Scientific paper

Green Synthesis of Bromo Organic Molecules and Investigations on Their Antibacterial Properties: An Experimental and Computational Approach

Naruti Longkumer,[1] Kikoleho Richa,[1] Rituparna Karmaker,[1] Visekhonuo Kuotsu,[2] Aola Supong,[1] Latonglila Jamir,[2] Pranjal Bharali[2] and Upasana Bora Sinha[1,*]

[1] *Department of Chemistry, Nagaland University, Lumami-798627, Nagaland, India*

[2] *Department of Environmental Science, Nagaland University, Lumami-798627, Nagaland, India*

* *Corresponding author: E-mail: upasanabsinha@gmail.com;*
Tel: +91-9436006754

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Abstract

A simple, environmentally benign methodology has been developed to synthesize some bromoorganic compounds which have potential as antimicrobial agents. The required compounds were obtained through microwave (MW) irradiation, on-water reactions and using cetyltrimethylammonium tribromide (CTMATB) as the bromine source. The high yield of the product could be achieved within short reaction times, thus representing the main attribute of the present synthetic approach. The compounds were evaluated for *in vitro* antibacterial activity against *Escherichia coli, Klebsiella pneumoniae*, *Staphylococcus aureus* and *Bacillus subtilis*. Further, *in silico* studies were carried out to elucidate the interactions of the compounds with the bacterial proteins.

Keywords: Bromo compounds; aqueous conditions; green chemistry; antibacterial activity, *in vitro* studies; molecular docking.

1. Introduction

Bromo derivatives, both naturally occurring as well as synthesised compounds, have been reported to have biological activities, such as feeding deterrent, antimicrobial, anti-diabetic, antioxidant, anti-inflammatory and enzyme inhibition.[1–7] Considering the importance of bromo organic compounds, new methods of their synthesis are always sought and literature enumerates a few reports of the use of quaternary ammonium tribromides (QATBs) under MW irradiation for their synthesis.[8,9] Among the tribromides reported so far, the efficacy and versatility of cetyltrimethylammonium tribromide (CTMATB) has been reported in many important organic transformations.[10–17] Its proven mildness as a brominating reagent and versatility towards various organic substrates added to its compatibility with the aqueous media is what prompted us to choose this reagent for the present study.

In recent years there has been an increasing emphasis on avoiding the use of solvents in organic reactions. It often happens that while many reaction strategies are efficient as well as benign, use of organic solvents in these reactions prevents them from being considered as perfectly green.[18] There is an extensive current debate over the relative "greenness" of the use of various solvent media, but water can undeniably be considered the cleanest solvent available, and the use and release of clean water clearly will have the least impact on the environment. Numerous publications report the combination of water as an environmentally benign solvent for chemical transformations with the use of MW irradiation as an efficient heating method.[19,20] In fact, MW heating has become a broadly accepted non-conventional energy source for performing organic synthesis[21–29] as well as in various aspects of inorganic chemistry and polymer chemistry.[30,31] Microwave heating is preferred in the context of environmentally benign synthesis because it is a more homogenous method and accelerates reaction processes as compared to the traditional heating methods (*e.g.* in an oil bath, heating mantle or hot air oven),[9,25,28,32] hence our choice of MW irradiation and use of water as the solvent medium.

While the presently synthesized compounds are examples of small molecules which are very common, small molecules have found significance as new-age pharmaceutical compounds due to their less challenging manufacturing procedure as compared to larger biologicals. Further, even though bromoorganic compounds have been commonly used as antimicrobial agents,[3–7] there seems to be no reports on the anti-microbial essay of the presently synthesized compounds in the literature. This led us to consider the prospects of such an investigation through experimental and computational approaches.

To explain the promising activity of these compounds, this work includes the molecular docking study of the synthesised compounds within the binding pockets of DNA gyrase subunit B (PDB ID: 1KZN) and dihydrofolate reductase (PDB ID: 3SRW). DNA gyrase is a bacterial protein of the topoisomerase family involved in DNA replication and transcription by catalysing the negative supercoiling of the closed-circular DNA. As this function is essential for DNA replication and transcription, gyrase is really a suitable target for antibacterial agents.[33] Dihydrofolate reductase (DHFR) is an important target in a number of therapeutic areas, including cancer and search for antiinfective compounds where it is used to generate antibacterial, antifungal and antiparasitic agents.[34]

2. Experimental

2. 1. General Chemistry

All the solvents and substrates were purchased from Merck, Spectrochem, Sigma-Aldrich, and S. D. Fine Chem. Hexane and ethyl acetate were distilled before the use in column chromatography, while the substrates were used without further purification. All reactions were monitored by TLC on silica gel HF_{254}. The microwave reactions were carried out in a scientific microwave system CATA 2R (single mode reactor) from Catalyst System (Pune, India). Melting points were determined by digital melting point apparatus. IR spectra were recorded with KBr pellets on a Perkin–Elmer FT-IR (spectrum two). ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL ECS-400 using $CDCl_3$ as the solvent and TMS as the internal standard.

2. 1. 1. Procedure for Synthesis of CTMATB

CTMATB was synthesised using a modified version of our method reported earlier.[17] In this procedure, a mixture of 4.89 g (41.07 mmol) of potassium bromide (KBr) and 5.00 g (13.74 mmol) of cetyltrimethylammonium bromide (CTMAB), and 0.057 g (0.53 mmol) of sodium carbonate (Na_2CO_3) were taken in a mortar and 10 mL (88.24 mmol) of 50% H_2O_2 added to the whole. The resultant mixture was grinded thoroughly and then was dissolved in 50 mL of water taken in a 100 mL beaker. The reaction solution was stirred at room temperature for 5 minutes and then 30 mL of 1 M H_2SO_4 was added drop-wise. An exothermic reaction followed and the CTMATB precipitated out. CTMATB formed was filtered using suction pump, washed with water many times till the filtrate contained no trace of acid (tested using litmus paper), and then initially air-dried and finally dried in a vacuum dessiccator.

$$\mathrm{CTMAB} \xrightarrow[\overset{+}{H}/\ KBr]{Na_2CO_3\ /\ H_2O_2} \mathrm{CTMATB} \qquad (1)$$

The compound was then dried in a vacuum desiccator using anhydrous calcium chloride ($CaCl_2$) as desiccant. The product was obtained as bright yellow micro-crystals which was further recrystallized from methanol. Yield of the product was 5.52 g (96%), m.p. 87–88 °C, m.p. (lit.) 87 or 88 °C.[35]

2. 1. 2. General Procedure for the Synthesis of Compounds 1a–9a.

A homogenous mixture of the reagent CTMATB (2 mmol) and substrate **1**–**9** (2 mmol) were taken in 1:1 ratio in a 50 mL round bottomed flask equipped with reflux condenser in the microwave reactor. 10 mL H_2O was added to the mixture and stirred thoroughly. The reaction mixture was placed inside the microwave reactor. The reactor was switched on and kept at a controlled power of P-7 which corresponds to 595 W. Reaction temperature was recorded using the flexible temperature probe attached to the microwave reactor, immediately after the completion of the reaction, and was found to be 90 °C. The progress of the reaction was monitored by TLC on silica gel HF_{254} using ethyl acetate–hexane solvent system (volume ratio varied for different substrates). After completion of the reaction, the product was extracted with 10 mL (2×) ethyl acetate and washed with 5 mL (2×) sodium bicarbonate solution. The crude product thus obtained was subjected to column chromatography over a pad of silica gel using ethyl acetate–hexane solvent system (volume ratio varied for different substrates) to obtain the desired products **1a**–**9a**.

2. 2. Antibacterial Studies

All the synthesized compounds were evaluated for their *in vitro* antibacterial activities against *Escherichia coli* and *Klebsiella pneumonia* as Gram negative bacteria, as well as *Staphylococcus aureus* and *Bacillus subtilis* as Gram positive bacteria. The antimicrobial properties of the synthesised compounds were evaluated by the determination of the zone of inhibition, using agar well diffusion method.[36] Subsequently minimum inhibitory concentrations (MIC) of the compounds were determined by the twofold broth dilution method in nutrient broth. DMSO was used as the control and the tests were performed at 10 mg/mL concentration using DMSO as the solvent. Streptomycin was used as the standard reagent. Each experiment was performed in triplicate and the average reading was taken.

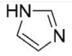
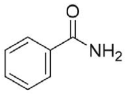
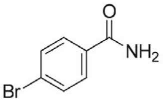
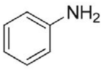
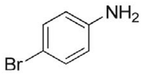
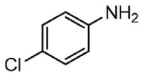
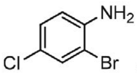
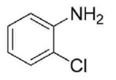
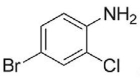
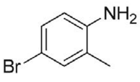
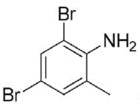
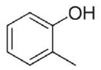
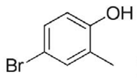
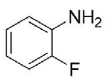
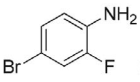
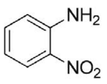
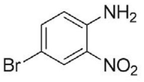
2. 3. Docking Studies

Molecular docking studies were conducted so as to validate the obtained data and to provide comprehensible evidence for the observed antibacterial activity of all synthesized compounds. In this study, molecular docking simulations were performed using Molegro Virtual Docker (MVD). The pdb file format of enzymes DNA Gyrase B (Pdb id: 1KZN) and dihydrofolate reductase (Pdb id: 3SRW) as receptors were obtained from the RCSB Protein Data Bank and were prepared for molecular docking. All the 3D structure of the ligands was drawn using ChemBioDraw as mol2 file. For molecular docking simulation, water molecules were removed and charges were assigned. By using MVD cavities were predicted and the ligands were docked against the target proteins and 30 independent runs were performed for each ligand.[37–40]

3. Results and Discussion

Cetyltrimethylammonium tribromide (CTMATB), having the molecular formula $C_{19}H_{42}NBr_3$ is a bright orange crystalline solid with sharp melting point at 87–88 °C. However, from thermogravimetric (TG) analysis it was revealed that the compound is stable even up to *ca.* 200 °C. One of the major implications of this property is that the tribromide may be very useful for the appropriate organic transformations at relatively high temperatures as well. It is an obvious fear that tribromides, upon heating, release bromine, which is an environmentally hazardous chemical. However, while investigating their thermal stability by

Table 1. Aqueous microwave bromination of organic substrates with CTMATB[a]

Substrate	Product[b]	Reaction time	Yield[c]
 **1**	 **1a**	4 min	70%
 **2**	 **2a**	5 min	75%
 **3**	 **3a**	4 min	80%
 **4**	 **4a**	4 min	80%
 **5**	 **5a**	5 min	62%
 **6**	 **6a**	2 min	69%
 **7**	 **7a**	3 min	60%
 **8**	 **8a**	5 min	69%
 **9**	 **9a**	4 min	86%

[a] Reactions maintained at 90 °C using controlled power P-7 of the MW reactor; all reactions were monitored by TLC; [b] Confirmed by IR, ^{1}H NMR and ^{13}CNMR; [c] Isolated yields.

TG experiments, it was observed that CTMATB loses Br_2 as the tail fragment at the temperature of 265–267 °C, which is much higher than the temperature at which brominations take place.[17]

In order to determine the efficiency of CTMATB in aqueous condition, different types of organic compounds were used and the reactions were performed under microwave conditions. These reactions, when performed in an oil bath under the same conditions, took longer time. As an example, **3a** took 8 minutes for its formation, while it took 4 minutes using MW reactor, thereby justifying our choice of MW irradiation. The results of the bromination reactions under microwave conditions are presented in Table 1. The products were identified by comparing their melting points and IR absorption spectra with that of authentic samples.[8,9,17,18,41]

The antibacterial activity of the synthesised compounds was tested against *Escherichia coli* and *Klebsiella*

Table 2. Zone of inhibition values (mm) of the synthesised compounds

Compounds	**Zone of inhibition (mm)**			
(10 mg/mL)	***E. coli***	***K. pneumoniae***	***S. aureus***	***B. subtilis***
1a	19	12	18	14
2a	24	15	21	18
3a	18	17	19	16
4a	12	10	15	>10
5a	10	>10	12	10
6a	19	15	16	12
7a	12	17	>10	14
8a	16	18	16	>10
9a	19	12	17	14
Streptomycin	32	30	34	30

Table 3. MIC (minimum inhibitory concentration in mg/mL) of the synthesised compounds

Compounds	**MIC (mg/ml)**			
(10 mg/mL)	***E. coli***	***K. pneumoniae***	***S. aureus***	***B. subtilis***
1a	0.117	0.468	0.117	0.234
2a	0.058	0.144	0.234	0.117
3a	0.117	0.144	0.117	0.144
4a	0.937	0.937	0.144	0.937
5a	0.937	0.937	0.468	0.937
6a	0.117	0.144	0.144	0.468
7a	0.468	0.117	0.937	0.234
8a	0.144	0.937	0.144	0.937
9a	0.117	0.937	0.144	0.234

Table 4. Docking score of the compounds with 1KZN

Ligand	**Moldock score**	**Rerank score**[a]	**Interaction**[b]	**Internal**[c]	**HBond**[d]	**LE1**[e]	**LE3**[f]
1a	−64.19	−49.54	−61.17	−3.01	−2.50	−8.02	−6.19
2a	−66.34	−57.59	−76.74	10.40	−2.29	−6.63	−5.76
3a	−56.97	−48.30	−66.03	9.06	−2.58	−7.12	−6.04
4a	−63.30	−52.11	−72.49	9.19	−2.02	−7.03	−5.79
5a	−62.87	−52.41	−72.86	9.99	−1.94	−6.99	−5.82
6a	−62.12	−52.74	−72.86	11.71	−2.08	−6.90	−5.86
7a	−62.72	−55.09	−75.60	12.87	0.00	−5.70	−5.01
8a	−62.50	−50.56	−73.12	10.61	−2.12	−6.25	−5.06
9a	−63.07	−54.09	−72.88	9.81	−3.31	−7.01	−6.01
Streptomycin	−101.15	−29.04	−150.03	48.87	−8.81	−2.53	−0.73

[a] The rerank score is a linear combination of E-inter (steric, Van der Waals, hydrogen bonding, electrostatic) between the ligand and the protein, and E-intra. (torsion, sp2-sp2, hydrogen bonding, Van der Waals, electrostatic) of the ligand weighted by pre-defined coefficients. [b] The total interaction energy between the pose and the protein (kJ/mol). [c] The internal energy of the pose. [d] Hydrogen bonding energy (kJ/mol). [e] Ligand efficiency 1: MolDock score divided by heavy atoms count. [f] Ligand efficiency 3: Rerank score divided by heavy atoms count.

Table 5. Docking score of the compounds with 3SRW

Ligand	Moldock score	Rerank score[a]	Interaction[b]	Internal[c]	HBond[d]	LE1[e]	LE3[f]
1a	−64.94	−49.76	−61.92	−3.02	−4.18	−8.12	−6.22
2a	−62.98	−54.19	−73.36	10.38	−3.19	−6.30	−5.42
3a	−50.44	−41.89	−59.50	9.06	−1.49	−6.30	−5.24
4a	−55.92	−46.30	−65.12	9.19	−1.43	−6.21	−5.14
5a	−55.86	−46.43	−65.85	9.99	−1.78	−6.21	−5.16
6a	−54.38	−46.44	−66.10	11.71	−1.91	−6.04	−5.16
7a	−64.85	−56.88	−78.04	13.19	−8.59	−5.90	−5.17
8a	−61.56	−51.24	−72.18	10.62	−2.38	−6.16	−5.12
9a	−60.34	−49.08	−70.15	9.81	−4.37	−6.70	−5.45
Streptomycin	−134.60	−39.20	−178.12	43.52	−9.39	−3.36	−0.98

[a] The rerank score is a linear combination of E-inter (steric, Van der Waals, hydrogen bonding, electrostatic) between the ligand and the protein, and E-intra. (torsion, sp2-sp2, hydrogen bonding, Van der Waals, electrostatic) of the ligand weighted by pre-defined coefficients. [b] The total interaction energy between the pose and the protein (kJ/mol). [c] The internal energy of the pose. [d] Hydrogen bonding energy (kJ/mol). [e] Ligand efficiency 1: MolDock score divided by heavy atoms count. [f] Ligand efficiency 3: Rerank score divided by heavy atoms count.

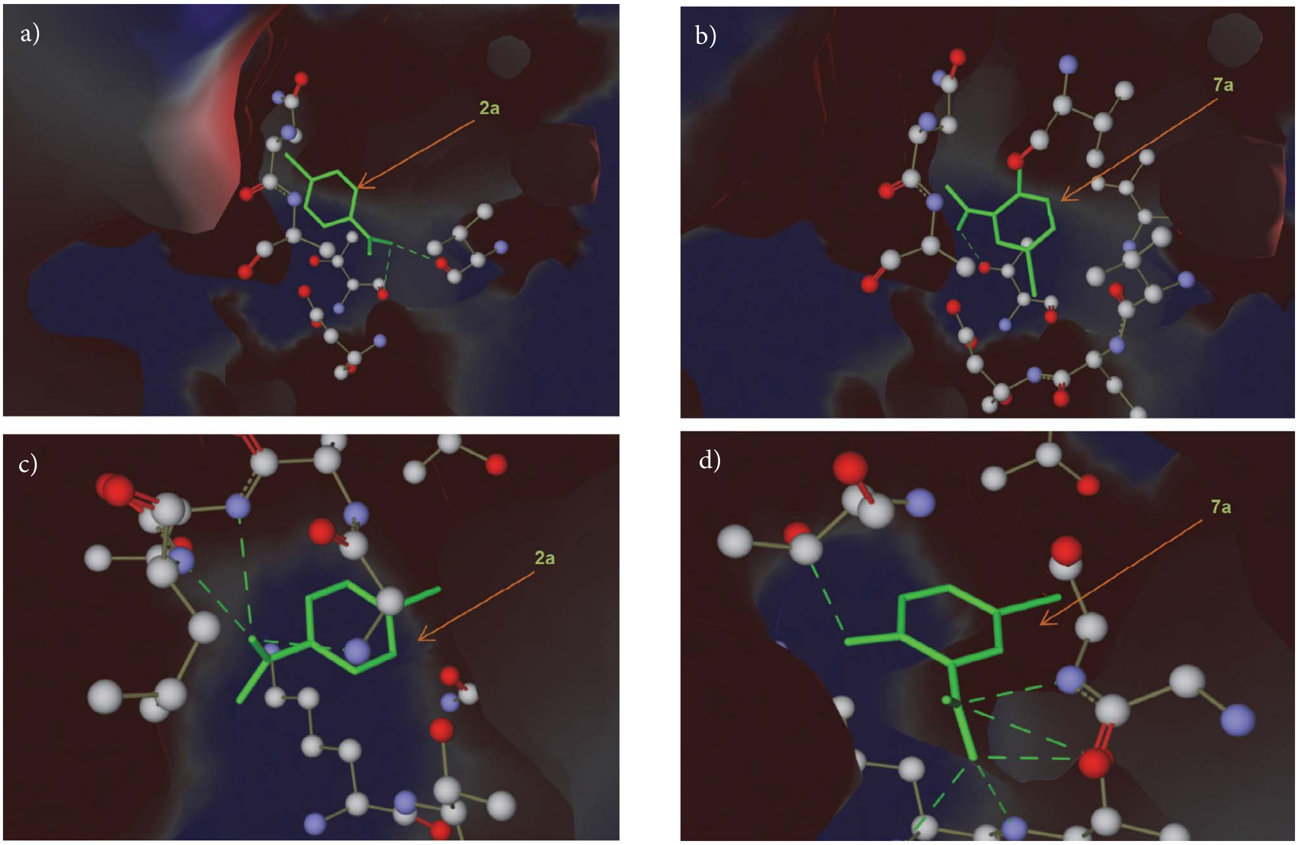


Figure 1. Molecular interaction of the compounds **2a** and **7a** at the active pockets of the protein 1KZN (a and b) and 3SRW(c and d) (green dotted lines indicate the mode of interaction with the protein).

pneumonia as Gram negative bacteria, as well as *Staphylococcus aureus* and *Bacillus subtilis* as Gram positive bacteria. The results of the primary screening are shown in Table 2. The investigation of the screening revealed that the compounds tested showed varying degree of activity against all the investigated microorganisms. Almost all the compounds showed moderate to potent activity against the strains. Subsequently, minimum inhibitory concentrations (MIC) of the compounds were determined to quantify the antibacterial potency of the compounds. The results of the MIC values of antibacterial activity are given in Table 3. Compound **2a** showed a better activity against *E. coli* with a MIC of 0.058 mg/mL and compounds **4a** and **5a** have lesser effectiveness against the bacterial strains. In comparison, compound **2a** showed the best activity indicating its promising broad spectrum of antibacterial property.

Docking studies were performed on known target proteins to understand the antibacterial mechanisms of bromo compounds using Molegro virtual docker (MVD). The proteins used as target were DNA gyrase B (Pdb id: 1KZN) from *Escherichia coli* and dihydrofolate reductase (Pdb id: 3SRW) from *Staphylococcus aureus*. The best pose of each compound were selected for ligand–protein interaction energy analysis as shown in Tables 4 and 5. The interaction energies of **2a** and **7a** were –76.74 kJ/mol and –75.60 kJ/mol as compared to streptomycin with –150.03 kJ/mol. This indicates that **2a** and **7a** also have a favourable ligand–protein interaction energy at the binding cavity of 1KZN. Similarly, the interaction energies of **2a** and **7a** were –73.36 kJ/mol and –78.04 kJ/mol as compared to streptomycin with –178.12 kJ/mol. This indicates that **2a** and **7a** also have a favourable ligand–protein interaction energy at the binding cavity of 3SRW. The snapshots of ligand–protein interaction depicting the binding mode of the best poses are shown in Fig. 1a, b, c and d. In this study, the molecular interaction analysis as shown in Table 6 established a common molecular interaction with Val71 and Thr165. Similarly, in Table 7, a common interaction with Thr122 and Asp121 in the compounds and streptomycin was established.

Table 6. Molecular interaction analysis of the compounds with the active site of 1KZN

Compound	Interaction (Protein···Ligand)	Interaction Energy (kJ/mol)	Interaction distance (Å)	Hybridisation (Protein)	Hybridisation (Ligand)
1a	Asp73(OD1)···N(4)	–2.5	2.785	sp^3(A)	sp^2(D)
2a	Val71(O)···N(8)	–2.409	2.589	sp^2(A)	sp^2(D)
	Thr165(O)···N(8)	–2.209	2.901	sp^2(A)	sp^2(D)
3a	Thr165(O)···N(6)	–2.5	2.928	sp^2(A)	sp^3(D)
	Val71(O)···N(6)	–2.5	2.815	sp^2(A)	sp^3(D)
4a	Val71(O)···N(0)	–2.5	2.676	sp^2(A)	sp^3(D)
5a	Val71(O)···N(0)	–2.5	2.663	sp^2(A)	sp^3(D)
6a	Val71(O)···N(0)	–2.5	2.683	sp^2(A)	sp^3(D)
7a	Thr165(OG1)···O(14)	–2.423	3.115	sp^3(B)	sp^2(A)
8a	Val71(O)···N(0)	–2.5	3.020	sp^2(A)	sp^3(D)
9a	Val167(N)···O(0)	–0.922	3.217	sp^2(D)	sp^3(B)
	Val71(O)···O(0)	–2.5	2.672	sp^2(A)	sp^3(B)
Streptomycin	Asn46(ND2)···N(36)	–2.5	2.866	sp^2(D)	sp^2(A)
	Asn46(ND2)···O(11)	–1.937	2.532	sp^2(D)	sp^3(B)
	Asp49(OD1)···N(38)	–0.377	3.524	sp^3(A)	sp^2(D)
	Asp49(OD1)···N(39)	–1.968	2.880	sp^3(A)	sp^2(D)
	Asn46(O)···N(39)	–1.153	3.396	sp^2(A)	sp^2(D)
	Asn46(O)···O(20)	–2.44	3.111	sp^3(A)	sp^3(B)
	Asp73(OD1)···O(20)	–2.5	2.676	sp^3(A)	sp^3(B)
	Thr165(OG1)···O(14)	–0.464	3.507	sp^3(B)	sp^3(A)
	Thr165(O)···O(35)	–0.335	3.009	sp^2(A)	sp^3(B)
	Val71(O)···O(35)	–2.5	2.621	sp^2(A)	sp^3(B)
	Val167(N)···O(35)	–0.890	3.112	sp^2(D)	sp^3(B)

(A): Acceptor (D): Donor (B): Both donor and acceptor

4. Conclusion

To conclude, microwave assisted aqueous reactions for the bromination of organic compounds as an attractive protocol due to its eco-friendly, efficient and economic nature are presented. The use of a CTMATB in the bromination reactions which is less toxic compared to using molecular bromine makes the process more environmentally benign. The antimicrobial study of these novel bromoorganic derivatives against Gram positive and Gram negative species showed that synthetic mimics of naturally occurring bromoorganic compounds can be of promise against drug-resistant bacteria. Docking studies revealed that both streptomycin and the synthesized compounds have a common interaction at the active sites of the protein and further studies on these compounds might increase their potency thereby enhancing their anti bacterial activity. Thus, this study adopts significance in view of simple molecules that are potent and easy to synthesize. Further studies on derivatives involving synthetic mimics of naturally occurring moieties would provide a lead in the development of novel bromoorganic-based antimicrobial compounds.

5. Acknowledgement

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Table 7. Molecular interaction analysis of the compounds with the active site of 3SRW

Compound	Interaction (Protein...Ligand)	Interaction Energy (kJ/mol)	Interaction distance (Å)	Hybridisation (Protein)	Hybridistion (Ligand)
1a	Gln96(N)···N(1)	–0.042	3.480	sp^{2}(D)	sp^{2}(A)
	Thr97(N)···N(1)	–2.210	3.157	sp^{2}(D)	sp^{2}(A)
	Thr97(OG1)···N(1)	–2.225	3.148	sp^{3}(B)	sp^{2}(A)
2a	Gly95(N)···O(7)	–0.175	2.944	sp^{2}(D)	sp^{2}
	Thr95(N)···O(7)	–0.510	3.223	sp^{2}(D)	sp^{2}
	Leu98(N)···O(7)	–2.5	3.027	sp^{2}(D)	sp^{2}
3a	Thr122(OG1)···N(6)	–2.5	2.867	sp^{3}(B)	sp^{3}(D)
	Asp121(OD1)···N(6)	–2.5	3.052	sp^{3}(A)	sp^{3}(D)
4a	Thr122(OG1)···N(0)	–2.5	2.883	sp^{3}(B)	sp^{3}(D)
5a	Thr122(OG1)···N(0)	–2.5	2.971	sp^{3}(B)	sp^{3}(D)
6a	Thr122(OG1)···N(0)	–2.5	2.956	sp^{3}(B)	sp^{3}(D)
7a	Thr97(OG1)···N(0)	–1.813	2.882	sp^{3}(B)	sp^{3}(D)
	Gly95(N)···N(13)	–2.208	2.932	sp^{2}(D)	sp^{3}(A)
	Thr47(OG1)···N(13)	–0.699	3.460	sp^{3}(B)	sp^{3}(A)
	Thr47(OG1)···O(14)	–2.5	2.813	sp^{3}(B)	sp^{2}(A)
	Thr47(N)···O(14)	–2.5	2.713	sp^{2}(D)	sp^{2}(A)
	Lys46(N)···O(14)	–0.280	3.402	sp^{2}(D)	sp^{2}(A)
8a	Thr122(OG1)···N(0)	–2.5	2.815	sp^{3}(B)	sp^{3}(D)
9a	Thr97(N)···O(0)	–0.673	3.110	sp^{2}(D)	sp^{3}(B)
	Gly95(N)···O(0)	–1.197	2.639	sp^{2}(D)	sp^{3}(B)
	Leu98(N)···O(0)	–2.5	2.746	sp^{2}(D)	sp^{3}(B)
Streptomycin	Ala8(N)···O(35)	–0.660	3.225	sp^{2}(D)	sp^{3}(B)
	Ala8(O)···O(34)	–1.812	2.517	sp^{2}(A)	sp^{3}(B)
	Gln20(O)···O(10)	–0.676	2.601	sp^{2}(A)	sp^{3}(B)
	Ser50(OG)···O(12)	–2.5	2.702	sp^{3}(B)	sp^{3}(B)
	Ser50 (OG)···O(22)	–2.5	2.607	sp^{3}(B)	sp^{2}(A)
	Thr47(OG1)···N(39)	–2.5	2.775	sp^{3}(B)	sp^{2}(D)
	Thr122(OG1)···N(3)	–2.5	3.085	sp^{3}(B)	sp^{2}(A)
	Thr122(OG1)···O(11)	–2.5	2.772	sp^{3}(B)	sp^{2}(B)
	Asp121(OD1)···N(2)	–2.5	3.053	sp^{3}(A)	sp^{2}(D)
	Asp121(OD1)···N (0)	–2.5	2.817	sp^{3}(A)	sp^{2}(D)
	Asn19(OD1)···N(2)	–2.093	3.181	sp^{2}(A)	sp^{2}(D)

(A): Acceptor (D): Donor (B): Both donor and acceptor

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Povzetek

Razvili smo enostavno in okolju prijazno metodologijo za sintezo nekaterih brhttps://doi.org/10.1021/jo050059ustavljale potencialne antimikrobne učinkovine. Zaželjene spojine smo pripravili s pomočjo mikrovalovnega obsevanja v reakcijah »na vodi« ter z uporabo cetiltrimetilamonijevega tribromida (CTMATB) kot vira broma. Visoki izkoristki reakcij, ki smo jih dobili že pri kratkih reakcijskih časih, so glavni atributi predstavljenega sinteznega pristopa. Spojinam smo določil *in vitro* antibakterijsko aktivnost proti *Escherichia coli, Klebsiella pneumoniae*, *Staphylococcus aureus* in *Bacillus subtilis*. Dodatno so *in silico* študije razložile interakcije med raziskovanimi spojinami in bakterijskimi proteini.