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Research Article

SYNTHESIS AND BIOLOGICAL EVALUATION OF BENZIMIDAZOLE

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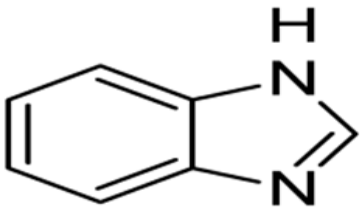
ABSTRACT

Benzimidazole and its derivatives have been showing promising activity in the treatment of several disease. For these reasons, they gained much attention as important pharmacophore and privileged structure in medicinal chemistry. I have attempted to combine aldehyde derivatives of heterocyclic with benzenamine to get some new Schiff base. The compounds synthesized were identified by UV, ^{1}HNMR, FTIR & MASS spectroscopic techniques. All compounds studied in this work were screened for their in vitro antibacterial activities against the standard strains: **Gram-negative are** *Pseudomonas aeruginosa, Escherichia coli,* **Gram- positive bacterium-** *Bacillus subtilis and* **Gram-positive spherical bacteria-** *Staphylococcus aureus.* The antibacterial activities of all test compounds were carried out by disc diffusion method. Compound BZ_5 and BZ_8 was found to be the most active antibacterial compound amongst the series of Compounds.

Keywords: Benzimidazole and Antibacterial.

INTRODUCTION

Bacterial resistance to the antibiotics is a big blow to humanity that's why continual search for newer chemotherapeutic agents is going on. the discovery of new drugs which are more potential and less toxic is essential for exploitation of synthetic derivatives for treating, management and diagnosis of diseases.Today more than 70% drugs used in practice.In this work we have endeavored to explore some new benzimidazole derivatives for their possible biological and pharmacological properties.



Hence, in the present work, we have attempted to combine aldehyde derivatives of heterocyclic with benzenamine to get some new Schiff base. All such compounds will be screened for antibacterial against various strains.

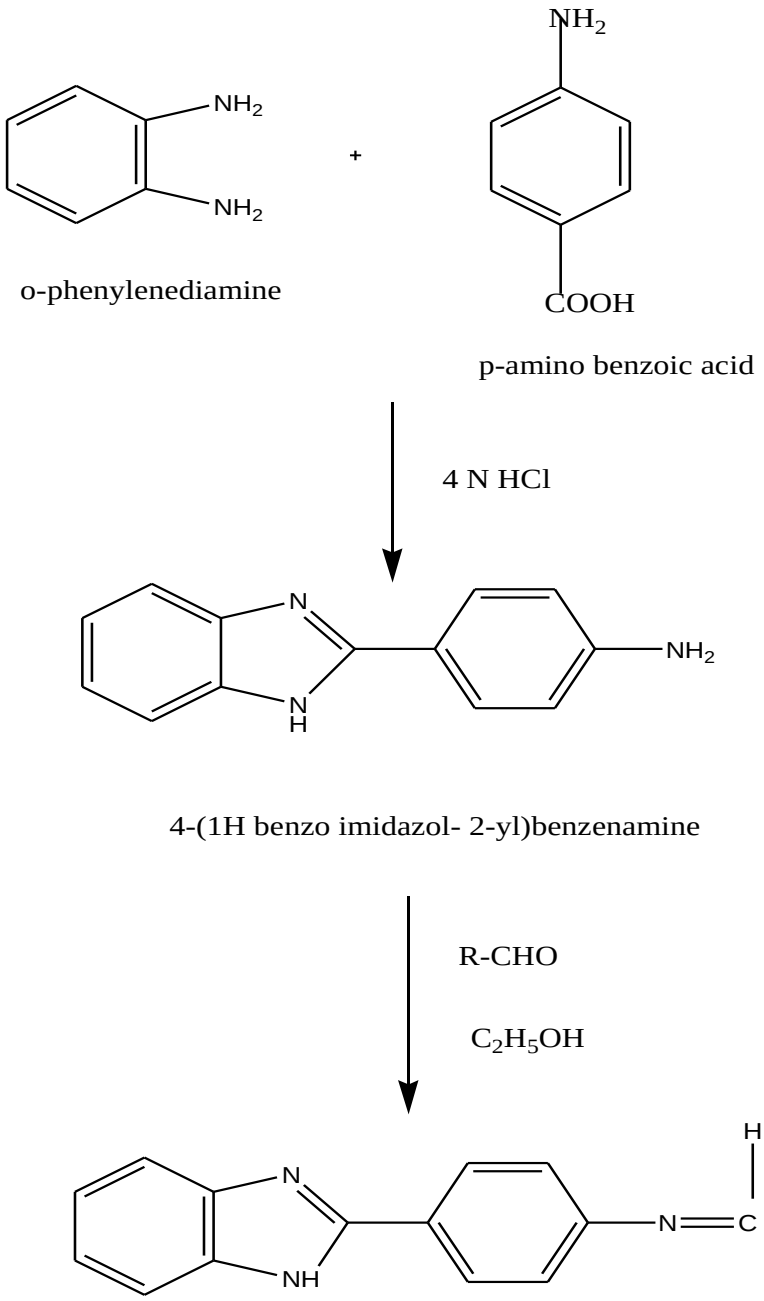
Experimental

MATERIAL AND REAGENTS

All chemicals All chemicals used in the synthesis were of synthetic grade and were supplied by Merck, Qualigens, Lobachemie, Changshuyangyuanchemical, China. Melting point of the synthesized compounds was done by theil tube capillary method. Purification of the compounds was checked by column chromatography by using **Ethyl acetate: Petroleum Ether (2:1)**.Spots were seen under iodine vapours. IR spectra were obtained on a Perkin-Elmer elmer spectrum version 10.03.05 administrator in B.H.U.

^{1}HNMR- spectra were recorded on JEOL AL-300 MHz FTNMR Spectrophotometer in DMSO or CDCl3 using TMS as the internal standard. (Chemical shift in δ ppm) &Mass Spectra were recorded on Water OPLC-TQDMS in positive mode ESI-MS Spectrophotometer.

Scheme



o-phenylenediamine

p-amino benzoic acid

4-(1H benzo imidazol- 2-yl)benzenamine

N-(4 substituted benzylidine)4(1 H benzo imidazol-2-yl)benzenamine

Procedure for the synthesis of N-(4-substituted benzylidine)-4-(1*H*-benzo[*d*]imidazol-2-yl) benzenamine (Bz_1-Bz_{10})

a. A mixture of o-phenylenediamine and *p*-amino benzoic acid (0.01mol) was dissoloved in 4N HCl (20mL) and refluxed for 4 hour. The mixture is cooled and filtered off. The residue is the 4- (1*H*-benzimidazol-2-yl) benzenamine.The product is recrystallized from absolute alcohol.This compound was obtained as a pale yellow solid.

b. A mixture of equimolar quantities of aromatic aldehyde and benzenamine derivatives was refluxed for 6 hour in 20 mL of ethanol. The reaction mixture was cooled and kept for 24 h. The crystals found was filtered and dried. The schiff base benzenamine was recrystallized from ethanol**.**

Antibacterial activity

The antibacterial activities of all test compounds were carried out by disc diffusion method .The concentrations of the test compounds were taken in DMSO and used in the concentration of 1mg and 2mg/disc.

The microorganisms were cultured in Mueller-Hinton broth (MHB). After 24 h the suspensions were adjusted to standard sub culture dilution. The Petri dishes containing Muller Hinton Agar (MHA) medium were cultured with diluted bacterial strain.

Disc made of Whatman filter paper No.1, diameter 6 mm was presterilized and was maintained in aseptic chamber. Each concentration was injected to the sterile disc papers. Then the prepared discs were placed on the culture medium. Standard drug Amikacin (30 µg) was used as a positive reference standard to determine the sensitivity of each microbial species tested.

Then the inoculated plates were incubated at 37 ºC for 24 h. The diameter of the clear zone around the disc was measured and expressed in millimeters as its anti-microbial activity.

Anti-bacterial activity of test compound was performed against **the *E. coli, S. aureus,P. aeruginosa* and *B.subtilis.***

Antibacterial activity

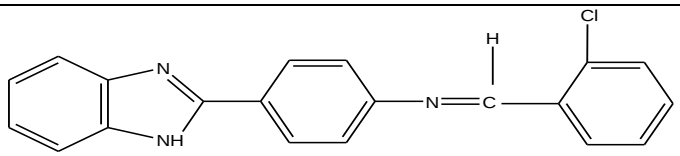
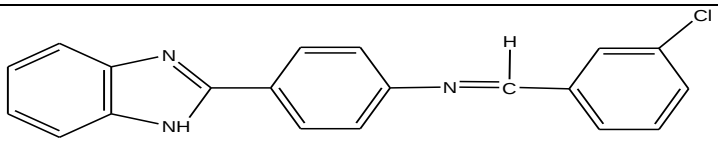
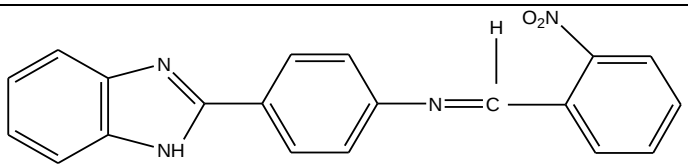
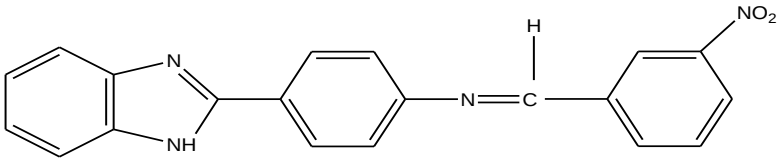
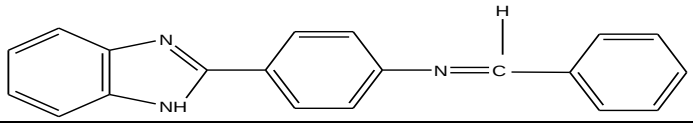
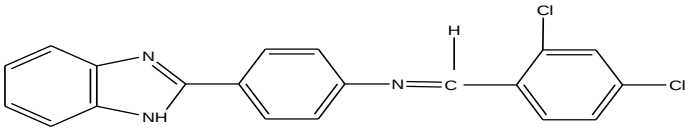
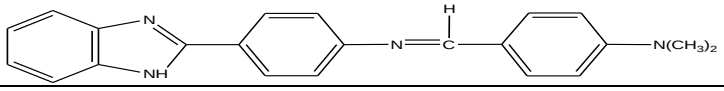
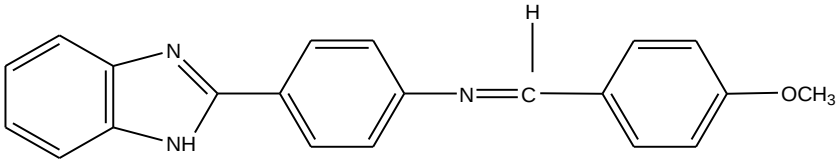
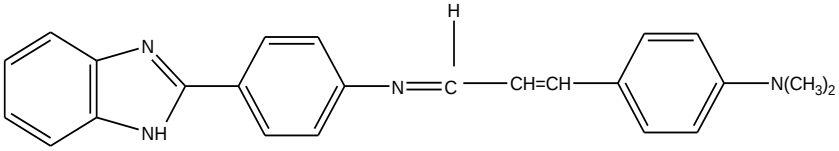
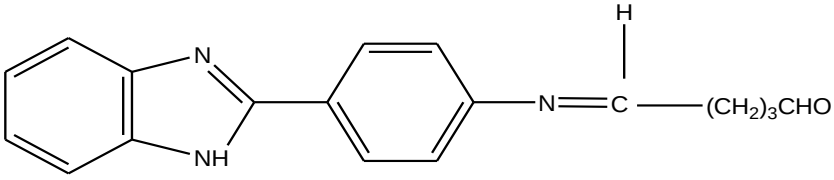
Compounds	Zone of Inhibition (mm)							
	S. aereus		***B. subtilis***		***E. coli***		***P. aerugenosa***	
	1mg	**2mg**	**1mg**	**2mg**	**1mg**	**2mg**	**1mg**	**2mg**
BZ-1	10	15	10	13	10	15	9	12
BZ-2	10	16	9	12	10	13	9	14
BZ-3	10	15	10	14	12	18	10	12
BZ-4	8	11	11	18	12	14	10	13
BZ-5	**20**	**25**	11	**22**	18	**22**	9	12
BZ-6	10	12	11	16	13	17	9	12
BZ-7	11	20	10	15	9	14	11	14
BZ-8	**23**	**30**	12	15	15	19	9	11
BZ9	12	15	11	13	13	15	9	13
BZ-10	12	17	10	15	10	14	11	15
Amikacin (30 µg)	**26**		**24**		**21**		**23**	

RESULT AND DISCUSSION

A novel series of N-(4-substituted benzylidine)-4-(1*H*-benzo[*d*]imidazol-2-yl) benzenamine derivatives (Bz_1-Bz_{10}) had been synthesized by using different types of aldehyde derivatives.

O-phenylenediamine and *p*-amino benzoic acid was dissoloved in 4N HCl (20mL) which was refluxed for 4 hour. The mixture is cooled and filtered off.Then the obtained product was refluxed with equimolar quantities of aromatic aldehyde for 6 hour in 20 mL of ethanol.The crystals found was filtered and recrystallized.All the synthesized derivatives were obtained in good yields and in a high state of purity. The reaction was monitored by TLC.Spots on the slides were detected in iodine chamber. Melting point of the synthesized compounds were taken by Theil tube method. The structures of newly synthesized compounds were established on the basis of IR, ^{1}H NMR and Mass spectroscopy.

Table 7.1 Structures and IUPAC name of compounds (BZ_1-BZ_{10})

Compoud Code	Structure	IUPAC name
BZ_1		N-(2-Chloro-benzylidine)-4-(1-H-Benzimidazol-2-yl)-benzenamine
BZ_2		N-(3-Chloro-benzylidine)-4-(1-H-Benzimidazol-2-yl)-benzenamine
BZ_3		N-(2-Nitro-benzylidine)-4-(1-H-Benzimidazol-2-yl)-benzenamine
BZ_4		N-(3-Nitro-benzylidine)-4-(1-H-Benzimidazol-2-yl)-benzenamine
BZ_5		4-(1H-benzo[d]imidazol-2-yl)-N-benzylidenebenzenamine
BZ_6		N-(2,4-diChloro-benzylidine)-4-(1-H-Benzimidazol-2-yl)-benzenamine
BZ_7		4-((4-(1H-benzo[d]imidazol-2-yl)phenylimino)methyl)-N,N dimethylbenzenamine
BZ_8		N-(4-methoxy-benzylidine)-4-(1-H-Benzimidazol-2-yl)-benzenamine
BZ_9		4-(3-(4-(1H-benzo[d]imidazol-2-yl)phenylimino)prop-1-enyl)-N,N-dimethylbenzenamine
BZ_{10}		5-(4-(1H-benzo[d]imidazol-2-yl)phenylimino)pentanal

Physical data of synthesized compounds (BZ_1-BZ_{10})

Compound Code	Melting Point(◦c)	Molecular Weight	Molecular Formula	Percentage yield	R_f value
BZ_1	250-255	332	$C_{20}H_{14}N_3Cl$	50%	0.39
BZ_2	230-250	332	$C_{20}H_{14}N_3Cl$	70%	0.41
BZ_3	180-200	342	$C_{20}H_{14}N_4O_2$	60%	0.67
BZ_4	220-240	342	$C_{20}H_{14}N_4O_2$	50%	0.76
BZ_5	140-160	297	$C_{20}H_{15}N_3$	50%	0.58
BZ_6	260-280	367	$C_{20}H_{13}N_3Cl_2$	60%	0.66
BZ_7	240-250	340	$C_{22}H_{20}N_4$	80%	0.78
BZ_8	200-210	327	$C_{21}H_{17}N_3O$	78%	0.81
BZ_9	100-120	366	$C_{24}H_{22}N_4$	40%	0.80
BZ_{10}	235-250	291	$C_{18}H_{17}N_3O$	50%	0.75

Spectral Data of the Synthesized Compounds (BZ_1-BZ_{10})
Study of I.R. & Mass Spectral data of Synthesized compound

Compound Code	I.R. Frequency in cm^{-1}	Type of vibration	m/z value
BZ_1	1556 1578 2908 741 742	C=C C=N N-H o-substitution C-Cl	269.1
BZ_2	1555 1398 813 741	C=N C-N m-substituted C-Cl	269.1
BZ_3	1615 1568 3414 1468 746	C-NO_2 Ar-NO_2 NH C=N O-substituted	240.1
BZ_4	3311 1416 1606 1563 705	NH Ar-NO_2 C-NO_2 C=N m-substituted	240
BZ_5	3202 1478 1380 1603	N-H C=N C-N C=C(Aromatic)	285
BZ_6	3383 1595 3045 764 831 670	N-H C=N Ar-H o-substituted p-substituted C-Cl	263
BZ_7	3314 2919 1599 1397	N-H Ar-H C=N C-N	238.1
BZ_8	3049 3336 1306 1597 1202	Ar-H N-H C-N C=N Ar-O-CH_3	225.1
BZ_9	3395 1602 1515 1277 837	N-H C=C C=N C-N p-substituted	173.1
BZ_{10}	3405 1531 1383 2919 1716	N-H C=N C-N C-H-O C=O	293.1

Study of N.M.R. Spectral data of Synthesized compound

Compound Code	Value in ppm	Type of peak	Functional group	No. of H
BZ_1	2.51 7.1 7.9	S D D	CHCl CH=CH (Ar-H) Ar-H	1 2 1
BZ_2	2.4 3.0 6.7 7.1 7.8	S M M M M	$R\text{-}NH_2$ CH-CL Ar-H CH=CH CH=CH	2 1 1 2 2
BZ_3	1.6 1.4 6.5 7.2	M M M S	CH-NHR CHNHR Ar-H CH=CH	2 2 1 2
BZ_4	1.2 4.4 7.2 8.3	M M M M	CHNHR C=CH CH(Benzene) CH(BZD)	2 1 1 1
BZ_5	1.2 2.5 7.2 7.7	M S M M	CHNHR C=CH(Benzene) CH(Benzaldehye) CH(Benzene)	2 1 1 1
BZ_6	1.2 2.5 4.1 7.6	M S M M	$CH_3(RNH_2)$ CH_2 C=CH Ar-H	3 2 1 1
BZ_7	1.6 3.1 6.6 7.2	S S M S	CHNHR CH_3 CH(Benzilidine) CH(Benzene)	2 3 1 1
BZ_8	3.9 2.5 7.5 8.3	D S M M	OCH_3 CH_3 CH CH	3 3 1 1
BZ_9	1.2 2.4 6.6 7.6	M S M M	CHNHR CH_3 C=CH CH(Benzene)	2 3 1 1
BZ_{10}	1.2 1.8 6.5 7.3	S M M S	CH_2 CHNHR Ar-H CH	2 2 1 1

CONCLUSION

The synthesis and antibacterial activity of novel benzimidazole derivatives were presented in this study. The biological profile of benzimidazole represents a fruitful matrix for better development of better medicinal agents. Hence, the structural exploitation may yield a safe therapeutic agent.

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