Synthesis, Molecular Docking, and In Vitro Antibacterial Activities of Some Novel Aminobenzylnaphthol Derivatives via One-Pot Three-Component Reaction

Shweta N. Dandekar[a], Onkar A. Lotlikar[a], M. M. V. Ramana[b], and Shrimant V. Rathod[a, 1]

[a] *Department of Chemistry, Bhavan's H. Somani College, Chowpatty, Mumbai, 400007 India*
[b] *Department of Chemistry, University of Mumbai, Santacruz (E), Mumbai, 400098 India*

Abstract—This work provides the first example of incorporating the thiazole moiety into the aminobenzyl-naphthol i.e. Betti base. A series of novel synthesized Betti bases via a one-pot three-component reaction of 2-amino-5-methyl thiazole, 2-naphthol, and substituted aldehydes are reported. The formation of desired products was confirmed using various spectroscopic techniques. The derivatives were screened in vitro for antibacterial activities. Molecular docking was also performed to predict the possible mode of action of these derivatives. The docking analysis ascertained that these derivatives regulate the antimicrobial potential via inhibition of DNA gyrase.

INTRODUCTION

Betti reaction is a special case of the Mannich reaction that produces aminobenzylnaphthol, known as Betti base [1]. The Betti bases serve as an important class of organic scaffolds. The reaction successfully procures the evolution of a new carbon−carbon bond along with one chiral carbon under mild experimental conditions. These optically active Betti bases have developed their importance as a ligand in asymmetric synthesis [2, 3]. Recent investigations have revealed their significance in pharmaceutical chemistry [4]. Betti bases have shown bioactivities including antibacterial [5], antitumor [6], bradycardiac [7], anti-inflammatory, and anthelmintic activities [8].

Multicomponent reactions (MCRs) represent an extraordinary tool for the construction of diverse and complex organic molecules. MCRs have their own advantages of saving time, energy, and raw materials [9]. Originally Betti bases were prepared in two steps, by the reaction of aldehyde, ammonia, and 2-naphthol in an ethanolic solution of KOH [10]. In recent years, one-pot synthesis is implemented for these reactions, with some catalysts thus making its synthetic pathway easy and rapid.

A critical analysis of the aforementioned reaction has prompted us to motif a novel Betti bases with 2-amino-5-methylthiazole, 2-naphthol, and substituted aldehydes. Present work deals with the synthesis, characterization, and molecular docking of a series of novel Betti bases. These compounds were then tested for in vitro antibacterial activities.

EXPERIMENTAL

Chemicals and reagents were purchased from S.D. Fine (Mumbai, India) and Sigma-Aldrich (United States) chemical companies. All the reactions were monitored by using thin-layer chromatography using Merck silica gel 60 F254 plates (TLC). Melting points were recorded on an Analab melting point apparatus. NMR (^{1}H and ^{13}C) spectra were recorded in a DMSO-d_6 solvent using Bruker Avance II (300 MHz) NMR spectrometer and TMS was taken as an internal standard. IR spectra were done by using Perkin Elmer, Frontier equipment with a diamond tip. Elemental analysis was performed on model EA300, Euro Vector.

General Procedure for the Synthesis of Betti Bases (IVa−j)

Equimolar concentrations of 5-methyl-thiazol-2-ylamine (**I**), substituted aromatic aldehyde (**II**), and 2-napthol (**III**) were taken in a round bottom flask and sequentially dissolved in glycerol. A catalytic amount of silica sulfuric acid (SSA) was added and the mixture

was kept on a water bath at 70−80°C for 30 min. The progress of the reaction was monitored on the TLC plate. After completion, the reaction mixture was quenched in water which results in the formation of a sticky mass. This sticky mass was freed using a pet ether and recrystallized using methanol.

1-[(2-Chloro-phenyl)-(5-methyl-thiazol-2-ylamino)-methyl]-naphthalen-2-ol (IVa). mp 168°C yield = 89.58% color = light yellow. **IR(v$_{max}$, cm^{-1}):** 3438 (−OH), 3368 (−NH), 3070 (Ar−H), 1542 (C=N), 742 (C−Cl). **^{1}H NMR (300 MHz, DMSO): δ** 10.09 (s, 1H, −OH), 8.11 (d, J = 8.6 Hz, 1H, **Ar−H**), 7.82 (s, 1H, **Ar−H**), 7.76−7.63 (m, 3H, **Ar−H**), 7.39 (t, J = 7.7 Hz, 1H, **Ar−H**), 7.31−7.21 (m, 1H, **Ar−H**), 7.18 (d, J = 8.9 Hz, 2H, **Ar−H**), 7.10 (t, J = 6.9 Hz, 2H, **Ar−H**), 6.88 (s, 1H,−NH), 6.63 (s, 1H, −CH), 2.21 (s, 3H, −CH$_3$). **^{13}C NMR (75 MHz, DMSO): δ** 167.12 (−**C=N**), 158.41, 153.27, 134.83, 132.13, 129.27, 129.15, 128.46, 128.38, 128.25, 126.17, 123.44, 122.85, 122.39, 120.33, 118.85, 117.95, 115.04, 114.75, 49.83 (**benzyl-C**), 11.71 (−**CH$_3$**). **Elemental analysis for C$_{21}$H$_{17}$ClN$_2$OS:** C, 66.22; H, 4.50; N, 7.35; found C, 66.36; H, 4.42; N, 7.46.

1-[(3-Chloro-phenyl)-(5-methyl-thiazol-2-ylamino)-methyl]-naphthalen-2-ol (IVb). mp 162°C yield = 84.34% color = light yellow. **IR (v$_{max}$, cm^{-1}):** 3445 (−OH), 3364 (−NH), 3059 (Ar−H), 1544 (C=N), 730 (C−Cl). **^{1}H NMR (300 MHz, DMSO): δ** 10.21 (s, 1H, −OH), 7.91 (d, J = 11.9 Hz, 2H, **Ar−H**), 7.72 (dd, J = 16.0, 8.4 Hz, 2H, **Ar−H**), 7.42-7.11 (m, 7H, **Ar−H**), 6.97 (s, 1H, −**NH**), 6.65 (s, 1H, −**CH**), 2.22 (s, 3H, −CH$_3$). **^{13}C NMR (75 MHz, DMSO): δ** 167.68 (−**C=N**), 153.31, 145.17, 134.68, 133.32, 132.10, 129.47, 129.37, 128.72, 128.50, 126.35, 126.12, 124.77, 123.18, 122.54, 120.40, 119.05, 119.00, 53.55 (**benzyl-C**), 11.74 (−**CH$_3$**). **Elemental analysis for C$_{21}$H$_{17}$ClN$_2$OS:** C, 66.22; H, 4.50; N, 7.35; found C, 66.16; H, 4.24; N, 7.44.

1-[(4-Chloro-phenyl)-(5-methyl-thiazol-2-ylamino)-methyl]-naphthalen-2-ol (IVc). mp 145°C yield = 90.28% color = light yellow. **IR (v$_{max}$, cm^{-1}):** 3423 (−OH), 3321 (−NH), 3056 (Ar−H), 1579 (C=N), 717 (C−Cl). **^{1}H NMR (300 MHz, DMSO): δ** 10.10 (s, 1H, −OH), 7.97−7.83 (m, 4H, **Ar−H**), 7.71−7.23 (m, 7H, **Ar−H**), 6.89 (s, 1H, −**NH**), 6.65 (s, 1H, −**CH**), 2.21 (s, 3H, −CH$_3$). **^{13}C NMR (75 MHz, DMSO): δ** 167.80 (−**C=N**), 153.36, 141.91, 134.69, 132.14, 130.75, 129.43, 128.50, 128.33, 126.31, 122.53, 120.41, 119.59, 119.14, 119.11, 53.66 (**benzyl-C**), 11.73 (−**CH$_3$**). **Elemental analysis for C$_{21}$H$_{17}$ClN$_2$OS:** C, 66.22; H, 4.50; N, 7.35; found C, 66.30; H, 4.64; N, 7.48.

1-[(5-Methyl-thiazol-2-ylamino)-(2-nitro-phenyl)-methyl]-naphthalen-2-ol (IVd). mp 190°C yield =

86.90% color = yellow. **IR (v$_{max}$, cm^{-1}):** 3430 (−OH), 3347 (−NH), 2980 (Ar−H), 1587 (C=N), 1538 (−NO$_2$). **^{1}H NMR (300 MHz, DMSO): δ** 9.87 (s, 1H, −OH), 7.91 (dd, J = 18.7, 9.9 Hz, 2H, **Ar−H**), 7.81−7.04 (m, 10H, **Ar−H** and −**NH**), 6.65 (s, 1H, −**CH**), 2.22 (s, 3H, −CH$_3$). **^{13}C NMR (75 MHz, DMSO): δ** 167.43 (−**C=N**), 164.19, 153.91, 149.28, 136.19, 134.98, 133.06, 131.72, 129.95, 129.49, 128.40, 127.60, 126.64, 123.92, 122.71, 122.52, 121.06, 119.01, 116.46, 52.08 (**benzyl-C**), 11.81 (−**CH$_3$**). **Elemental analysis for C$_{21}$H$_{17}$N$_3$O$_3$S:** C, 64.43; H, 4.38; N, 10.73; found C, 64.58; H, 4.26; N, 10.80.

1-[(5-Methyl-thiazol-2-ylamino)-(3-nitro-phenyl)-methyl]-naphthalen-2-ol (IVe). mp 168°C yield = 91.58% color = yellow. **IR (v$_{max}$, cm^{-1}):** 3441 (−OH), 3346 (−NH), 3019 (Ar−H), 1599 (C=N), 1548 (−NO$_2$). **^{1}H NMR (300 MHz, DMSO): δ** 10.30 (s, 1H, −OH), 8.26 (s, 1H, **Ar−H**), 8.01 (d, J = 8.0 Hz, 1H, **Ar−H**), 7.91 (s, 1H, **Ar−H**), 7.74−7.26 (m, 8H, **Ar−H**), 7.05 (s, 1H, −**NH**), 6.69 (s, 1H, −**CH**), 2.25 (s, 3H, −**CH$_3$**). **^{13}C NMR (75 MHz, DMSO): δ** 167.76 (−**C=N**), 153.50, 148.03, 145.21, 134.69, 132.91, 132.02, 129.90, 128.95, 128.88, 128.67, 126.64, 122.90, 122.75, 121.27, 121.09, 120.98, 119.13, 118.65, 53.80 (**benzyl-C**), 11.83 (−**CH$_3$**). **Elemental analysis for C$_{21}$H$_{17}$N$_3$O$_3$S:** C, 64.43; H, 4.38; N, 10.73; found C, 64.50; H, 4.44; N, 10.84.

1-[(5-Methyl-thiazol-2-ylamino)-(4-nitro-phenyl)-methyl]-naphthalen-2-ol (IVf). mp 180°C yield = 94.39% color = yellow. **IR (v$_{max}$, cm^{-1}):** 3445 (−OH), 3355 (−NH), 3066 (Ar−H), 1587 (C=N), 1540 (−NO$_2$). **^{1}H NMR (300 MHz, DMSO): δ** 10.21 (s, 1H, −OH), 8.06 (d, J = 8.5 Hz, 2H, **Ar−H**), 7.84 (d, J = 8.8 Hz, 2H, **Ar−H**), 7.74−7.17 (m, 7H, **Ar−H**), 7.06 (s, 1H, −**NH**), 6.68 (s, 1H, −**CH**), 2.24 (s, 3H, −CH$_3$). **^{13}C NMR (75 MHz, DMSO): δ** 167.66 (−**C=N**), 153.45, 146.18, 134.69, 132.03, 129.83, 128.82, 128.60, 127.25, 126.54, 122.99, 122.69, 120.89, 119.03, 118.66, 53.87 (**benzyl-C**), 11.79 (−**CH$_3$**). **Elemental analysis for C$_{21}$H$_{17}$N$_3$O$_3$S:** C, 64.43; H, 4.38; N, 10.73; found C, 64.54; H, 4.36; N, 10.77.

1-[(3-Methoxy-phenyl)-(5-methyl-thiazol-2-ylamino)-methyl]-naphthalen-2-ol (IVg). mp 165°C yield = 87.65% color = brown. **IR (v$_{max}$, cm^{-1}):** 3434 (−OH), 3368 (−NH), 3062 (Ar−H), 1580 (C=N), 1238 (−OCH$_3$). **^{1}H NMR (300 MHz, DMSO): δ** 10.27 (s, 1H, −OH), 7.90 (d, J = 5.2 Hz, 2**Ar−H**), 7.70 (dd, J = 16.9, 8.1 Hz, 2H, **Ar−H**), 7.32−6.94 (m, 7H, **Ar−H**), 6.73 (m, 1H, −**NH**), 6.64 (s, 1H, −**CH**), 3.68 (s, 3H, −**OCH$_3$**), 2.21 (s, 3H, −CH$_3$). **^{13}C NMR (75 MHz, DMSO): δ** 168.01 (−**C=N**), 159.23, 153.34, 143.97, 134.56, 132.21, 129.21, 128.92, 128.79, 128.42, 126.12,

123.40, 122.46, 120.18, 119.59, 119.20, 118.70, 112.64, 110.89, 101.57, 54.82 (−OCH$_3$), 54.20 (**benzyl-C**), 11.75 (−**CH$_3$**). **Elemental analysis for C$_{22}$H$_{20}$N$_2$O$_2$S:** C, 70.19; H, 5.35; N, 7.44; found C, 70.25; H, 5.42; N, 7.56.

1-[(5-Methyl-thiazol-2-ylamino)-p-tolyl-methyl]-naphthalen-2-ol (IVh). mp 156°C yield = 92.88% color = buff. **IR (v$_{max}$, cm$^{−1}$):** 3442 (−OH), 3350 (−NH), 3060 (Ar−H), 1581 (C=N). **^{1}H NMR (300 MHz, DMSO):** δ 10.29 (s, 1H, −**OH**), 7.88 (d, *J* = 14.6 Hz, 2H, **Ar−H**), 7.70 (dd, *J* = 18.1, 8.4 Hz, 2H, **Ar−H**), 7.41−7.02 (m, 7H, **Ar−H**), 6.84 (s, 1H, −**NH**), 6.65 (s, 1H, −**CH**), 2.26 (s, 3H, −**CH$_3$**), 2.22 (s, 3H, **CH$_3$**). **^{13}C NMR (75 MHz, DMSO):** δ 168.15 (**C=N**), 153.38, 139.06, 135.51, 132.22, 129.16, 128.86, 128.59, 128.44, 126.19, 126.10, 125.48, 122.47, 120.19, 119.73, 119.34, 54.41 (**benzyl-C**), 20.77 (−**CH$_3$**), 11.78 (−**CH$_3$**). **Elemental analysis for C$_{22}$H$_{20}$N$_2$OS:** C, 73.30; H, 5.59; N, 7.77; found C, 73.38; H, 5.72; N, 7.83.

1-(((4-Methylthiazol-2-yl)amino)(thiophen-2-yl)-methyl)naphthalen-2-ol (IVi). mp 166°C yield = 88.64% color = brown. **IR (v$_{max}$, cm$^{−1}$):** 3435 (−OH), 3355 (−NH), 3068 (Ar−H), 1598 (C=N). **^{1}H NMR (300 MHz, DMSO):** δ 10.45 (s, 1H, −**OH**), 8.00 (d, *J* = 8.5 Hz, 1H, **Ar−H**), 7.81 (s, 1H), 7.72 (dd, *J* = 17.0, 8.4 Hz, 2H, **Ar−H**), 7.39 (t, *J* = 7.5 Hz, 1H, **Ar−H**), 7.31−7.19 (m, 2H, **Ar−H**), 7.15 (d, *J* = 4.9 Hz, 1H, **Ar−H**), 7.03 (s, 1H, **Ar−H**), 6.87−6.82 (m, 1H), 6.79 (s, 1H, −**NH**), 6.67 (s, 1H, −**CH**), 2.22 (s, 3H, −**CH$_3$**). **^{13}C NMR (75 MHz, DMSO):** δ 172.51 (−**C=N**), 158.31, 151.65, 139.60, 137.01, 134.52, 133.63, 133.44, 131.40, 131.32, 129.10, 128.96, 127.76, 127.58, 125.74, 124.14, 123.87, 56.97 (**benzyl-C**), 16.72 (−**CH$_3$**). **Elemental analysis for C$_{19}$H$_{16}$N$_2$OS$_2$:** C, 64.74; H, 4.58; N, 7.95; found C, 64.79; H, 4.65; N, 7.92.

1-(Benzo[D] [1, 3]dioxol-5-yl((4-methylthiazol-2-yl)amino)methyl)naphthalen-2-ol (IVj). mp 174°C yield = 84.45.19% color = brown. **IR (v$_{max}$, cm$^{−1}$):** 3422 (−OH), 3349 (−NH), 3063 (Ar−H), 1576 (C=N). **^{1}H NMR (300 MHz, DMSO):** δ 10.33 (s, 1H, −**OH**), 7.90 (d, *J* = 8.6 Hz, 1H, **Ar−H**), 7.78−7.65 (m, 3H, **Ar−H**), 7.41−7.33 (m, 1H, **Ar−H**), 7.24 (dd, *J* = 18.3, 8.1 Hz, 2H, **Ar−H**), 6.81 (d, *J* = 5.0 Hz, 2H, **Ar−H**), 6.68 (s, 1H, −**NH**), 6.67 (s, 1H, −**CH**), 2.23 (s, 3H, −**CH$_3$**). **Elemental analysis for C$_{22}$H$_{18}$N$_2$O$_3$S:** C, 67.67; H, 4.65; N, 7.17; found C, 67.78; H, 4.60; N, 7.25.

Biological Evaluation

Antibacterial activity. Antimicrobial activity of the synthesized derivatives was determined using disk diffusion methods on four nonpathogenic organisms *S. aureus*, *E. coli*, *P. aeruginosa*, and *B. substilus*. The selected bacterial suspension was inoculated on agar plates, and the plates were then allowed to dry for 5 minutes. The sterile filter paper disks (Whatman no. 1, diameter = 6 mm) were soaked in each sample solution. Ciprofloxacin disk was used as a positive control. The Petri plates were incubated for 18 h at 35±2°C. After incubation, the MIC of compounds was determined [15].
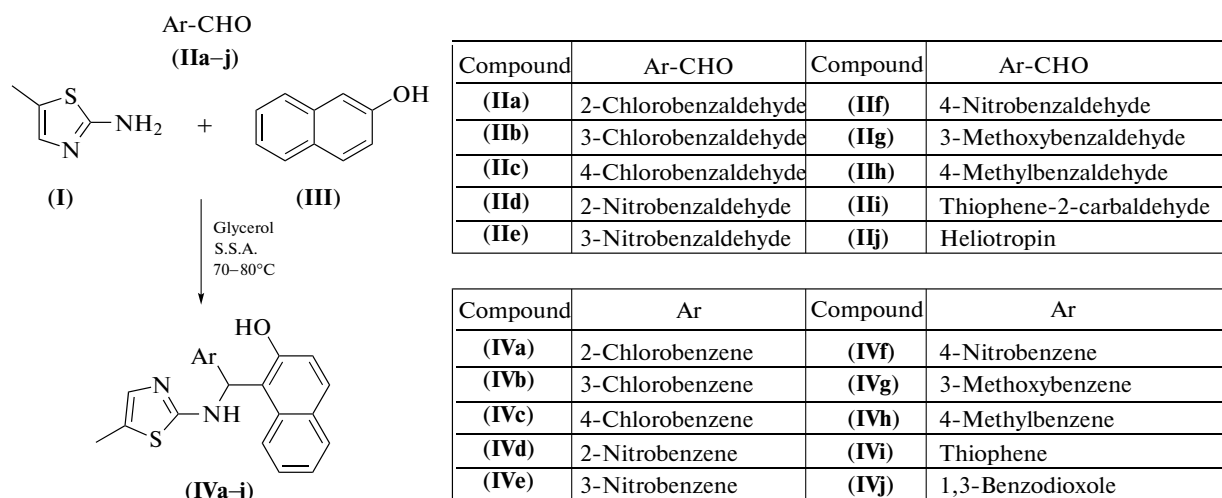
Molecular docking. Molecular docking was carried out using the structure of the *S. aureus* DNA gyrase (PDB ID 6QX1) which was downloaded from the free protein-free protein database (http://www.rcsb.org). Biopredicta module of Vlife MDS v. 4.6 was utilized for the docking analysis [16, 17].

RESULTS AND DISCUSSIONS

Chemist ry

Synthesis of aminobenzylnaphthol (Betti base) was carried out using a general pathway outlined in Scheme 1. The one-pot reaction was incorporated for the synthesis of Betti bases using silica sulfuric acid (SSA) as a catalyst. 2-Amino-5-methylthiazole, 2-naphthol, and substituted aldehydes were initially dissolved in glycerol. To this small portion of SSA was added and the mixture was allowed to heat at 70−80°C. The products obtained were characterized using IR, ^{1}HNMR, ^{13}C NMR, and elemental analysis. The characterization data of synthesized novel compounds are presented in the experimental section.

IR data for Betti bases reveals a characteristic absorption band in the range of 3420−3430 cm$^{−1}$ for phenolic −OH stretching while a band at 3350−3360 cm$^{−1}$ was observed for −NH stretching. ^{1}H NMR spectra depict the presence of singlet for phenolic proton, −NH and chiral −CH at δ ~10.20 ppm, δ ~7.00 ppm, and δ ~6.60 ppm respectively. A singlet that corresponds to three protons of methyl in thiazole moiety was observed at δ ~2.20 ppm. In ^{13}C NMR spectra, a peak around δ ~167 ppm indicates the presence of the C=N group of thiazole. The two characteristic peaks for chiral benzyl carbon and methyl carbon were evidenced at δ ~53 ppm and δ ~11.7 ppm respectively [11]. As further, elemental analysis of C, N, and H was obtained for synthesized compounds and the experimental composition was in good agreement with the theoretical values.

Compound	Ar-CHO	Compound	Ar-CHO
(IIa)	2-Chlorobenzaldehyde	**(IIf)**	4-Nitrobenzaldehyde
(IIb)	3-Chlorobenzaldehyde	**(IIg)**	3-Methoxybenzaldehyde
(IIc)	4-Chlorobenzaldehyde	**(IIh)**	4-Methylbenzaldehyde
(IId)	2-Nitrobenzaldehyde	**(IIi)**	Thiophene-2-carbaldehyde
(IIe)	3-Nitrobenzaldehyde	**(IIj)**	Heliotropin

Compound	Ar	Compound	Ar
(IVa)	2-Chlorobenzene	**(IVf)**	4-Nitrobenzene
(IVb)	3-Chlorobenzene	**(IVg)**	3-Methoxybenzene
(IVc)	4-Chlorobenzene	**(IVh)**	4-Methylbenzene
(IVd)	2-Nitrobenzene	**(IVi)**	Thiophene
(IVe)	3-Nitrobenzene	**(IVj)**	1,3-Benzodioxole

Scheme 1. Schematic representation for the route of synthesis of Schiff's base.

Antibacterial Activity

Antibacterial activity of the synthesized derivatives was performed via the disc diffusion method on four different organisms *S. aureus*, *B. substilus*, *E. coli*, and *P. aeruginosa*, using ciprofloxacin as a standard. Table 1 shows the minimum inhibitory concentration (MIC) in μg/mL for all the compounds and standards. The result reveals that the bacterial activity depends not only on nature but also on the position of the substit-

uents on the benzene ring of Betti bases. Although the results were not so great, among all the synthesized compounds **(IVa–f)** has depicted satisfactory results against all microbial cultures which emphasize the importance of the electron-withdrawing group. It was also noted that the withdrawing group at the ortho position raises the bacterial activity as compared to the meta and para position. This is due to the meta and para substitutions gives conformation restriction to fit

Table 1. Evaluation of the antibacterial activity of synthesized compounds **(IVa–j)**

Compound	Minimum inhibitory concentration (MIC, μg/mL)			
	[a](G+) bacteria		[b](G−) bacteria	
	S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*
(IVa)	500	250	250	500
(IVb)	500	500	500	500
(IVc)	250	1000	500	250
(IVd)	500	500	500	250
(IVe)	500	750	750	500
(IVf)	750	500	500	500
(IVg)	1000	1000	1000	750
(IVh)	1000	1000	1000	750
(IVi)	250	1000	1000	750
(IVj)	750	750	500	500
Ciprofloxacin	**2.2**	**1**	**1.7**	**0.5**

[a](G+) Gram-positive bacteria, [b](G−) gram-negative bacteria.
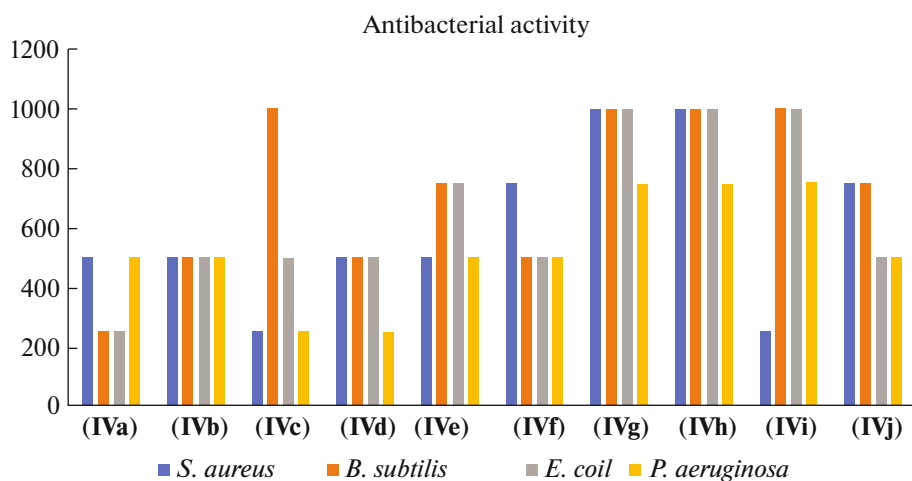
Antibacterial activity

Fig. 1. Bar graph of comparative antibacterial activity of synthesized derivatives **(IVa–j)**.
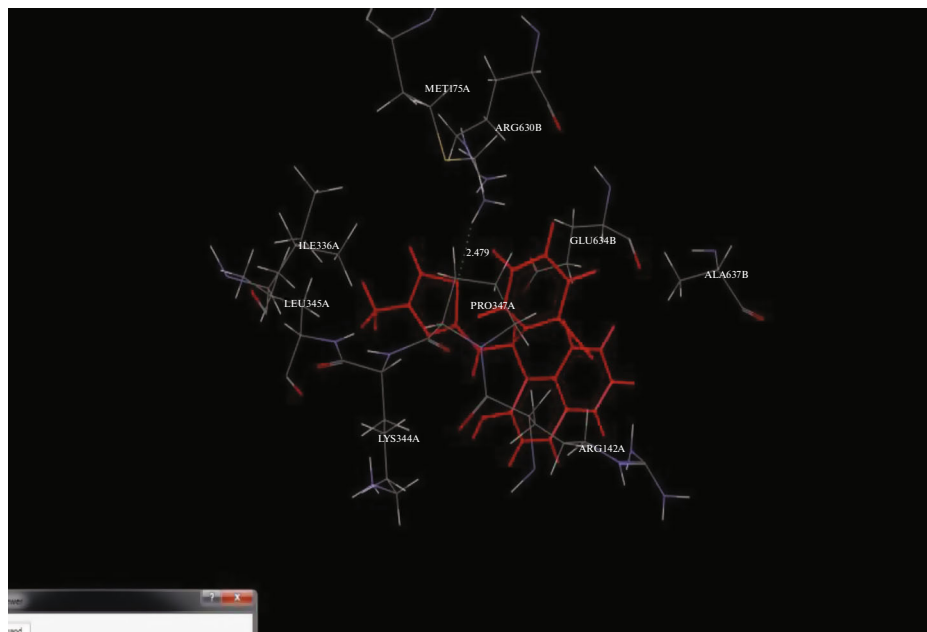

Fig. 2. Docking interaction of **(IVa)**.

in the receptor pocket. On the other hand, compounds **(IVg)** and **(IVh)** have exhibited less activity against all microbial cultures as they have electron-donating substituents on benzene i.e. methoxy and methyl respectively. The comparative bar graph of the antibacterial study is shown in Fig. 1.

Antimicrobial Docking

Docking analysis was performed to ascertain the mechanism of action of the synthesized derivatives. The crystal structure of DNA gyrase was utilized for the docking simulations. All the molecules were found

to have a good binding affinity towards the DNA gyrase. Interactions of all synthesized derivatives are shown in Table S1 (Supplementary Information). Some of the most promising derivatives **(IVa, IVc, and IVd)** and their interactions with protein are elaborated below.

A molecule **(IVa)** shows hydrogen bond interaction with ARG630 and hydrophobic interactions with GLU634, ILE336, ARG342, LYS344, LEU345 (Fig. 2).

A molecule **(IVc)** shows hydrogen bond interaction with PRO343 and hydrophobic interactions with GLU634, ASP635, ALA637, VAL638, ARG342 (Fig. 3).
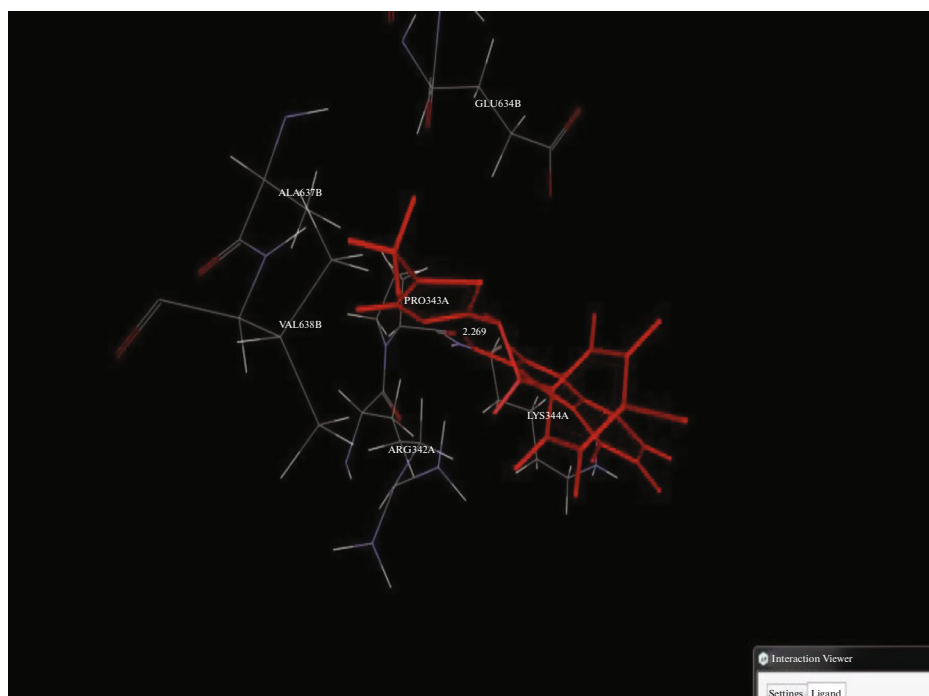
Fig. 3. Docking interaction of (**IVc**).

A molecule (**IVd**) shows hydrogen bond interaction with ARG630 hydrophobic interaction with ILE633, GLU634, ALA637, ILE30, MET179 (Fig. 4).

Insilico ADMET Prediction

All the synthesized derivatives were scrutinized for in silico ADMET prediction using admetSAR server (http://lmmd.ecust.edu.cn/admetsar2/about/) and the results are listed in Table 2. All the derivatives were marked under category III (500 mg kg^{-1} < LD$_{50}$ ≤ 5000 mg kg^{-1}) for acute oral toxicity which indicates that these derivatives are nontoxic [12]. The nitro, methoxy, and methyl substituted derivatives (**IVd–h**) were indicated for possible carcinogenicity (trinary).

Table 2. In silico ADME prediction

| Compounds	Alog$P$	Water solubility	Acute oral toxicity, kg/mol	Carcinogenicity (binary)	Carcinogenicity (trinary)
(**IVa**)	6.17	−4.79	2.429	0.8857	0.3982
(**IVb**)	6.17	−4.79	2.814	0.8857	0.3982
(**IVc**)	6.17	−4.79	2.755	0.8857	0.3982
(**IVd**)	5.42	−3.442	2.393	0.9286	0.3807
(**IVe**)	5.42	−3.569	2.502	0.9286	0.3807
(**IVf**)	5.42	−3.569	2.496	0.9286	0.3807
(**IVg**)	5.52	−4.459	2.587	0.9429	0.3776
(**IVh**)	5.82	−4.294	2.459	0.9143	0.3586
(**IVi**)	5.57	−4.142	2.726	0.9143	0.3742
(**IVj**)	5.24	−3.948	2.422	0.9429	0.4479
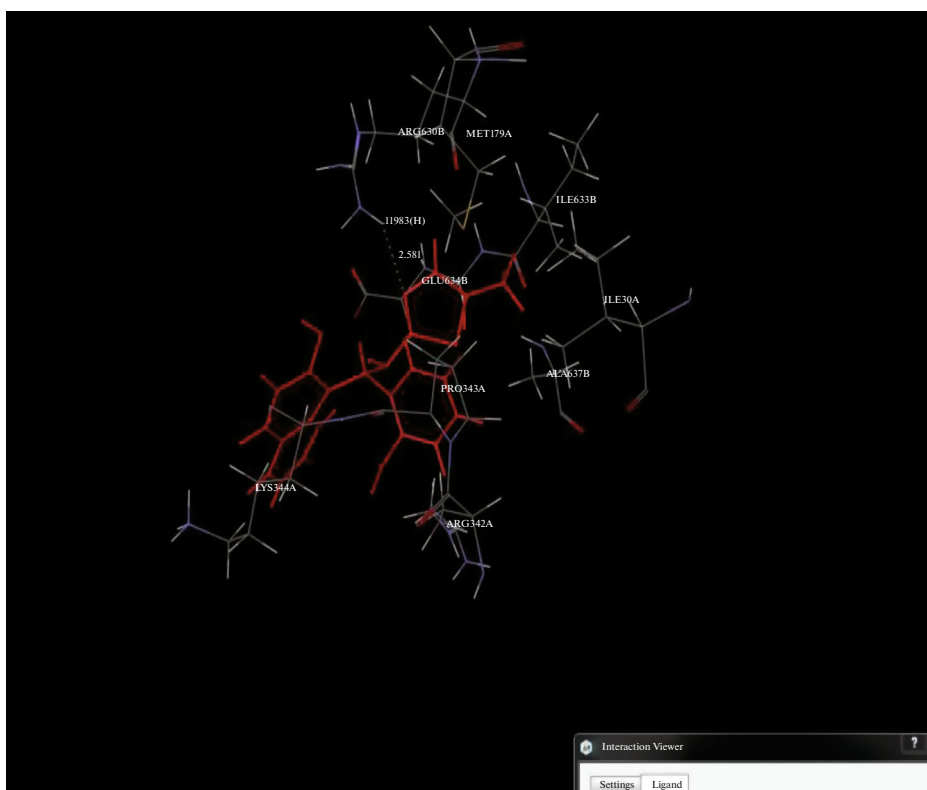
Fig. 4. Docking interaction of **(IVd)**.

No Lipinski rule violation was observed for any molecule, thus making it suitable for oral consumption [13, 14].

CONCLUSION

In conclusion, the novel derivatives of Betti bases **(IVa–j)** were synthesized using SSA as an acid catalyst and characterized using FTIR, NMR, and Elemental analysis. These aminobenzylnaphthol derivatives i.e. Betti bases were screened for in vitro antibacterial activity which affirms that the electron-withdrawing groups are more potent than electron-donating groups as well as a substitution at ortho position shows most effectual activity than others. Molecular docking simulations were performed to ascertain the mechanism of action of these derivatives. The docking analysis brings to light that, these molecules are exhibiting action via inhibition of DNA gyrase for antibacterial potential. In silico ADMET prediction reveals that no violation of the Lipinski rule was observed as well the acute oral toxicity was marked under category III for all molecules.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interests. The authors declare that they have no conflicts of interest.

Statement on the welfare of humans or animals. This article does not contain any studies involving animals performed by any of the authors.

SUPPLEMENTARY INFORMATION

The online version contains supplementary material available at https://doi.org/10.1134/S1068162021040075.

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