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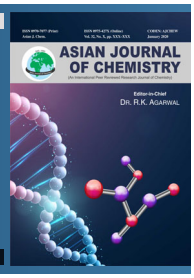

Design, Synthesis, Molecular Docking and Antimicrobial Evaluation of Some Tosyl Carbamate Derivatives

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A series of tosyl carbamates have been synthesized and screened for their antibacterial and antifungal activities. All the synthesized compounds were characterized by spectral techniques (IR, ^{1}H, ^{13}C NMR and mass) and elemental analysis. *in silico* Molecular docking method was performed to study their antimicrobial activity against the target protein 1T9U. Compound **27** showed good antibacterial activity against Gram-positive and Gram-negative bacterial strains and compound **19** showed good antifungal activity. Molecular docking results revealed that the compound **19** exhibits minimum CDOCKER energy. Tosyl carbamate derivatives having good antimicrobial activities compared to that standard and all the synthesized compounds exhibits moderate CDOCKER scores.

Keywords: Tosyl carbamates, Molecular docking, Protein 1T9U, CDOCKER energy.

INTRODUCTION

Carbamate molecules play a vital role in modern drug discovery and medicinal chemistry. Structurally, carbamate functionality is related to amide ester hybrid functions and, in standard displays good chemical and proteolytic stabilities. Organic carbamates serve a crucial characteristic as optimum protecting groups for amines and amino acids in organic synthesis and peptide chemistry [1]. Carbamates are traditionally prepared from chloroformates or isocyanates through emerging phosgene or its substitutes as starting materials [2]. The reaction of alcohols with isocyanates giving carbamates (urethanes) and its utility to polyfunctional alcohols and isocyanates is the basis of the polyurethane industry [3]. Several attempts were made to replace the classical synthesis, which involves the direct reaction of alcohols with phosgene or its derivative isocyanates with new methodologies employing less toxic and dangerous reagents [4]. Carbamates are beneficial in biologically active compounds. There are some drugs in the markets containing carbamate functional group [5]. For example, a large number of molecules with carbamate motifs had been found to possess various bioactive potentials and have been developed into marketed drugs that treat arrhythmias [6], seizures [7], asthma [8-11] and AIDS [12-15]. Organic carbamates have regularly been employed as demandable pharmaceuticals in the kinds of drugs and pro drugs. They represent an important class of compounds displaying various exciting properties [16]. The importance of the present findings, chemistry provides an efficient and practical approach to synthesize carbamates, which play very crucial and also ubiquitous roles in pharmaceutical drugs [17-22], agrochemicals [23] (pesticides, herbicides, insecticides, fungicides, *etc*.) as intermediates in organic synthesis [24] and material terrains [25]. Compounds containing sulfonyl groups were studied recognition because of their organic significance, chemical applications and a number of aryl sulfonamide derivatives are a common place substructure magnificence found in a huge number of active pharmaceutical ingredients (APIs) [26]. The sulfonyl carbamate functional group is an easily accessible carboxylic acid bioisostere and traditionally brought inside the *N*-acylation of sulfonamides with carbonic acid derivatives such as chloroformate or anhydride [27]. Sulfonyl carbamates are also used as nitrogen nucleophiles in Mitsonobu reaction [28] as shielding groups for alcohols [29] and as dehydrating agents [30]. Sulfonamide based medicines are antimicrobial agents, still widely used for the treatment of numerous bacterial, protozoal and fungal infections [31] and the first effective chemotherapeutic agents to be available in safe therapeutic dosage ranges [32]. The

applications of sulfonyl carbamate moiety has greatly extended from their primary function as potent antibacterial [33], antimicrobial [34], antitumor [35], hypoglycemic [36], antithyroid [37], anticarbonic anhydrase [38], anti-inflammatory [39], lipid regulating [40], diuretic [41], COX-inhibitors, dihydropteroate synthetase (DHPS), a key enzyme involved in folate synthesis, anti-impotence drugs [42] and also have been used as azo dyes for achieving improved light stability, water solubility, and fixation to fiber properties [43]. Recently, several reports have indicated that carbamate linkage present in between the active pharmacophores of various structurally diverse molecules increases mani-fold biological activities of semi-synthetic, natural/synthetic molecules [44].

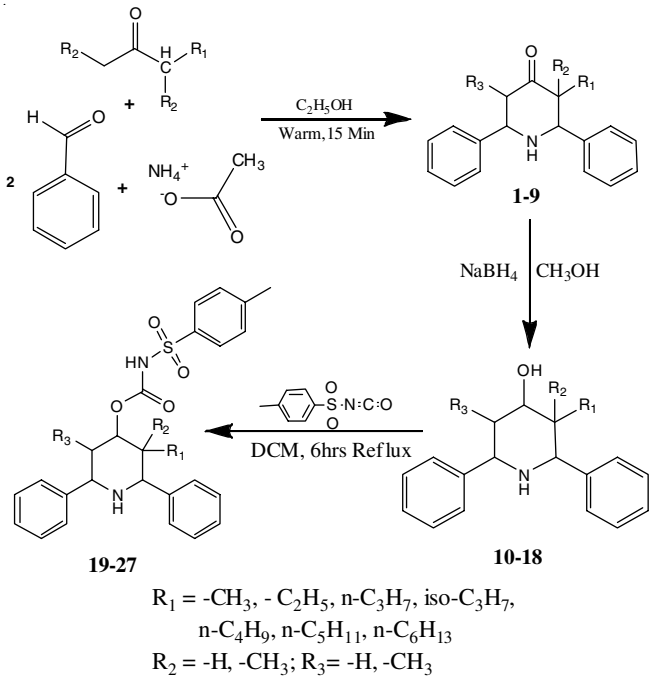
EXPERIMENTAL

All the chemicals were purchased from Avra chemicals. Melting points of synthesized compounds were determined in open capillaries and are uncorrected. IR spectra were recorded in Agilent Cary 650 IR Spectrophotometer using the ATR method. ^{1}H spectra (400 MHz) and ^{13}C spectra (100 MHz) were recorded on BRUKER AVANCE III NMR spectrometer in DMSO with tetramethylsilane the internal standard and the chemical shifts were reported in parts per million scales. Mass spectra were studied using API 3000 series mass spectrometer. The purity of the compounds was checked by TLC on silica gel and spots were developed using ultraviolet light and iodine chamber.

3,5-Dialkyl-2,6-diarylpiperidin-4-ones (**1-9**) compounds were synthesized by a condensation reaction of appropriate aldehydes, ketones and ammonium acetate in 2:1:1 ratio [45].

Synthesis of 4-hydroxy-3,5-dialkyl-2,6-diarylpiperidine (10-18): Sodium borohydride (0.1 mmol) was added slowly to a solution of appropriate 3,5-dialkyl-2,6-diarylpiperidin-4-ones (0.01mol) in methanol and the mixture was stirred at room temperature until the reaction completes. The reaction mixture was poured into crushed ice and the solid obtained was filtered and dried.

General synthesis of 3,5-dialkyl-2,6-diaryl piperidine-4-yltosyl carbamate (19-27): A stirred solution of 4-hydroxy-3,5-dialkyl-2,6-diaryl-piperidine (0.01mol), *p*-toluene sulfonyl isocyanate (0.01mol) and triethylamine in dichloromethane were refluxed for 4-6 h and the reaction was monitored by TLC. Then the mixture was extracted with chloroform and washed with water. The chloroform layer was dried over anhydrous sodium sulfate and distilled off under vacuum. Purifications with silica gel column chromatography with petroleum ether: ethyl acetate mixture yielded the product (**Scheme-I**).



Scheme-I: Synthesis of 3,5-dialkyl-2,6-diaryl piperidine-4-yl tosyl carbamate

Spectral data

3-Methyl-2,6-diphenylpiperidin-4-yltosyl carbamate (19): White solid, m.p.: 174-178 ºC. Yield: 82.90 %, m.w.: 464. FT-IR (KBr, ν_{max}, cm^{-1}): 3469 (amide-NH), 3311 (pip-NH), 3058 (Ar C-H), 2975 (aliph.ph. C-H), 1666 (C=O), 1378, 1142 (SO_2). ^{1}H NMR (400 MHz, DMSO-d_6): (δ, ppm) 7.2-7.7 (m, 14H), 4.7 (s, NH), 4.0 (d, 2H), 3.8 (d, 1H), 3.2 (d, 1H), 2.5 (s, 3H), 1.9 (s, 1H), 1.4 (m, 1H), 0.6 (d, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 170.92, 142.40, 141.79, 140.66, 129.78, 128.82, 128.57, 127.75, 126.07, 72.38, 66.1, 60.27, 59.39, 21.3, 14.47. Elemental analysis for $C_{26}H_{28}N_2O_4S$ (%): C, 67.22; H, 6.07; N, 6.03; O, 13.78; S, 6.90.

3,3-Dimethyl-2,6-diphenylpiperidine-4-yltosyl carbamate (20): White solid, m.p.: 172-174 ºC, Yield: 72.5 %, m.w.: 478. FT-IR (KBr, ν_{max}, cm^{-1}): 3488 (amide-NH), 3345 (pip-NH), 3058 (Ar C-H), 2976 (aliph. C-H), 1646 (C=O), 1351, 1144 (SO_2). ^{1}H NMR (400 MHz, DMSO-d_6): (δ, ppm) 7.1-7.7 (m, 14H), 5.03 (s, NH), 3.8 (d, 1H), 2.5 (s, 3H), 2.3 (s, 1H), 1.9 (s, 2H), 0.47 (dd, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 157.36, 142, 140, 126.08- 129.77, 65.79, 62.25, 38.39, 21.3, 14.23. Elemental analysis for $C_{27}H_{30}N_2O_4S$ (%): C, 67.76; H, 6.32; N, 5.85; O, 13.37; S, 6.70.

3,5-Dimethyl-2,6-diphenylpiperidine-4-yltosyl carbamate (21): White solid, m.p.: 172-176 ºC. Yield: 72 %, m.w.: 478. FT-IR (KBr, ν_{max}, cm^{-1}): 3491 (amide-NH), 3347 (pip-NH), 3062 (Ar C-H), 2976 (aliph. C-H), 1647 (C=O), 1351, 1142 (SO_2). ^{1}H NMR (400 MHz, DMSO-d_6): (δ, ppm) 7.3-7.6 (m, 14H), 5.01 (s, NH), 2.5 (s, 3H), 2.3 (s, 1H), 0.47 (dd, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 157, 141, 140, 126.08-129.77, 65.79, 62.25, 38.39, 21.3, 14.23. Elemental analysis for $C_{27}H_{30}N_2O_4S$ (%): C, 67.76; H, 6.32; N, 5.85; O, 13.37; S, 6.70.

3-Ethyl-2,6-diphenylpiperidin-4-yltosyl carbamate (22): White solid, m.p.: 168-170 ºC. Yield: 77.09 %, m.w.: 478. FT-IR (KBr, ν_{max}, cm^{-1}): 3567 (amide-NH), 3472 (pip-NH), 3041 (Ar C-H), 2963 (aliph. C-H), 1637 (C=O), 1354, 1146 (SO_2). ^{1}H NMR (400 MHz, DMSO-d_6): (δ, ppm) 7.5-7.2 (m, 14H), 4.8 (s, NH), 4.3 (dd, 2H), 4.2 (d,2H), 4.0 (d, 1H), 2.5 (s, 3H), 2.0 (s, NH), 1.9, 1.2, 0.8-0.9. ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 157, 126-129, 63.32, 62.35, 58.99, 56.08, 21.3, 19.5, 11. Elemental analysis for $C_{27}H_{30}N_2O_4S$ (%): C, 67.76; H, 6.32; N, 5.85; O, 13.37; S, 6.70.

2,6-Diphenyl-3-propylpiperidin-4-yltosyl carbamate (23): White solid, m.p.: 174-176 ºC. Yield: 68.3 % m.w.: 492.

FT-IR (KBr, ν_{max}, cm^{-1}): 3428 (-NH), 3036 (Ar C-H), 2956 (aliph. C-H), 1637 (C=O), 1354,1144 (SO_2). ^{1}H NMR (400 MHz, DMSO-d_6): (δ, ppm) 7.2-7.7 (m, 14H), 5.01 (NH), 4.3 (dd, 2H), 3.9 (d, 1H), 2.5 (s, 3H), 2.3 (s, H), 2.08 (s, NH), 1.97 (d, 2H), 0.5-0.8 (m, 7H). ^{13}C NMR (100 MHz, DMSO-d_6): (δ, ppm) 156.27 (CO), 142.3, 141.8, 140.3, 129.7, 128.9, 126.6, 62.44, 56.10, 46.13, 41.80, 21.3, 29.43, 14.2. Elemental analysis for $C_{28}H_{32}N_2O_4S$ (%): C, 68.27; H, 6.55; N, 5.69; O, 12.99; S, 6.51.

3-Isopropyl-2,6-diphenylpiperidin-4-yltosyl carbamate (24): White solid, m.p.: 174-178 ºC. Yield: 74.76 %, m.w.: 464. FT-IR (KBr, ν_{max}, cm^{-1}): 3421 (amide NH), 3210 (pip-NH), 2953 (aliph. C-H), 1633 (C=O), 1325, 1151 (SO_2). ^{1}H NMR (400 MHz, DMSO-d_6): (δ, ppm) 7.2-7.6 (m, 14H), 4.7 (s, 1H), 4.3 (dd, 2H), 2.5 (s, 3H), 2.3 (s, 1H), 2.1 (s, NH), 1.92 (d, 2H), 1.2 (m, 1H), 0.7 (d, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): (δ, ppm): 159.86, 141.99, 137.77, 129.78, 129.02, 128.89, 128.36, 127.23, 126.85, 126.08, 63.06, 61.10, 58.72, 56.10, 21.3, 20.9, 17.67. Elemental analysis for $C_{28}H_{32}N_2O_4S$ (%): C, 68.27; H, 6.55; N, 5.69; O, 12.99; S, 6.51.

3-Butyl-2,6-diphenylpiperidin-4-yltosyl carbamate (25): White solid, m.p.: 208-212 ºC. Yield: 76.6 %, m.w.: 506. FT-IR (KBr, ν_{max}, cm^{-1}): 3431 (-NH), 3036 (Ar C-H), 2955 (aliph. C-H), 1638 (C=O), 1353, 1144 (SO_2). ^{1}H NMR (400 MHz, DMSO-d_6): (δ, ppm) 7.2-7.5 (m, 14H), 5.0 (NH), 4.3 (dd, 2H), 3.9 (d, 1H), 2.5 (s 3H), 2.3 (1H), 2.08 (d, 2H), 2.05 (s, 1H), 1.9, 0.8-1.0 (m, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 157, 140.49, 126.72-129.09, 62.44, 56.18, 27.94, 26.72, 22.35, 21.31, 13.99. Elemental analysis for $C_{29}H_{34}N_2O_4S$ (%): C, 68.75; H, 6.76; N, 5.53; O, 12.63; S, 6.33.

3-Pentyl-2,6-diphenylpiperidin-4-yltosyl carbamate (26): White solid, m.p.: 192-196ºC. Yield: 69 %, m.w.: 520. FT-IR (KBr, ν_{max}, cm^{-1}): 3437 (-NH), 3039 (Ar C-H), 2951 (aliph. C-H), 1637 (C=O), 1352, 1143 (SO_2). ^{1}H NMR (400 MHz, DMSO-d_6): (δ, ppm) 7.2-7.5 (m, 14H), 4.7 (NH), 4.3 (d, 2H), 4.03 (d, 1H), 2.5 (s, 3H), 2.3 (1H), 2.08 (d, 2H), 2.0 (NH), 1.9 (d, 2H), 0.5-1.08 (m, 11H). ^{13}C NMR (100 MHz, DMSO-d_6): (δ, ppm): 157, 142, 141, 126.78-129.07, 62.43, 56.15, 41.79, 31.51, 27.07, 25.43, 22.1, 21.3, 14.2. Elemental analysis for $C_{30}H_{36}N_2O_4S$ (%): C, 69.20; H, 6.97; N, 5.38; O, 12.29; S, 6.16.

3-Hexyl-2,6-diphenylpiperidin-4-yltosyl carbamate (27): White solid, m.p.: 188-190ºC. Yield: 70 %, m.w.: 534. FT-IR (KBr, ν_{max}, cm^{-1}): 3464 (-NH), 3064 (Ar C-H), 2929 (aliph. C-H), 1678 (C=O), 1354, 1143 (SO_2). ^{1}H NMR (400 MHz, DMSO-d_6): (δ, ppm): 7.7-7.1 (m, 14H), 4.7 (s, NH), 3.9 (dd, 2H), 3.6 (d, 1H), 2.5 (s, 3H), 2.0 (s, NH), 1.0-1.1 (m, 13H). ^{13}C NMR (100 MHz, DMSO-d_6): (δ, ppm): 157, 142.34, 141.8, 124-129, 71.04, 64.70, 59.45, 31.4, 29.69, 27.7, 25.67, 22.43, 21.37, 14.36. Elemental analysis for $C_{31}H_{38}N_2O_4S$ (%): C, 69.63; H, 7.16; N, 5.25; O, 11.97; S, 6.00.

Molecular docking studies: A molecular docking study was performed using the Biovia discovery studio 2016 program [46]. For the present investigation, the CDOCKER (CHARMm based DOCKER) is grid-based molecular docking protocol that operates on the CDOCKER algorithm utilizing CHARMm force field and offers full flexibility to ligands including dihedral, angles and bonds [47]. Docking was performed to investigate the best binding compounds depends on a variety of scoring functions, such as CDOCKER energy and CDOCKER interaction and hydrogen bond interaction. The best binding poses are selected as the lowest binding energy and least energy difference between cdocker interaction energy and cdocker energy of interacting compounds with targeted protein.

For the present investigation, X-ray crystal structure of AcrB (PDB ID: 1T9U) were downloaded from the protein data bank (PDB) based on the good resolution of 3.5 Å. AcrB is a major multidrug exporter in *Escherichia coli* [48]. The retrieved 3D crystal structure of AcrB (1T9U) was prepared and energy minimized to stabilize the structure was followed by CHARMm force field to avoid steric overlap and to relax the conformation [49].

The compounds were drawn in Chem Draw 12.0. Three-dimensional structure of the compounds was obtained by the Chem Draw 3D Ultra 12.0 software. The designed ligands were saved as mol format and examined as to generate the best pose was determined the binding interactions. The co-factors, unwanted water molecules and chains are removed.

***in vitro* Antimicrobial activity:** The newly synthesized compounds were assayed for *in vitro* antimicrobial activities by filter paper disc diffusion method [50]. The bacterial species (Gram-positive and Gram-negative) and fungal species were incubated at 48 ºC for 24 h. The bacterial and fungal cultures were grown in nutrient agar medium and subcultured for the better growth and subcultured into the petri plates for the experiments. The cultures were diluted with sterilized saline and the compounds were diluted in DMSO for biological assays. The bacterial and fungal cultures containing discs were placed on the media and incubated at 48 ºC for 24 to 48 h for better observation. The sterile filter paper discs of 6 mm in diameter were impregnated with a variety of test compounds and the results were compared with the activity of standards ciprofloxacin and amphotericin B. The results were measured and expressed as a zone of inhibition in mm. In agar disc diffusion method, test compounds were introduced into the discs and allowed to dry at 48 ºC. The discs were positioned below the nutrient agar petri plates previously seeded with a suspension of each bacterial and fungal strain. The petri dishes were incubated for 24 h at 37 ºC and the diameter of zone of inhibition was observed and measured.

RESULTS AND DISCUSSION

The parent compound, piperidine-4-one derivative was synthesized by the Mannich reaction as shown in **Scheme-I**. Then it was reduced to hydroxyalkyl piperidine derivatives using sodium borohydride. The reduced compound was further reacted with *p*-toluene sulfonyl isocyanate. The obtained product was subjected to column chromatography using pet ether:ethyl acetate (1:3) as an eluent and good yielded. The formation of tosyl carbamates (**19-27**) was confirmed by recording their FT-IR, ^{1}H & ^{13}C NMR and mass spectrometry.

In the FT-IR spectra of the synthesized compounds, **19-27** contained absorption bands in the range of 3469-3311 cm^{-1} due to stretching vibrations of the NH group, 1666 cm^{-1} due to the presence of CO stretching and at 1378 and 1142 cm^{-1} were confirmed the presence of SO_2 asymmetric and symmetric

stretching vibrations. In ^{1}H NMR, compounds **19-27** (DMSO-d_6) revealed the following signals: a singlet equivalent to one proton in the δ 5.0 and 2.0 ppm range assigned for the amide NH and piperidone protons, a singlet equivalent to three protons at δ 2.5 ppm assigned tosyl CH_3 protons, a doublet at δ 0.45 ppm assigned of piperidone methyl protons, and a multiplet at δ 7.39-7.66 ppm assigned for the aromatic protons, respectively. In ^{13}C NMR, compounds **19-27** show the chemical shift values of carbon atoms appear δ 157 ppm due to carbonyl atom, δ 126.08- 129.77 ppm due to aromatic carbons atoms, δ 65.7-62.25 ppm due to piperidone ring carbon atoms and δ 14.23 ppm is due to piperidone ring attached methyl carbon atom, respectively. Molecular and fragmented ion peaks in the mass spectra have given further evidence for the structural elucidation of the compounds.

Molecular docking studies: The comparative and automated docking studies with the compounds on AcrB (PDB ID: 1T9U) were performed with the CDOCKER algorithm in the docking program over the Discovery studio. The better interacting compounds were decided based on the binding compatibility of the compound. The strength of the protein-ligand interaction was analyzed based on the docking score, the number of hydrogen bonds and binding energy. The top-ranked compounds with lowest docked binding affinities and high docking were selected and summarized in Table-1. The conformation with the lowest binding energy was considered as the most favourable docking pose. From that result, synthesized compound **19** shows a good cdocker energy (kcal/mol) and cdocker interaction energy (kcal/mol). A two-dimensional structure of synthetic ligands (**19-27**) is produced using discovery studio (v 16.1.0.15350) (Fig. 1) in the two-dimensional structure, dotted lines represent van der Waals interactions, hydrogen bonding and pi-alkyl interactions. Docking of these compounds against the AcrB (1T9U) structure of the active site residues is performed by the discovery studio. Compound **21** shows interaction with the amino acid residues. An interaction of docked structure **21** is shown in Figs. 2 and 3. Out of nine docked compounds, **19**, **22** and **24** compounds showed lowest cdocker energy with the amino acid residues of the receptor molecule.

TABLE-1
DOCKING RESULTS OF THE DESIGNED COMPOUNDS (**19-27**) TOWARDS 1T9U

S. No.	Entry	-CDOCKER energy (kcal/mol)	-CDOCKER interaction energy (kcal/mol)
1	19	23.87	38.25
2	20	26.37	37.55
3	21	26.79	37.73
4	22	24.17	38.70
5	23	26.45	39.86
6	24	24.17	40.42
7	25	27.90	42.42
8	26	27.03	40.14
9	27	30.70	47.38

***in vitro* Antimicrobial activity:** *in vitro* Antimicrobial activity (antibacterial and antifungal activities) of synthesized tosyl carbamate derivatives (**19-27**) were investigated using the disc diffusion method. Two Gram-positive (*Staphylococcus aureus* and *Bacillus subtilis*) and three Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa* and *Proteus morganii*) bacterial strains and five fungal strains (*Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida tropicalls* and *Candida parapsilosis*) had been chosen to display the antimicrobial activity. Ciprofloxacin and amphotericin B were used as the standards in the antibacterial and antifungal activities, respec-

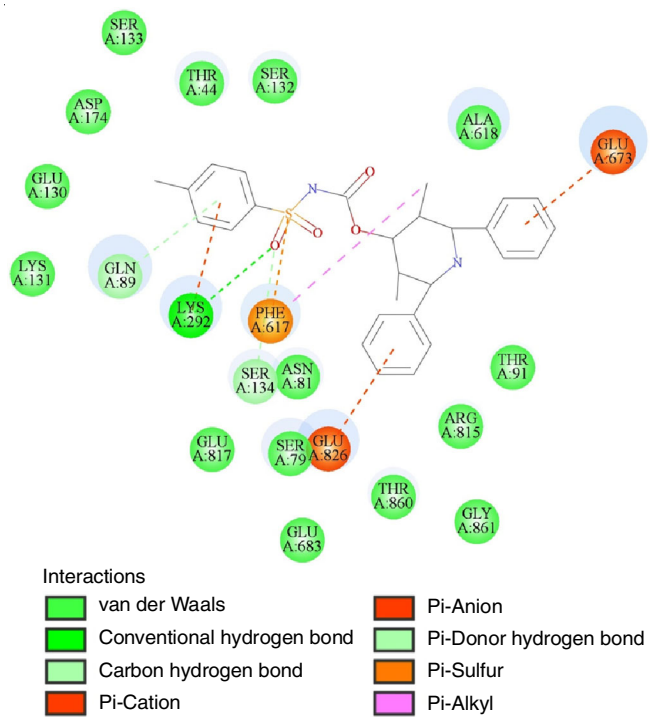


Fig 1. Two-dimensional diagram of compound **21** docked with 1T9U protein

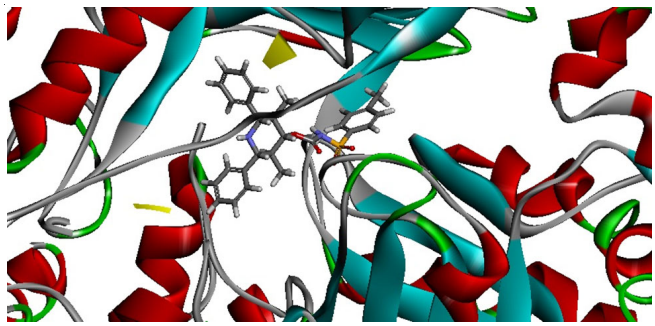


Fig. 2. Structure of 1T9U protein in complex with compound **21**

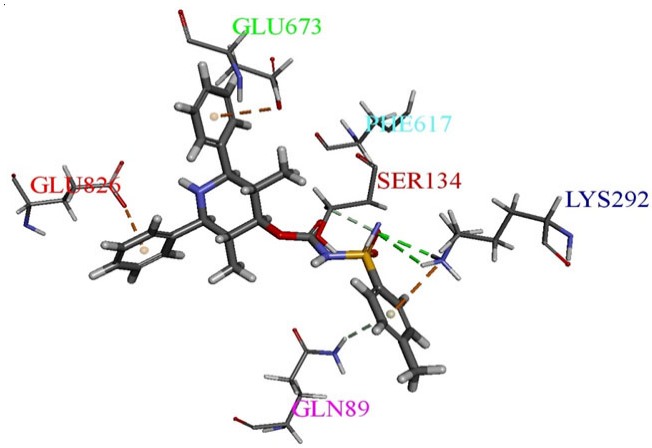


Fig. 3. Docking interactions of 1T9U protein with compound **21**

TABLE-2
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES OF SYNTHESIZED COMPOUNDS (**19-27**) BY DISC DIFFUSION METHOD

Compounds	Zone of inhibition (mm)									
	Antibacterial activity					Antifungal activity				
	B. subtilis	*S. aureus*	*E. coli*	*P. aeruginosa*	*P. morganii*	*C. albicans*	*C. glabrata*	*C. parapsilosis*	*C. krusei*	*C. tropicalis*
19	09	20	18	13	19	21	10	23	20	17
20	10	16	12	17	11	18	14	19	17	09
21	08	19	16	13	14	09	19	24	18	16
22	12	15	22	06	22	14	09	19	13	14
23	11	20	13	17	10	17	13	08	09	10
24	20	18	15	15	19	11	20	22	19	23
25	21	17	16	19	20	08	16	23	20	16
26	15	14	07	09	15	09	17	13	09	08
27	17	20	20	19	20	16	16	20	21	18
Ciprofloxacin	18	25	23	21	26	–	–	–	–	–
Amphotericin B	–	–	–	–	–	22	18	26	20	19

tively and the samples were prepared in DMSO. The zone inhibition of compounds (**19-27**) against the bacterial strains is given in Table-2. Compounds **19**, **23** and **27** against *S. aureus*; and compounds **22** and **27** against *E. coli* showed significantly high antibacterial activity at a diameter zone of inhibition compared to the standard drug ciprofloxacin. Compounds **19**, **20** and **21** exhibited moderate antibacterial activity, similarly, compounds **19**, **20**, **21** and **24** exhibited better antifungal activities against *C. parapsilosis*, *C. krusei* and *C. tropicalls* as compared to the standard drug amphotericin B (Table-2).

Conclusion

In conclusion, a new sequence of nine substituted tosyl carbamates has been synthesized reasonably in good yields and evaluated for their molecular docking studies and *in vitro* antimicrobial studies. Finally, the molecular docking studies of the synthesized compounds were docked with target protein 1T9U were carried out and the results of such studies were reported. *in silico* Studies revealed that synthesized compounds **19** and **21** have relatively lesser CDOCKER energy scores. The synthesized compounds were tested *in vitro* antimicrobial activity by disc diffusion method. All the compounds demonstrated mild to the moderate zone of inhibition against the standard drugs.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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