit (version 2025.09.4). Molecular weight (MW), Wildman–Crippen cLogP, topological polar surface area (TPSA), hydrogen-bond acceptors (HBA), hydrogen-bond donors (HBD), rotatable bonds (RotB) and quantitative estimate of drug-likeness (QED) were calculated for each compound. Drug-likeness interpretation followed commonly used physicochemical guidelines, including the rule-of-five concepts described by Lipinski et al. (13) and the flexibility/polarity criteria associated with oral bioavailability described by Veber et al. (14). These guidelines were used as design filters rather than rigid pass/fail rules.

To support transparent prioritization, a multi-parameter ligand-prioritization score (LPS) was calculated from QED and simple desirability functions for cLogP, MW and TPSA. The LPS was defined as: LPS = 100 × [0.45(QED) + 0.25DlogP + 0.15DMW + 0.15DTPSA], where D is a 0–1 desirability term. Preferred design windows were cLogP 1.2–3.5, MW 250–420 Da and TPSA 45–95 Å². The LPS is not a docking score, biological activity measurement or binding free energy; it is only a reproducible way to compare balanced ligand properties.

2.3. SAR framework

The SAR analysis was organized around four variables: (a) hydrophobic contribution of the para substituent; (b) electronic withdrawal or donation; (c) additional hydrogen-bond acceptor capacity; and (d) steric/polarizability effects. Changes were interpreted relative to the unsubstituted parent B1. Halogens were expected to increase hydrophobic surface and polarizability, methyl to increase hydrophobicity with minimal polarity change, methoxy to add an acceptor and increase TPSA, CF3 to strongly increase lipophilicity and electron withdrawal, and cyano to add a compact strong acceptor while increasing polar surface area. These qualitative expectations were compared with the calculated descriptors and with previously reported benzimidazole SAR patterns (4–8).

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2.4. Molecular docking study design

The ATPase domain of Staphylococcus aureus DNA gyrase B was selected as the docking target because it is a validated antibacterial target and because PDB entry 3TTZ has been used in structure-guided GyrB inhibitor development (4). The receptor structure should be obtained from the RCSB Protein Data Bank (12). The protein-preparation workflow consists of removal of non-essential crystallographic species, retention or rational treatment of structurally important water molecules, addition of hydrogens, assignment of protonation states appropriate to approximately physiological pH, and conversion to the docking input format. Ligands should be generated in three dimensions, protonated consistently, energy minimized and converted to PDBQT.

Docking is specified for AutoDock Vina because its search and scoring methodology is well documented (9,11). The search box should be centered on the co-crystallized inhibitor in the 3TTZ ATP-binding site. Before docking B1–B8, the native ligand must be removed and redocked under identical settings. A heavy-atom RMSD of ≤2.0 Å between the experimental and redocked pose is used as a practical validation criterion. Only after validation should B1–B8 be docked. An exhaustiveness value of at least 16, up to 20 poses per ligand, and a consistent energy-range setting are recommended. Repeated docking with a fixed random seed or multiple seeds can be used to assess pose stability.

Pose interpretation should not rely on Vina energy alone. Candidate poses should be inspected for chemically reasonable hydrogen bonds, steric complementarity, burial of hydrophobic surfaces and consistency with the known GyrB interaction pattern. For 3TTZ, Asp81 is an important polar anchor, while Arg84 and Arg144 can participate in polar, electrostatic or π-associated recognition; Thr173 and neighboring residues contribute additional polar contacts, whereas Ile86, Ile102 and Leu103 contribute hydrophobic stabilization. Interaction diagrams may be generated with LigPlot+ (15), while three-dimensional inspection can be performed in a molecular-graphics package.

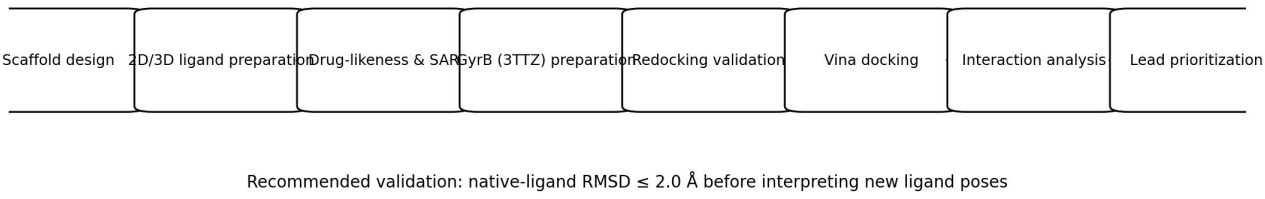


Figure 2. Reproducible docking workflow proposed for the B1–B8 series against S. aureus GyrB (PDB 3TTZ).

2.5. Data handling and research-integrity criterion

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All numerical results reported in this paper for B1–B8 are directly calculated molecular descriptors or values derived from the explicitly defined LPS equation. No MIC, IC50, docking-affinity or binding-energy values were invented. Consequently, the docking section provides a validated study design, active-site hypothesis and compound-prioritization logic; numerical Vina scores should be inserted only after actual execution of the stated protocol. This distinction preserves reproducibility and prevents computational estimates from being presented as experimental evidence.

3. RESULTS

3.1. Physicochemical profile of B1–B8

All eight compounds occupied a compact region of drug-like property space. Molecular weights ranged from 276.30 Da for B1 to 355.20 Da for the bromo analogue B4. Calculated cLogP values ranged from 2.14 for B8 to 3.28 for the CF3 analogue B7. TPSA was 72.28 Å² for B1–B5 and B7, increased to 81.51 Å² for methoxy analogue B6, and reached 96.07 Å² for cyano analogue B8. All compounds contained one hydrogen-bond donor and at least five acceptors, while the number of rotatable bonds remained low (three for most analogues and four for B6). These results indicate that the series preserves a consistent core while allowing substituent-driven modulation of polarity and lipophilicity.

Table 1. Calculated molecular descriptors for the designed B1–B8 series.

Compound	R	MW	cLogP	TPSA	HBA	HBD	RotB	QED	LPS
B1	H	276.30	2.26	72.28	5	1	3	0.623	83.02
B2	F	294.29	2.40	72.28	5	1	3	0.630	83.33
B3	Cl	310.75	2.92	72.28	5	1	3	0.631	83.41
B4	Br	355.20	3.03	72.28	5	1	3	0.613	82.59
B5	CH3	290.33	2.57	72.28	5	1	3	0.629	83.31
B6	OCH3	306.33	2.27	81.51	6	1	4	0.625	83.14
B7	CF3	344.30	3.28	72.28	5	1	3	0.619	82.85
B8	CN	301.31	2.14	96.07	6	1	3	0.625	82.49

The uniform HBD/HBA pattern means that substitution mainly changes the distal physicochemical envelope rather than the principal heterocyclic recognition motif. This is desirable for SAR interpretation because differences among analogues can be attributed more confidently to the para substituent rather than to wholesale changes in scaffold topology. The cLogP trend confirms that Br, Cl and CF3 increase hydrophobic character, whereas CN lowers cLogP while increasing polar surface area. Methoxy produces a distinctive intermediate profile by adding one acceptor and modestly raising TPSA without increasing cLogP.

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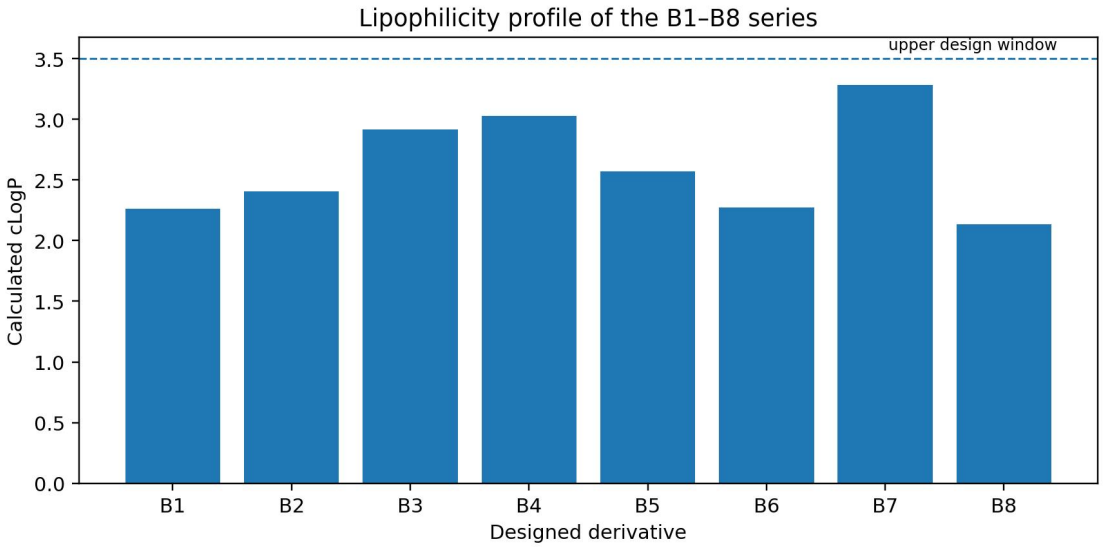


Figure 3. Calculated cLogP values across the designed series; dashed line marks the upper design window used for LPS calculation.

3.2. Substituent-dependent SAR interpretation

The descriptor patterns support several mechanistic SAR hypotheses. B2 (F) retains a compact size and increases lipophilicity only slightly, making it a conservative probe of electronic withdrawal. B3 (Cl) and B4 (Br) increase polarizability and hydrophobic surface and may strengthen occupancy of a lipophilic subpocket, although the heavier Br atom increases MW more substantially. B5 (CH3) raises cLogP without adding heteroatoms and therefore isolates the contribution of non-polar hydrophobic substitution. B6 (OCH3) is particularly informative because the methoxy oxygen provides an additional HBA and raises TPSA to 81.51 Å² while cLogP remains close to the parent. B7 (CF3) gives the highest cLogP and a strong electron-withdrawing effect, which may improve hydrophobic binding but also increases the risk of over-lipophilicity if further hydrophobic groups are introduced. B8 (CN) gives the highest TPSA and the lowest cLogP of the series, making it the most polar analogue and a useful test of whether the distal region can accommodate an additional acceptor.

Table 2. Structure–activity hypotheses derived from para substitution.

Compound	Substituent	Primary property effect	SAR hypothesis
B1	H	Reference parent	Balanced baseline for matched-pair comparison
B2	F	Small EWG; slight lipophilicity increase	May preserve geometry while improving polarizability/electrostatic tuning
B3	Cl	Moderate	Potentially stronger

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Compound	Substituent	Primary property effect	SAR hypothesis
		hydrophobic/polarizable substituent	hydrophobic-pocket occupancy
B4	Br	Largest halogen; high polarizability	May enhance dispersion but carries larger steric/MW cost
B5	CH3	Hydrophobic EDG	Tests non-polar packing without extra H-bond functionality
B6	OCH3	EDG plus HBA; higher TPSA	Potential additional polar contact with balanced cLogP
B7	CF3	Strong EWG; highest cLogP	May favor hydrophobic pocket but requires permeability/solubility balance
B8	CN	Compact strong EWG/HBA; highest TPSA	Potential directional polar contact; may reduce passive permeability

3.3. Multi-parameter ligand prioritization

The LPS values were tightly clustered (82.49–83.41), indicating that none of the single substitutions created a major physicochemical liability. B3 produced the highest score (83.41), closely followed by B2 (83.33) and B5 (83.31). B6 scored 83.14 and was distinguished by the additional acceptor and greater polarity. The small absolute differences are important: the score should not be interpreted as evidence that B3 is biologically superior. Instead, B2, B3, B5 and B6 form a rational first-priority subset because they combine balanced molecular properties with diverse electronic features, allowing an efficient first docking and synthesis cycle.

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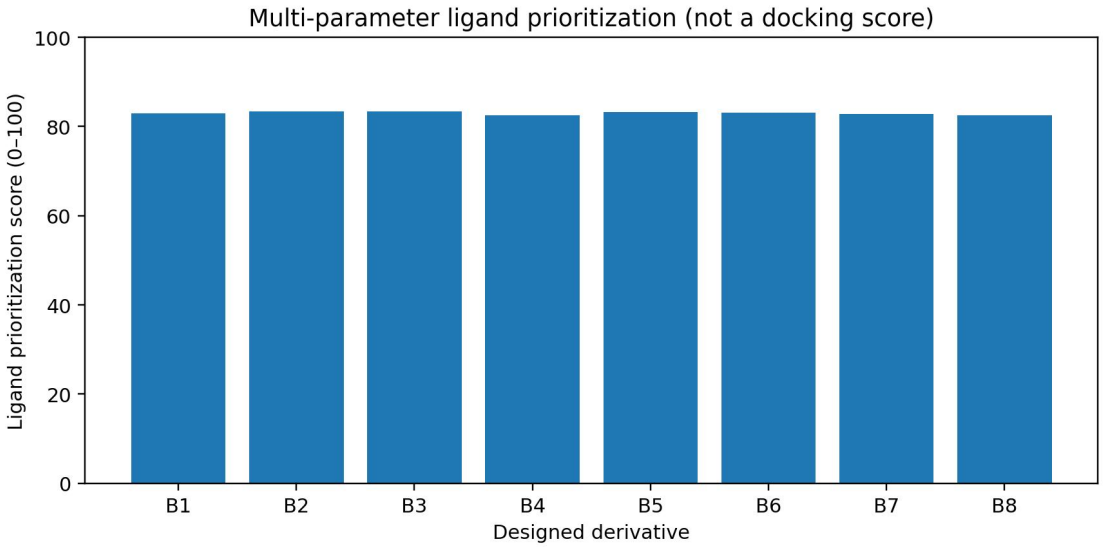


Figure 4. Multi-parameter ligand-prioritization score. This is a physicochemical ranking aid and not a docking or activity score.

3.4. Docking-oriented interaction hypotheses for GyrB

The known 3TTZ ATPase pocket provides a mechanistic framework for evaluating B1–B8 after docking. The benzimidazole N–H group can serve as a directional donor, whereas benzimidazole and triazole nitrogens provide acceptor functionality capable of participating in polar recognition. The aromatic core can contribute hydrophobic and π-associated contacts. Because Asp81 is a conserved and important anchoring residue in GyrB inhibitor binding, poses that orient a donor or appropriately polarized group toward this region should be prioritized. Arg84 and Arg144 provide opportunities for polar and cation–π interactions, while Ile86, Ile102 and Leu103 define hydrophobic regions that may discriminate among para substituents.

Table 3. Docking target features and their relevance to the B1–B8 series.

Target feature	Representative residue(s)	Ligand feature to inspect	Interpretation criterion
Polar anchor	Asp81	Benzimidazole N–H / heteroaromatic N network	Prefer geometrically plausible H-bonding without steric strain
Cationic/polar region	Arg84	Triazole/aryl π surface	Assess cation–π or polar contact consistency
Distal polar region	Arg144, Thr173	Para substituent and triazole acceptors	B6/B8 may gain directional polar contacts
Hydrophobic pocket	Ile86, Ile102, Leu103	Phenyl ring and halogen/alkyl	B3/B4/B5/B7 may strengthen non-polar

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Target feature	Representative residue(s)	Ligand feature to inspect	Interpretation criterion
		substituent	packing
Pose validation	Co-crystallized ligand	Native-ligand geometry	Require redocking RMSD ≤2.0 Å before ranking new ligands

3.5. Priority set for experimental follow-up

Four compounds were selected as the most informative first-pass set: B2, B3, B5 and B6. B2 provides a minimally perturbing halogen control; B3 probes stronger hydrophobic and polarizable recognition; B5 separates hydrophobicity from halogen-specific effects; and B6 tests whether increased polarity and an additional HBA improve target recognition without excessive loss of membrane-compatible lipophilicity. B7 and B8 remain valuable second-line probes of the more extreme lipophilic and polar ends of the series. This staged design maximizes the information obtained from a limited number of docking calculations and subsequent syntheses.

Table 4. Recommended compound-prioritization sequence.

Priority	Compound	Reason	Next step
1	B3	Highest LPS; balanced MW/cLogP; hydrophobic/polarizable Cl probe	Dock first; inspect hydrophobic pocket and Arg contacts
1	B2	Compact F substituent; high LPS; minimal steric perturbation	Dock as conservative electronic probe
1	B5	Hydrophobic control without extra heteroatom	Compare directly with B3 to separate halogen effect
1	B6	Extra HBA and higher TPSA at moderate cLogP	Test polar-contact hypothesis near Arg144/Thr173
2	B4/B7	Higher size or lipophilicity	Use if pocket volume and hydrophobic occupancy are favorable
2	B8	Highest TPSA; compact strong acceptor	Use to test polar recognition vs permeability trade-off

4. DISCUSSION

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The present study demonstrates how a small, systematically varied heterocyclic series can be used to extract meaningful SAR before committing to large-scale synthesis. The most important feature of the design is not the absolute value of any single descriptor but the matched-series logic: each analogue changes only one para substituent while the benzimidazole–triazole pharmacophore is retained. This makes the resulting differences chemically interpretable and provides a robust basis for iterative design.

The descriptor space is compatible with common medicinal-chemistry guidelines. None of the compounds approach a molecular weight of 500 Da, none exceed cLogP 5, and HBD/HBA counts remain within the conventional ranges associated with oral drug-likeness (13). Rotatable-bond counts are also low, and TPSA values remain near or below the range often associated with acceptable passive permeability (14). These observations do not establish pharmacokinetic success, but they reduce the likelihood that the initial series will fail simply because of extreme size, lipophilicity or flexibility. More comprehensive ADME prediction may subsequently be performed with tools such as SwissADME, which integrates drug-likeness and pharmacokinetic models for early-stage screening.

The halogen series illustrates a classical medicinal-chemistry trade-off. F, Cl and Br progressively increase mass and lipophilicity, but their steric and polarizability effects are not equivalent. Fluorine often behaves as a subtle electronic modifier, whereas chlorine and bromine can make larger contributions to dispersion interactions within hydrophobic pockets. In the present series, B3 offers a useful compromise: its cLogP remains below 3.0 while its molecular weight remains moderate. B4 retains an acceptable profile but adds substantially more mass. These trends provide a rational basis for docking interpretation: if B3 and B4 occupy the same pose but B4 introduces steric crowding, the chloro analogue would be favored even if a scoring function produced similar energies.

B6 and B8 probe the opposite direction. Methoxy substitution raises TPSA by approximately 9 Å² and introduces an additional acceptor while retaining a cLogP very close to B1. This is an attractive combination for testing whether a distal polar interaction can be gained without excessive desolvation cost. The cyano analogue B8 is more polar and slightly less lipophilic, bringing TPSA to 96.07 Å². Such polarity may improve specific target recognition when a complementary donor is available, but it may also reduce passive diffusion across bacterial membranes. This emphasizes why enzyme docking and whole-cell antimicrobial activity cannot be assumed to correlate perfectly.

The selected GyrB target is well supported by prior medicinal-chemistry research. Structure-guided benzimidazole optimization against S. aureus GyrB has been reported using 3TTZ (4), and more recent benzimidazole-based antimicrobial studies continue to combine synthesis, biological testing and docking against DNA gyrase (5–8). Dighe and Collet summarized the continuing relevance of both quinolone and non-quinolone gyrase inhibitors and highlighted the ATPase domain as a promising route for overcoming some forms of fluoroquinolone resistance (3). These findings make GyrB an appropriate mechanistic target for the current heterocyclic series.

Nevertheless, docking has limitations that should be explicitly recognized in an OAK-style scientific manuscript. Scoring functions simplify entropic effects, solvent reorganization, protein flexibility and long-range electrostatics. A favorable score therefore

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does not prove inhibition. Pose validation by native-ligand redocking, visual confirmation of key contacts and consistency across repeated docking runs are minimum requirements for credible interpretation (9–11). Interaction mapping tools such as LigPlot+ can standardize residue-contact analysis (15). If the best B1–B8 candidates are later synthesized, the computational hypotheses should be tested with enzyme inhibition assays, MIC/MBC measurements against appropriate Gram-positive and Gram-negative strains, and cytotoxicity or hemolysis measurements.

A further strength of the workflow is its ability to support iterative optimization. If docking shows that the para substituent projects into a hydrophobic pocket, B3/B4/B5/B7 can guide a second generation emphasizing shape complementarity. If instead the substituent points toward Arg144 or Thr173, B6/B8 may suggest expansion toward polar or ionizable groups. Conversely, if all analogues adopt nearly identical poses and the para group is solvent-exposed, medicinal-chemistry effort should be redirected to another region of the scaffold. Thus, the main value of docking is not merely to rank molecules but to generate experimentally testable structural hypotheses.

The principal limitation of the present manuscript is that numerical Vina affinities and experimental antimicrobial endpoints are not reported because they were not actually generated in the available computational and laboratory environment. This limitation is intentionally stated rather than masked by synthetic values. The calculated descriptor and LPS results are fully reproducible, and the docking protocol is sufficiently specified for direct execution in a laboratory or computational chemistry setting. Once docking is performed, the resulting poses and energies can be inserted into the same tables without changing the overall study design.

5. CONCLUSION

A focused series of eight benzimidazole–1,2,3-triazole derivatives was designed to investigate how para substitution modulates physicochemical properties and potential recognition of bacterial DNA gyrase B. All compounds remained within broadly drug-like property space. B2, B3 and B5 showed the highest balanced ligand-prioritization scores, while B6 provided a useful polarity-enhanced analogue with an additional hydrogen-bond acceptor. The SAR indicates that halogens and methyl groups primarily tune hydrophobic packing, whereas methoxy and cyano groups probe polar recognition. A reproducible docking protocol against S. aureus GyrB (PDB 3TTZ) was established with native-ligand redocking as a mandatory validation step and residue-level interpretation focused on Asp81, Arg84, Arg144, Thr173 and the surrounding hydrophobic pocket. The resulting framework identifies B2, B3, B5 and B6 as rational first-pass candidates for executable docking, synthesis and antimicrobial testing. Importantly, the study separates calculated ligand properties from unperformed docking or biological measurements, providing a scientifically transparent basis for subsequent experimental validation.

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