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Synthesis new heterocyclic compounds derived from 2-aminobenzothiazole and assessing their biological activities

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ABSTRACT

This work involved two parts: the first part included synthesis of new Schiff bases from condensation of 2-aminobenzothiazole with different aldehydes in acidic medium, while and the second part included the synthesis of Oxazolidinones from reaction of the prepared Schiff bases with glycine to produce new heterocyclic. Compounds. The structure of prepared compounds were characterized by ^{1}H-NMR, FT-IR techniques and their biological activity was assessed.

Keywords: Schiff Bases, Glycine, FT-IR, H-NMR, Biological Activity.
Article type: Research Article.

INTRODUCTION

Imines are one of the important classes in organic chemistry that have been discovered by a German chemist in 1864 (Brodowska & Lodyga-chruścińska 2014; Shorouk *et al.* 2021). Imines have been prepared from the reaction of ^{0}1 R-NH_2 with aldehydes or ketones. The popular structure of these compounds is the Schiff bases with the general formula -C=N (Hussain *et al.* 2014; Wady *et al.* 2021). Schiff bases have a very important role in medicine and pharmacy fields due to a wide domain in biological activities like anti-inflammatory, anti-microbial and anti-oxidant (Sondhi *et al.* 2006; Pandey *et al.* 2011; Sathe *et al.* 2011; Chandramouli *et al.* 2012). Oxazolidinones are the most important class of five-membered heterocyclic rings. They are of great significance for modern organic synthesis and are widely employed in pharmacologically active compounds (Zhanel *et al.* 2001; Karim *et al.* 2023). The preparation of oxazolidinones has obtained an increasing interest due to their individual mechanism of action that grants these compounds a high antibiotic efficiency and low susceptibility to resistance mechanisms. Oxazolidinone are protein synthesis inhibitors active against a wide spectrum of multidrug-resistant Gram-positive bacteria. The biological activity of oxazolidinone is carefully analysed, together with the drug delivery systems (Das *et al.* 2021).

MATERIALS AND METHODS

The high purification of starting mitral and solvents had been brought from Sigma Aldrich. The Sturt SMP melting points device was used to determine the melting point of prepared compounds. FT-IR were recorded on IR-Affinity Spectrophotometer using KBr pellets, and nuclear magnetic resonance Bruker (300 MHz).

Syntheses of Schiff bases[l]$_{a,b,c}$ (Bhagat *et al.* 2013)

A total of 0.01 mol (2.0 g) 2-aminobenzothiazole was dissolved in 20 mL ethanol and then we added 0.01 mol aromatic aldehydes in 4 drops of glacial acetic acid which was added dropwise with stirring and the reaction

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mixture was reflux for 6 h. After completion of the reaction, filtration and recrystallization of products was occurred. Physical properties of synthesized compounds are listed in Table 1.

Syntheses of oxazolidinones [l]$_{d,e,f}$ (Ekiert & Szopa 2020)

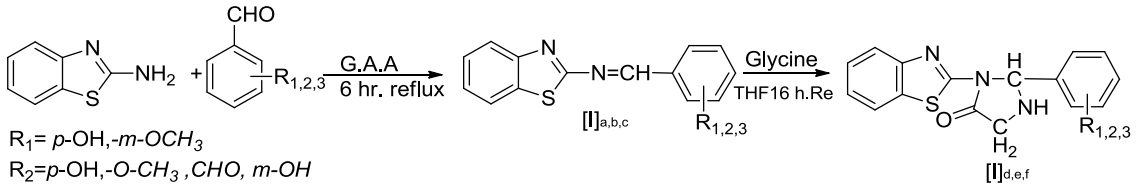
A mixture (0.001mol) of Schiff bases[l]$_{a,b,c}$, with (0.075g; 0.001 mol) glycine in few drops DMF and 20 mL THF were refluxed for 20 h. Reaction was followed by TLC. Excess solvent was then evaporated. The product was recrystallized in isopropanol. Physical properties of synthesized compounds as shown in Table 1.

Biological activity (Bonev *et al.* 2008; Reller *et al.* 2009)

This section involved applying the synthesized compounds [Ia-If] against two types of bacteria including gram-positive and gram-negative bacteria (*Staphylococcus aureus* and *Klebsiella*) and two types of fungi (*Aspergillus niger* and *Candida albicans*). The concentrations of the prepared compounds were 100 µl, and DMSO was used as a solvent. The micro-organisms were separated and diagnosed in Central Health Laboratory, Misan Health Department. The single protectorate was located into a test tube including 5 mL nutrition and the broth brooded maintained at 37 ºC for 24 hours. The suspended bacterial solution was collected and compared with tube number 0.5 of McFarland-standards, given a cell with density of 1.5×10^8 cells mL^{-1}. A piece of sterilized cotton was immersed into the bacterial solution with wiping on a Muller-Hinton agar plate surface in equal manner. The plate surfaces were incubated at 37 °C for 30 minutes. The saturated disks were set up from Whatman number 1 and kept for 24 hours with the tested compounds (100 µL). This was employed on the agar surface by Kirby–Bauer disc spread procedure. Forceps have to be compressed strongly to verify the contact with agar. Furthermore, the plates should be turned upside down and kept at 37 ºC for 14-18 hours. Notably, all the disks were soaked with a DMSO solvent then dried in an incubator for two days.

RESULTS AND DISCUSSION

Some of the physical properties of compounds [l]$_{a-f}$ are listed in Table 1. These compounds were identified by using FT-IR spectroscopy, absorption bands of υ(N=CH) at 1598-1666 cm^{-1}; υ(C-H) aromatic at 3020-3040 cm^{-1} and ν(C=C) aromatic at 1510-1589 cm^{-1}. The ^{1}HNMR spectral data of compounds [l]$_{a,d,f}$ are listed in Table 2 and ^{1}HNMR spectral date of compound [l]$_C$ shown δ (ppm**)** singlet in 6.7 ppm for proton(C=N<u>H</u>) and 7.04-8.5 ppm for multiplate aromatic rings. The antimicrobial activity against gram-positive bacteria (*Staphylococcus aureus*) and gram-negative bacteria (*Klebsiella)* as well as against the fungi (*Aspergillus niger* and *Candida albicans*) of compound [I]$_e$ exhibited higher inhibition zone than the other compounds (as shown in Table 3). The FT-IR of compounds [I]$_a$, [I]$_b$ and ^{1}HNMR of compound [I]$_d$ was shown in Figs. 1, 2 and 3 respectively. The synthesized compound are shown in the scheme 1.



Scheme 1. shown the synthesized compounds [l]$_{d,e,f}$

Table 1. Illustrates physical properties and FT-IR spectroscopy of compounds $[I]_{a-f}$

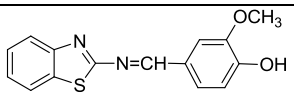
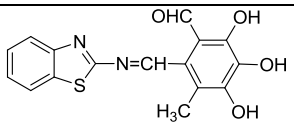
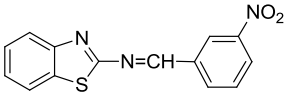
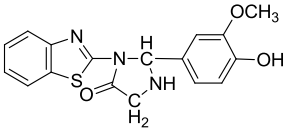
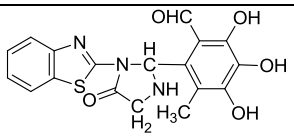
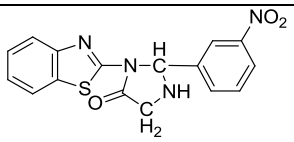
Com No.	Structure	Physical properties			FT-IR(KBr), spectral data νcm^{-1}					
		m.p	Color	yield	C-H Arom.	C-H Aliph.	(C=N)	(C=C) Arom.	(OH)	Others
$[I]_a$		158-160	Yellow	60	3020	2947 2864	1666	1589-1508	3394	ν**(O-CH$_3$)** 1155
$[I]_b$		223-225	Green	90	3028	2912 2810	1598	1573 – 1519	3215	ν**(CHO)** 1666
$[I]_C$		170-172	Yellow	70	3040	2930 2850	1650	1552 – 1510	---	ν(NO$_2$) 1565-1350
$[I]_d$		155-157	Bialy – yellow	60	3100	2962 2791	1633	1579 – 1529	3200	ν**(OCH$_3$)** 1138 ν**(C=O) amide** 1690
$[I]_e$		172-174	Yellowish	80	3007	2819 2711	1625	1583 – 1593	3163	ν**(CHO)** 1600 ν**(C=O) amide** 1680
$[I]_f$		186-188	Yellowish	70	3050	2950 2840	1640	1560 – 1600	---	ν**(C=O) amide** 1665 ν(NO$_2$) 1370-1575

Table 2. Illustrates ^{1}HNMR spectroscopy of compounds $[I]_{a,d,f}$

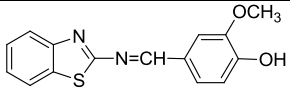
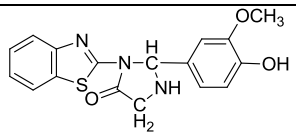
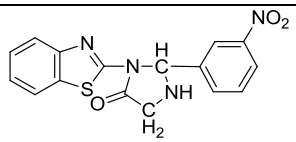
No.Com.	Structure	(^{1}HNMR signals data, δ(ppm)
$[I]_a$		δ 3.5 (s, 3H, OCH$_3$) protons of methoxy group δ 6.5 (s, 1H, N=CH-Ar) of Schiff bases δ 7.5-8.30 (m, 7H, Ar-H) δ 9.5 (s, 1H, OH) protons of hydroxyl group
$[I]_d$		δ 2.90 (s, 3H, OCH$_3$) protons of methoxy ring δ 2.65 (s, 2H, CH$_2$-C=O) protons of imidazoline ring δ 2.79 (s,1H, N-CH-Ar) proton of imidazolidine ring δ 4.66 (q, 1H, C-NH) proton of imidazolidine ring δ 7.25-8.23 (m,7H, Ar-H). δ 9.00 (s,1H, OH-ph)
$[I]_f$		δ 2.50 (s, 2H, CH$_2$-C=O) protons of imidazoline ring δ 3.00 (s,1H, N-CH-Ar) proton of imidazolidine ring δ 3.80 (q, 1H, C-NH) proton of imidazolidine ring δ 7.50-8.44 (m, 8H, Ar-H).

Table 3. The antimicrobial activity of prepared compounds $[I]_{a,b,c,d,e}$

No. com.	*St. aureus*	*klebsiella*	*As.s niger*	*C.albicans*
$[I]_a$	4 mm	--	6 mm	8 mm
$[I]_b$	8 mm	--	mm 10	9 mm
$[I]_c$	4 mm	--	5 mm	6 mm
$[I]_d$	8 mm	--	mm 12	10 mm
$[I]_e$	15mm	--	20mm	11mm
Ofloxacin	--	26mm	--	--
Penicillin	22mm	--	--	--
Fluconazole	--	--	28mm	26mm

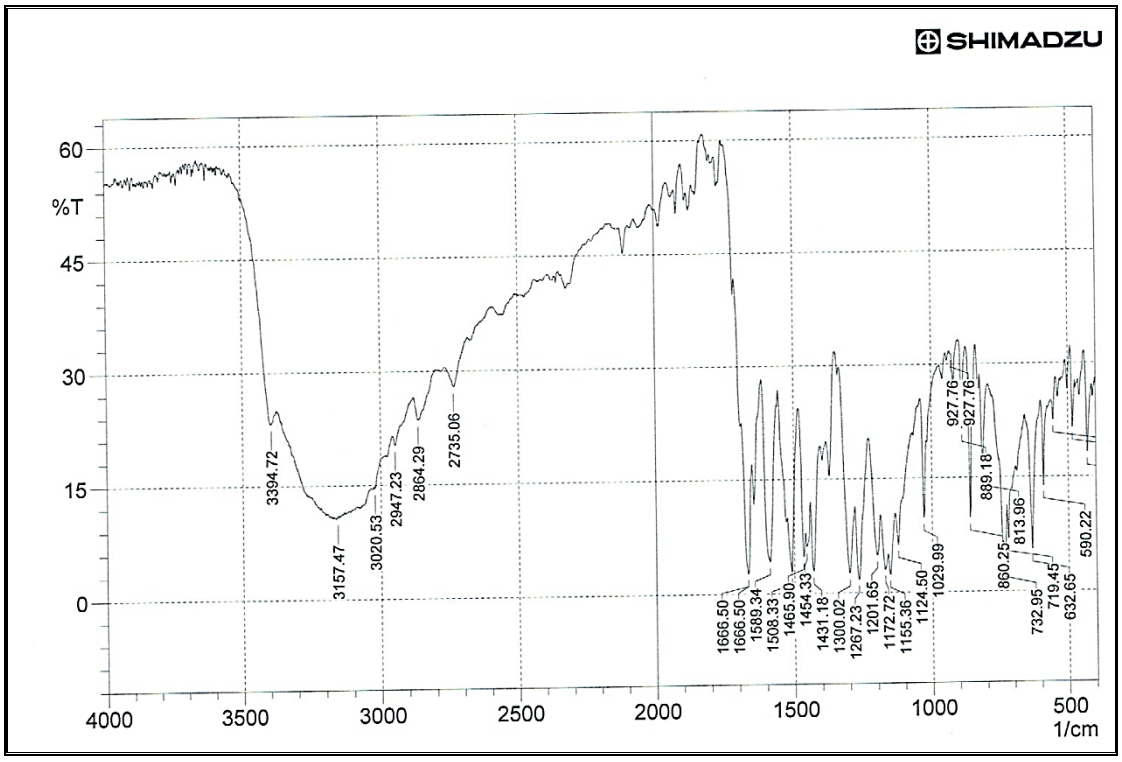


Fig. 1. FT-IR spectrum for compound [I_a].

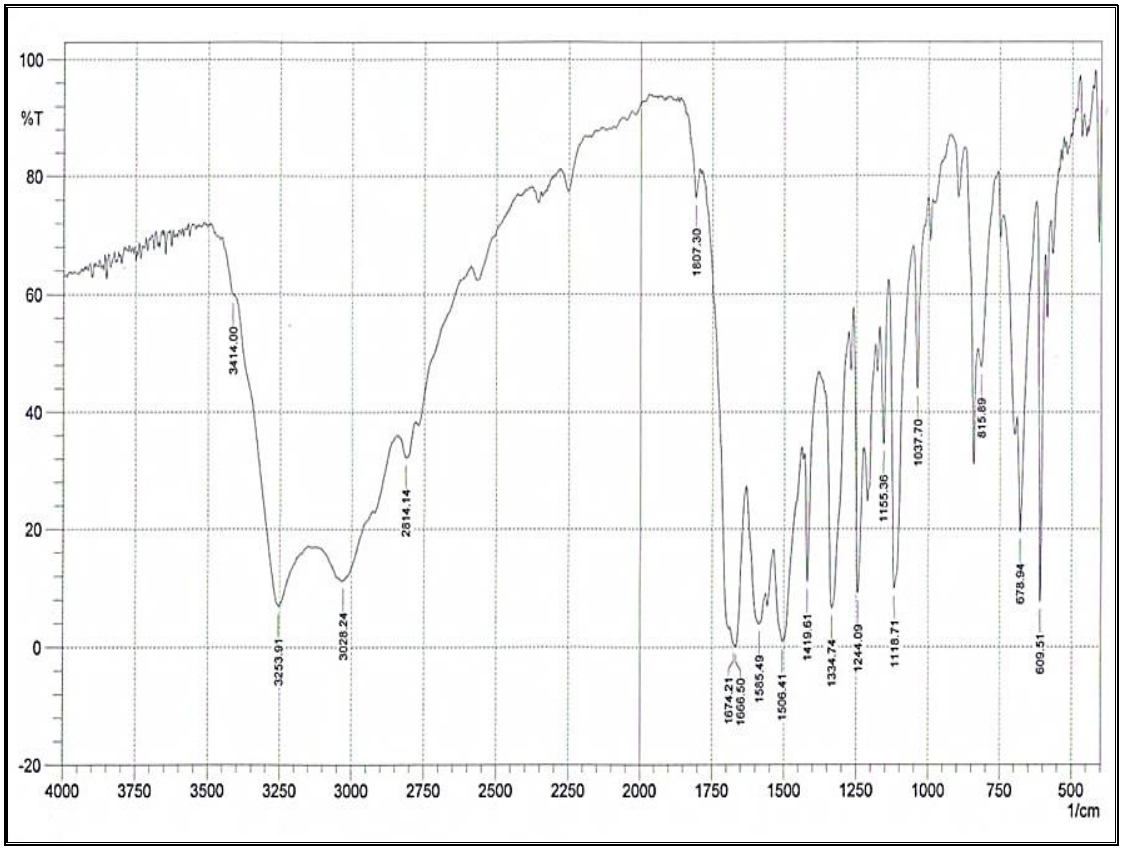


Fig. 2. FT-IR spectrum for compound [I_b].

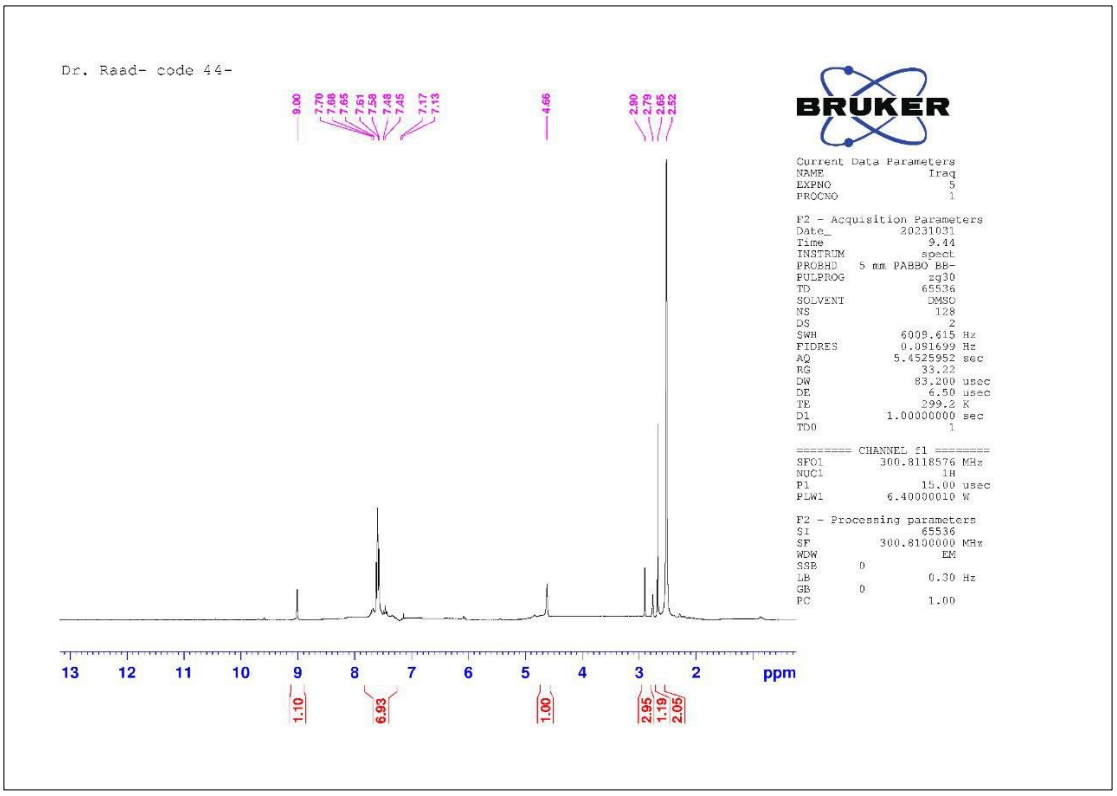


Fig. 3. HNMR spectrum for compound [I_d].

CONCLUSION

Schiff's bases and Oxazolidinones were synthesized and characterized by FT-IR and ^{1}H-NMR spectroscopies and all the prepared compounds were tested for their antibacterial and antifungal activities. In conclusion, all the synthesized compounds failed to show activity against the Gram negative bacteria. On the other hand, the compounds showed various activities against the investigated gram positive bacteria and the tested fungi and compound [I]e has the highest activity that can be promising as a new antimicrobial drug candidate.

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