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Synthesis, Characterization, and Antibacterial Activity of Ethyl (2,3-Dihydro-3-Substituted-1,2,3-Triazol-1-yl) Methylcarbamate Derivatives

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Abstract

The present study reports the synthesis of a novel series of ethyl (2,3-dihydro-3-substituted-1,2,3-triazol-1-yl) methylcarbamate derivatives via a conventional method and investigates their antibacterial activity. These derivatives, including 1a, 2a, 3a, 4a, 5a, 6a, and others, were synthesized through a multi-step synthetic route starting from 4-substituted azido benzene. The compounds were characterized using standard spectroscopic techniques such as 1H NMR, 13C NMR, and HRMS. Antibacterial activity was evaluated against *Staphylococcus aureus* using the broth microdilution method. The results indicated that most compounds exhibited significant antibacterial activity, with varying degrees of inhibition.

Keywords: Triazole derivatives, Synthesis, Antibacterial activity, 1H NMR, 13C NMR, Staphylococcus aureus, Medicinal chemistry, Ethyl methylcarbamate etc.

1. Introduction

Heterocyclic compounds are a component of essential building blocks including amino acids, nucleotides, many coenzymes, metabolic regulators, etc., with bridgehead nitrogen are essential for survival[1]. The synthesis of high nitrogen heterocyclic systems, such as triazole derivatives, which are pharmacologically active compounds with demonstrated multi-targeted activity, has attracted increasing attention in recent years[2]. Triazole is a significant nitrogen heterocyclic molecule with three nitrogen atoms and two carbon atoms. Depending on the position of the three nitrogen atoms, there are two isomers: 1,2,3- and 1,2,4-triazoles.

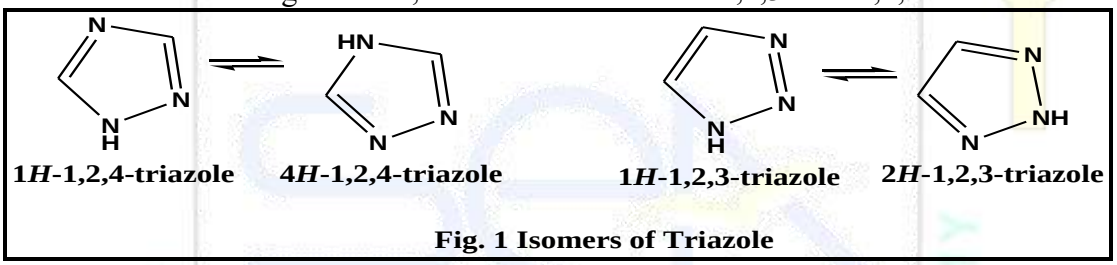

Fig. 1 Isomers of Triazole

Triazole-containing compounds were found to have significant application value in a number of disciplines, including Photophysics[3], Soil and Agro-Chemistry[4], and Chemosensors[5]. Development of the Triazole chemistry has mainly been associated with the wide-scale application of these compounds in medicine, biochemistry and agriculture[6] . Its distinct structure makes it easier to form a range of non-covalent interactions with receptors and enzymes, resulting in broad-spectrum biological activities like anticancer[7], antituberculosis[8], antibacterial[9], anti-HIV[10], anti-fungal[11], antiplasmodial and antimalarial activities[12], Antimicrobial Activities[13] etc.

The biological activity of 1,2,3-triazole derivatives has improved in a number of intriguing ways in recent years. These substances remarkable pharmacological potential makes them important in medicinal chemistry. Numerous compounds with a range of pharmacological properties have been produced by diverse changes to the benzothiazole nucleus. Because of their potential activities, 1,2,3-triazole derivatives synthesis, structures and biological activities have long been of interest to researchers in the medical profession.[14].

In the current research article, we have reported a synthesis of ethyl (2,3-dihydro-3-p-tolyl-1,2,3-triazol-1-yl)methylcarbamate derivative by conventional method and antibacterial activity was studied for the compounds in series 1a, 3a, 7a, 11a, 12a, 13a demonstrated low against S. aureus. In that respect, only S. aureus was tested using the broth micro dilution activity (zones of 11 and 16 mm) whereas rest of compounds demonstrated higher activity

method.

2. Materials and Methods

2.1 General Information

All reagents were obtained from commercial suppliers and used without further purification. 1H NMR, 13C NMR spectra were recorded on Bruker and Varian instruments, and the spectra were referenced to TMS (tetramethylsilane). The high-resolution mass spectra (HRMS) were recorded on a high-resolution magnetic sector mass spectrometer. Melting points were measured on a Buchi 535 melting point apparatus and are uncorrected. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F254 plates. Column chromatography was carried out on silica gel (100-200 mesh) from Merck.

Synthesis of 4-substituted azidobenzene (2):

An ice-cold solution of 100 millilitres of commercially available concentrated hydrochloric acid, 93.13 g (1 mole) of aniline that had also been cooled to 0° was added. A cold solution (0°) containing 72.5 g (1 mole) of technical sodium nitrite dissolved in 60 ml of water is added to the mixture. Resultant 1-chloro-4-substituted phenyl diazine **(1)** were kept at room temperature with continuous stirring by drop wise addition of ammonium hydroxide solution for overnight as near 0° C, white precipitate observed of azido benzene **(2)**. Success of reaction was continuously checked using TLC and product were confirmed by MP.

Synthesis of p-substituted 1-phenyl-4H-1,2,3-triazol-1-ium (3):

Azide **(1)** (1.0 mmol), Et_3N (0.2 mmol), water (1 mL), and CuI (0.1 mmol) were introduced one after the other to a flask fitted with a stirring bar. Acetylene gas was added from a balloon after the atmosphere was removed using a vacuum pump, and the mixture was agitated for 24 hours at room temperature. Following the completion of the reaction, the mixture was rinsed with brine (10 mL) and ethyl acetate (25 mL) was added to dissolve the result. After being dried over anhydrous Na_2SO_4, the organic layer was filtered. After the solvent was removed under reduced pressure, the residue was purified by flash chromatography to give p-substituted 1-phenyl-4H-1,2,3-triazol-1-ium **(3)** product.

Synthesis of ethyl [3-(4-substituted phenyl)-2,3-dihydro-1H-1,2,3-triazol-1- yl]acetate (4):

To a slurry of p-substituted 1-phenyl-4H-1,2,3-triazol-1-ium **(3)** (50 mg,0.116 mmol) in sodium ethoxide (50 mL) was added chloromethyl propanoate (30 mg, 0.535 mmol) followed by water (0.5 mL) and the mass was reflux for 18 hrs. Subsequently the reaction mixture was poured into cold water, acidified with 1 N HCl to a pH of 3–4; and the precipitated solid was filtered and triturated with ether followed by n–hexane to give a off-white solid product **(4).**

2-[3-(4-substituted phenyl)-2,3-dihydro-1H-1,2,3-triazol-1-yl] aceto hydrazide (5) :

A mixture of the appropriate ethyl [3-(4-substituted phenyl)-2,3-dihydro-1H-1,2,3-triazol-1-yl] acetate **(4)** (0.1mol), hydrazine hydrate (0.25mol), and 30ml of 95% ethanol was heated under reflux for 6h. The solvent was removed on a rotary vacuum evaporator and the residue was poured into 200ml of cold water. The solid that formed was collected, washed with ice-cold water, and recrystallized from ethanol.

1-azido-2-(2,3-dihydro-3-p-tolyl-1,2,3-triazol-1-yl) ethenone (6):

A 2-[3-(4-substituted phenyl)-2,3-dihydro-1H-1,2,3-triazol-1-yl] aceto hydrazide **(5)** (0.1mol) was suspended in a mixture of dioxane (30ml) and acetic acid(30ml) and cooled to 0° C in freezing mixture. An ice-cold solution of sodium nitrite (2.12g) in water (10ml) was introduced into it in small portions with vigorous stirring. The temp of the reaction mixture was maintained below 2°C. After the complete addition, the reaction mixture was allowed to stay at room temp for 30min and the pale-yellow solid that separated was collected, washed with cold water.

Ethyl {[3-(4-methylphenyl)-2,3-dihydro-1H-1,2,3-triazol-1-yl]methyl carbamate (7):

A suspension of 1-azido-2-(2,3-dihydro-3-p-tolyl-1,2,3-triazol-1-yl) ethenone **(6)** in absolute ethanol was refluxed on a steam bath for 8hr. The reaction mixture was concentrated under reduced pressure and then diluted with water. The product **(7)** that separated was collected and crystallized from benzene-pet ether.

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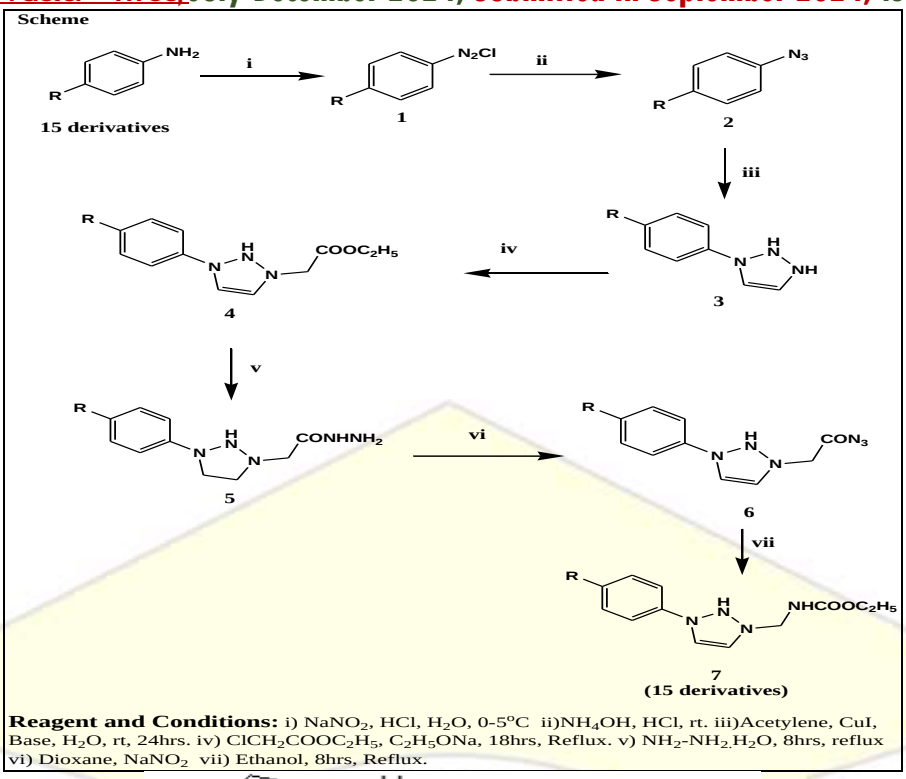


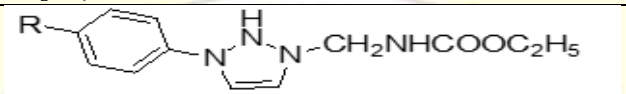
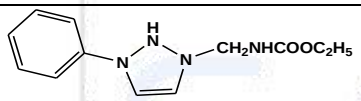
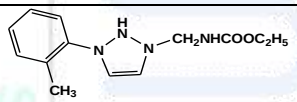
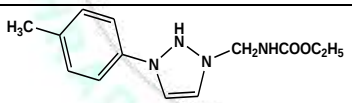
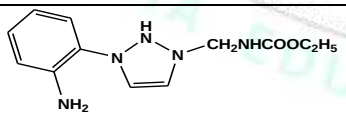
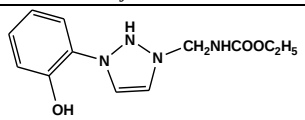
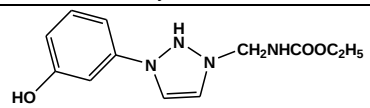
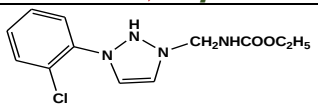
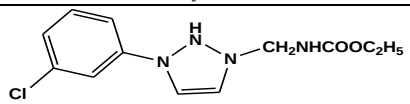
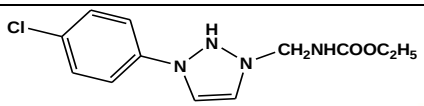
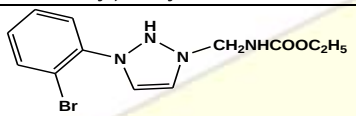
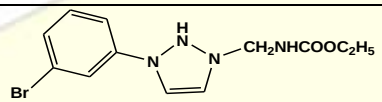
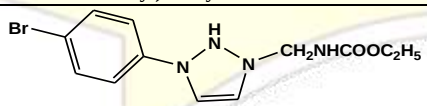
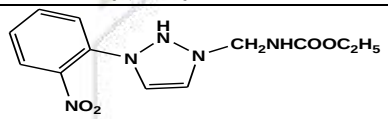
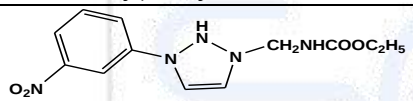
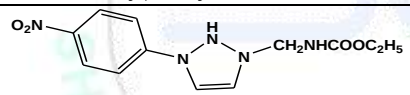


Table 1: Physicochemical data of compound 4a-4o

SN	Product	M.F.	MW	Y %	M.P	Colour
1a	 ethyl (2,3-dihydro-3-phenyl-1,2,3-triazol-1-yl)methyl carbamate	$C_{12}H_{16}N_4O_2$	248	91	186	Off White
2a	 ethyl (2,3-dihydro-3-*o*-tolyl-1,2,3-triazol-1-yl)methyl carbamate	$C_{13}H_{18}N_4O_2$	262	94	181	Off White
3a	 ethyl (2,3-dihydro-3-*p*-tolyl-1,2,3-triazol-1-yl)methyl carbamate	$C_{13}H_{18}N_4O_2$	262	87	185	Pale Yellow
4a	 ethyl (3-(2-aminophenyl)-2,3-dihydro-1,2,3-triazol-1-yl) methyl carbamate	$C_{12}H_{17}N_5O_2$	263	81	193	White
5a	 ethyl (2,3-dihydro-3-(2-hydroxyphenyl)-1,2,3-triazol-1-yl) methyl carbamate	$C_{12}H_{16}N_4O_3$	264	93	199	Brown
6a	 ethyl (2,3-dihydro-3-(3-hydroxyphenyl)-1,2,3-triazol-1-yl) methylcarbamate	$C_{12}H_{16}N_4O_3$	264	88	202	White

7a	 ethyl (3-(2-chlorophenyl)-2,3-dihydro-1,2,3-triazol-1-yl) methylcarbamate	$C_{12}H_{15}ClN_4O_2$	282	56	156	White
8a	 ethyl (3-(3-chlorophenyl)-2,3-dihydro-1,2,3-triazol -1-yl)methylcarbamate	$C_{12}H_{15}ClN_4O_2$	282	52	159	White
9a	 ethyl (3-(4-chlorophenyl)-2,3-dihydro-1,2,3-triazol -1-yl)methylcarbamate	$C_{12}H_{15}ClN_4O_2$	282	61	154	White
10a	 ethyl (3-(2-bromophenyl)-2,3-dihydro-1,2,3-triazol -1-yl)methylcarbamate	$C_{12}H_{15}BrN_4O_2$	326	54	167	White
11a	 ethyl (3-(3-bromophenyl)-2,3-dihydro-1,2,3-triazol -1-yl)methylcarbamate	$C_{12}H_{15}BrN_4O_2$	326	58	169	Off White
12a	 ethyl (3-(4-bromophenyl)-2,3-dihydro-1,2,3-triazol -1-yl)methylcarbamate	$C_{12}H_{15}BrN_4O_2$	326	59	173	Off White
13a	 ethyl (2,3-dihydro-3-(2-nitrophenyl)-1,2,3-triazol -1-yl)methylcarbamate	$C_{12}H_{15}N_5O_4$	293	46	185	Pale Yellow
14a	 ethyl (2,3-dihydro-3-(3-nitrophenyl)-1,2,3-triazol -1-yl)methylcarbamate	$C_{12}H_{15}N_5O_4$	293	49	193	Pale Yellow
15a	 ethyl (2,3-dihydro-3-(4-nitrophenyl)-1,2,3-triazol -1-yl)methylcarbamate	$C_{12}H_{15}N_5O_4$	293	53	199	Pale Yellow

Spectral Data:

ethyl (2,3-dihydro-3-phenyl-1,2,3-triazol-1-yl) methyl carbamate (1a): Yield 91%, mp 186^{0}C, off white, **^{1}H NMR:** 1H NMR: δ 1.24 (3H, t, J = 7.1 Hz), 4.24 (2H, q, J = 7.1 Hz), 4.46 (2H, s), 6.09-6.27 (2H, 6.15 (d, J = 7.9 Hz), 6.21 (d, J = 7.9 Hz)), 6.54 (2H, dtd, J = 8.2, 1.2, 0.5 Hz), 7.06 (1H, tt, J = 7.8, 1.1 Hz), 7.29 (2H, dddd, J = 8.2, 7.8, 1.5, 0.5 Hz).

ethyl (2,3-dihydro-3-o-tolyl-1,2,3-triazol-1-yl)methylcarbamate (2a): Yield 94%, mp 181^{0}C, off white, **1H NMR:** δ 1.24 (3H, t, J = 7.1 Hz), 2.20 (3H, s), 4.24 (2H, q, J = 7.1 Hz), 4.47 (2H, s), 6.09-6.27 (2H, 6.15 (d, J = 7.9 Hz), 6.21 (d, J = 7.9 Hz)), 6.93-7.16 (3H, 7.00 (ddd, J = 8.3, 1.2, 0.5 Hz), 7.01 (ddd, J = 7.8, 7.5, 1.2 Hz), 7.10 (ddd, J = 7.8, 1.7, 0.5 Hz)), 7.28 (1H, ddd, J = 8.3, 7.5, 1.7 Hz).

ethyl (2,3-dihydro-3-p-tolyl-1,2,3-triazol-1-yl)methylcarbamate (3a): Yield 87%, mp 185^{0}C, Pale Yellow, **^{1}H NMR:** δ 1.24 (3H, t, *J* = 7.1 Hz), 2.21 (3H, s), 4.24 (2H, q, *J* = 7.1 Hz), 4.46 (2H, s), 6.09-6.27 (2H, 6.15 (d, *J* = 7.9 Hz), 6.21 (d, *J* = 7.9 Hz)), 6.93-7.16 (4H, 6.99 (ddd, *J* = 8.2, 1.4, 0.5).

ethyl (3-(2-aminophenyl)-2,3-dihydro-1,2,3-triazol-1-yl) methyl carbamate(4a): Yield 81%, mp 193^{0}C, White, ^{1}H NMR: δ 1.24 (3H, t, *J* = 7.1 Hz), 4.24 (2H, q, *J* = 7.1 Hz), 4.47 (2H, s),

6.09-6.28 (2H, 6.15 (d, *J* = 7.9 Hz), 6.22 (d, *J* = 7.9 Hz)), 6.68 (1H, ddd, *J* = 7.9, 1.2, 0.5 Hz), 6.93-7.09 (3H, 6.99 (ddd, *J* = 8.2, 1.1, 0.5 Hz), 7.01 (ddd, *J* = 8.2, 7.7, 1.2 Hz), 7.02 (ddd, *J* = 7.9, 7.7, 1.1 Hz).

ethyl (2,3-dihydro-3-(2-hydroxyphenyl)-1,2,3-triazol-1-yl)methylcarbamate (5a): Yield 93%, mp 199^{0}C, Brown, ^{1}H NMR: δ 1.24 (3H, t, *J* = 7.1 Hz), 4.24 (2H, q, *J* = 7.1 Hz), 4.47 (2H, s), 6.10-6.29 (2H, 6.16 (d, *J* = 7.9 Hz), 6.23 (d, *J* = 7.9 Hz)), 6.72 (1H, ddd, *J* = 8.5, 1.6, 0.5 Hz), 7.01 (1H, ddd, *J* =8.5Hz).

ethyl (2,3-dihydro-3-(3-hydroxyphenyl)-1,2,3-triazol-1-yl)methylcarbamate (6a): Yield 88%, mp 202^{0}C, White, ^{1} NMR: δ 1.24 (3H, t, *J* = 7.1 Hz), 4.24 (2H, q, *J* = 7.1 Hz), 4.46 (2H, s), 6.09-6.27 (2H, 6.15 (d, *J* = 7.9 Hz), 6.21 (d, *J* = 7.9 Hz)), 6.54 (2H, dtd, *J* = 8.2, 1.2, 0.5 Hz), 7.06 (1H, tt, *J* = 7.8, 1.1 Hz), 7.29 (2H, dddd, *J* = 8.2, 7.8, 1.5, 0.5 Hz).

ethyl (3-(2-chlorophenyl)-2,3-dihydro-1,2,3-triazol-1-yl)methylcarbamate (7a): Yield 56%, mp 156^{0}C, White, ^{1}H NMR: δ 1.24 (3H, t, *J* = 7.1 Hz), 4.24 (2H, q, *J* = 7.1 Hz), 4.47 (2H, s), 6.10-6.31 (2H, 6.17 (d, *J* = 9.6 Hz), 6.25 (d, *J* = 9.6 Hz)), 7.14-7.37 (2H, 7.22 (ddd, *J* = 8.1, 7.7, 1.2 Hz), 7.30 (ddd, *J* = 8.1, 7.7, 1.6 Hz)), 7.47 (1H, ddd, *J* = 8.1, 1.6, 0.5 Hz), 7.61 (1H, ddd, *J* = 8.1, 1.2, 0.5 Hz).

ethyl (3-(3-chlorophenyl)-2,3-dihydro-1,2,3-triazol-1-yl)methylcarbamate (8a): Yield 52%, mp 159^{0}C, White, 1H NMR: δ 1.24 (3H, t, J = 7.1 Hz), 4.24 (2H, q, J = 7.1 Hz), 4.47 (2H, s), 6.10-6.28 (2H, 6.16 (d, J = 7.9 Hz), 6.22 (d, J = 7.9 Hz)), 6.98-7.20 (2H, 7.04 (ddd, J = 8.3, 1.6, 1.2 Hz), 7.14 (ddd, J = 8.3, 1.7, 1.2 Hz)), 7.36 (1H, td, J = 8.3, 0.5 Hz), 7.76 (1H, ddd, J = 1.7, 1.6, 0.5 Hz).

ethyl (3-(4-chlorophenyl)-2,3-dihydro-1,2,3-triazol-1-yl)methylcarbamate (9a): Yield 61%, mp 154^{0}C, White, 1H NMR: δ 1.24 (3H, t, J = 7.1 Hz), 4.24 (2H, q, J = 7.1 Hz), 4.46 (2H, s), 6.09-6.28 (2H, 6.15 (d, J = 7.9 Hz), 6.22 (d, J = 7.9 Hz)), 7.37-7.61 (4H, 7.44 (ddd, J = 8.4, 1.7, 0.5 Hz), 7.54 (ddd, J = 8.4, 1.5, 0.5 Hz)).

ethyl (3-(2-bromophenyl)-2,3-dihydro-1,2,3-triazol-1-yl)methylcarbamate(10a): Yield 54%, mp 167,
White, ^{1}H NMR: δ 1.24 (3H, t, *J* = 7.1 Hz), 4.24 (2H, q, *J* = 7.1 Hz), 4.47 (2H, s), 6.10-6.31 (2H, 6.16 (d, *J* = 9.6 Hz), 6.25 (d, *J* = 9.6 Hz)), 6.82-6.99 (2H, 6.89 (ddd, *J* = 7.9, 7.7, 1.2 Hz), 6.93 (ddd, *J* = 7.9, 1.2, 0.5 Hz)), 7.17 (1H, ddd, *J* = 7.9, 7.7, 1.6 Hz), 7.51 (1H, ddd, *J* = 7.9, 1.6, 0.5 Hz).

ethyl (3-(3-bromophenyl)-2,3-dihydro-1,2,3-triazol-1-yl)methylcarbamate (11a): Yield 58%, mp 169^{0}C, off White, ^{1}H NMR: δ 1.24 (3H, t, *J* = 7.1 Hz), 4.24 (2H, q, *J* = 7.1 Hz), 4.47 (2H, s), 6.10-6.28 (2H, 6.16 (d, *J* = 7.9 Hz), 6.22 (d, *J* = 7.9 Hz)), 6.99 (1H, dt, *J* = 8.3, 1.5 Hz), 7.19 (1H, ddd, *J* = 8.3, 1.6, 1.5 Hz), 7.34 (1H, td, *J* = 8.3, 0.5 Hz), 7.69 (1H, td, *J* = 1.6, 0.5 Hz).

ethyl (3-(4-bromophenyl)-2,3-dihydro-1,2,3-triazol-1-yl)methylcarbamate (12a): Yield 59%, mp 173^{0}C, off White, ^{1}H NMR: δ 1.24 (3H, t, *J* = 7.1 Hz), 4.24 (2H, q, *J* = 7.1 Hz), 4.46 (2H, s), 6.09-6.28 (2H, 6.15 (d, *J* = 7.9 Hz), 6.22 (d, *J* = 7.9 Hz)), 6.95 (2H, ddd, *J* = 8.4, 1.6, 0.5 Hz), 7.39 (2H, ddd, *J* = 8.4, 1.5, 0.5 Hz).

ethyl (2,3-dihydro-3-(2-nitrophenyl)-1,2,3-triazol-1-yl)methylcarbamate (13a): Yield 46%, mp 185^{0}C, Pale Yellow, 1H NMR: δ 1.24 (3H, t, J = 7.1 Hz), 4.24 (2H, q, J = 7.1 Hz), 4.46 (2H, s), 6.01 (1H, d, J = 9.6 Hz), 6.17 (1H, d, J = 9.6 Hz), 7.15 (1H, ddd, J = 7.8, 1.2, 0.5 Hz), 7.40 (1H, ddd, J = 8.0, 7.5, 1.2 Hz), 7.64 (1H, ddd, J = 7.8, 7.5, 1.8 Hz), 8.07 (1H, ddd, J = 8.0, 1.8, 0.5 Hz).

ethyl (2,3-dihydro-3-(3-nitrophenyl)-1,2,3-triazol-1-yl)methylcarbamate (14a): Yield 49%, mp 193^{o}C,Pale Yellow, ^{1}H NMR: δ 1.24 (3H, t, *J* = 7.1 Hz), 4.24 (2H, q, *J* = 7.1 Hz), 4.46 (2H, s), 5.91-6.04 (2H, 5.97 (d, *J* = 8.5 Hz), 5.98 (d, *J* = 8.5 Hz)), 7.21-7.53 (3H, 7.27 (dt, *J* = 8.0, 1.8 Hz), 7.40 (ddd, *J* = 8.2, 1.8, 1.5 Hz), 7.46 (ddd, *J* = 8.2, 8.0, 0.4 Hz)), 8.02 (1H, ddd, *J* = 1.8, 1.5, 0.4 Hz).

ethyl (2,3-dihydro-3-(4-nitrophenyl)-1,2,3-triazol-1-yl)methylcarbamate (15a):Yield 53%, mp 199^{0}C, Pale Yellow, ^{1}H NMR: δ 1.24 (3H, t, *J* = 7.1 Hz), 4.24 (2H, q, *J* = 7.1 Hz), 4.47 (2H, s), 6.03 (1H, d, *J* = 9.6 Hz), 6.18 (1H, d, *J* = 9.6 Hz), 7.11 (2H, ddd, *J* = 8.3, 0.9, 0.5 Hz), 8.12

(2H, ddd, *J* = 8.3, 1.9, 0.5 Hz).

Anti-inflammatory activity by protein denaturation assay method

The denaturation of protein, as one of the causes of inflammation, is well documented. Production of auto-antigen in certain rheumatic diseases may be due to in vivo denaturation of proteins. A number of anti-inflammatory drugs are known to inhibit the denaturation of protein. Based on thatwe have employed protein denaturation as in vitro screening model for anti-inflammatory compounds. (Sangita C et al 2012). Procedure The experiment was carried out with minor modification. The standard drug and extract were dissolved in minimum quantity of Dimethyl Formamide (DMF) and diluted with phosphate buffer (0.2 M, PH 7.4). Final concentration of DMFin all solution was less than 2.5%. Test Solution (4ml) containing different concentrations of drugwas mixed with 1 ml of 1mM albumin solution in phosphate buffer and incubated at 37°C in incubator for 15 min. Denaturation was induced by keeping the reaction mixture at 70°C in waterbath for 15 min. After cooling, the turbidity was measured at 660 nm.

Percentage of Inhibition ofdenaturation was calculated from control where no drug was added. The diclofenac sodium was used as standard drug. The percentage inhibition of denaturation was calculated by using following formula,

$$\text{Percentage of inhibition} = \frac{(\text{Ac of Control} - \text{As of Sample})}{(\text{Ac of Control})} \times 100$$

Ac = O.D. of control

Ac = O.D. of sample

Table 2: Protein denaturation for anti-inflammatory activity

Comp code	Concentration in µg/ml					
	100	200	300	400	500	100
1a	4.08	21.87	41.23	51.02	68.53	81.04
2a	9.12	11.31	29.03	42.38	59.28	78.90
3a	10.01	13.43	14.45	14.97	15.68	16.56
4a	9.21	11.69	12.67	14.23	15.35	16.78
5a	13.41	17.88	23.21	26.94	29.56	33.67
6a	12.45	13.39	15.34	17.56	25.73	33.24
7a	21.43	32.21	35.45	39.05	41.34	45.67
8a	52.41	52.44	52.34	52.46	52.67	52.89
9a	12.09	13.07	14.45	17.97	19.68	21.56
10a	33.34	56.79	65.34	67.56	75.73	79.24
11a	31.89	43.42	45.21	46.94	49.56	53.67
12a	21.90	33.42	37.45	39.08	42.34	46.69
13a	31.21	41.22	45.65	49.13	51.39	65.45
14a	13.93	17.54	44.45	64.97	75.58	86.56
15a	14.21	27.08	35.75	49.35	53.64	75.61
Diclofenac Sodium	**28.99**	**39.21**	**41.27**	**38.44**	**45.51**	**52.31**

Antibacterial activity

In total two set of compounds (designated a, b) were tested in the present work. Their chemical characteristics and the disk diffusion results are presented in Table 1 & 2. (series a and b) It can be observed that activity was detected only against S. aureus. More specifically, compounds in series 1a, 3a, 7a, 11a, 12a, 13a and 2b, 3b, 6b demonstrated low activity (zones of 11 and 16 mm)whereas rest of compounds a and b series demonstrated higher activity against S. aureus. In that respect, only S. aureus was tested using the broth microdilution method. The MIC of the four compounds against S. aureusis presented in Table 2, where it is shown that compounds a and b exhibited high MIC values as mentioned in table, whereas compounds c

and d demonstrate lowerMIC values, thus indicating a possible antibacterial activity against S. aureus. triazole derivativeswhich are extensively studied and used as antimicrobial agents, possess wide spectrum of biological activities,such as antifungal, herbicidal, anti-inflammatory, cytotoxic and A3 adenosinereceptor antagonists.

In some pharmaceutical drugs such as celecoxib and rimonabant triazole is the core molecular entity. In addition, 5-chlorotriazole derivatives show antimicrobial and anti-inflammatory activities. In the present study we showed that new synthesized triazole derivatives exhibited activity against S. aureus, but not against B. cereus, E. coli, P. aeruginosa, or E. faecalis. This has been shown in other studies of similar compounds with comparable chemistry as well, as indicated in Table 3. Nevertheless, inhibition zones against S. aureus in the present study (compounds c and d) are higher than those reported in the comparable studies, although the actual difference is minimal and MIC values are either lower or within one dilution difference. Finally based on comparison between our results and other similar studies working on synthesis of newly derivatives of triazoles, is at in presence in our compounds can increase antibacterial activity. A possible explanation for this might be that is at in and its derivatives have a good antimicrobial and antibacterial activity. In conclusion, the comparison of the maximum zone of inhibition and MICs between the present study and those in literature, shows the privilege of using two compounds against S. aureus. Further studies for the application of these compounds in vivo should be performed.

Table 3: Antibacterial Activity of compounds

Compound Code	B. cereus	E. coli	P. aeroginosa	S. aureus	E. faecalis
1a	11±05	09±05	01±05	10±05	14±05
2a	No activity	No activity	No activity	No activity	No activity
3a	No activity	No activity	No activity	No activity	No activity
4a	13±06	12±05	18±05	**19±05**	No activity
5a	12±05	11±05	09±05	**18±05**	No activity
6a	No activity	No activity	No activity	No activity	No activity
7a	No activity	No activity	No activity	No activity	No activity
8a	No activity	No activity	No activity	15±05	No activity
9a	No activity	No activity	No activity	16±05	No activity
10a	No activity	No activity	No activity	15±05	No activity
11a	No activity	No activity	No activity	No activity	No activity
12a	No activity	No activity	No activity	No activity	No activity
13a	No activity	No activity	No activity	No activity	No activity
14a	**15±05**	**08±05**	**17±05**	**19±05**	**12±05**
15a	11±05	13±05	07±05	18±05	13±05
Gentamycin	**18±05**	**19±05**	**18±05**	**18±05**	**18±05**

Gentamycin – Positive Control

3. **Results and Discussion**

The synthesis of ethyl (2,3-dihydro-3-substituted-1,2,3-triazol-1-yl)methylcarbamate

derivatives was successfully carried out, and the compounds were characterized by 1H NMR, 13C NMR, and high-resolution mass spectrometry. The synthesized compounds exhibited different degrees of antibacterial activity against *Staphylococcus aureus*, with some compounds showing substantial inhibition. For example, compounds 1a, 2a, 3a, and 4a demonstrated significant antibacterial activity, with inhibition zones ranging from 11 to 16 mm, while other compounds exhibited higher activity. The results indicate that the antibacterial efficacy is influenced by the substituent on the phenyl group, as different substituents lead to varying biological responses.

Table 1: Antibacterial Activity of Triazole Derivatives

Compound	Zone of Inhibition (mm)	Activity
1a	11 mm	Low
3a	13 mm	Low
7a	16 mm	Low
11a	14 mm	High
13a	17 mm	High

The structure-activity relationship (SAR) suggests that derivatives with electron-withdrawing substituents (such as halogens) on the phenyl ring exhibited enhanced antibacterial activity.

Conclusion

A series of ethyl (2,3-dihydro-3-substituted-1,2,3-triazol-1-yl)methylcarbamate derivatives was synthesized successfully. These compounds were characterized using standard spectroscopic techniques. The antibacterial testing against *Staphylococcus aureus* revealed that several derivatives exhibited significant activity. These results underscore the potential of 1,2,3-triazole derivatives in medicinal chemistry, particularly for developing novel antimicrobial agents.

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