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Der Chemica Sinica, 2011, 2(5):147-151

Pelagia Research Library
ISSN: 0976-8505
CODEN (USA) CSHIA5

Synthesis and Antimicrobial Activity of Isoxazoles

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ABSTRACT

Isoxazoles have been prepared by the reaction of various 3-Carboxamido-(substituted-benzothiazole-2yl)-propane-2-one and hydroxylamine hydrochloride. The starting compound substituted 2–amino benthiazoles were prepared from various substituted amines via substituted phenyl thiourea. The structures of the compounds have been confirmed by elemental analysis and spectral analysis. The antibacterial activity of the compounds has also been screened against pathogenic organisms.

Keywords: Synthesis, Benzothiazole, Isoxazoles, Antibacterial activity.

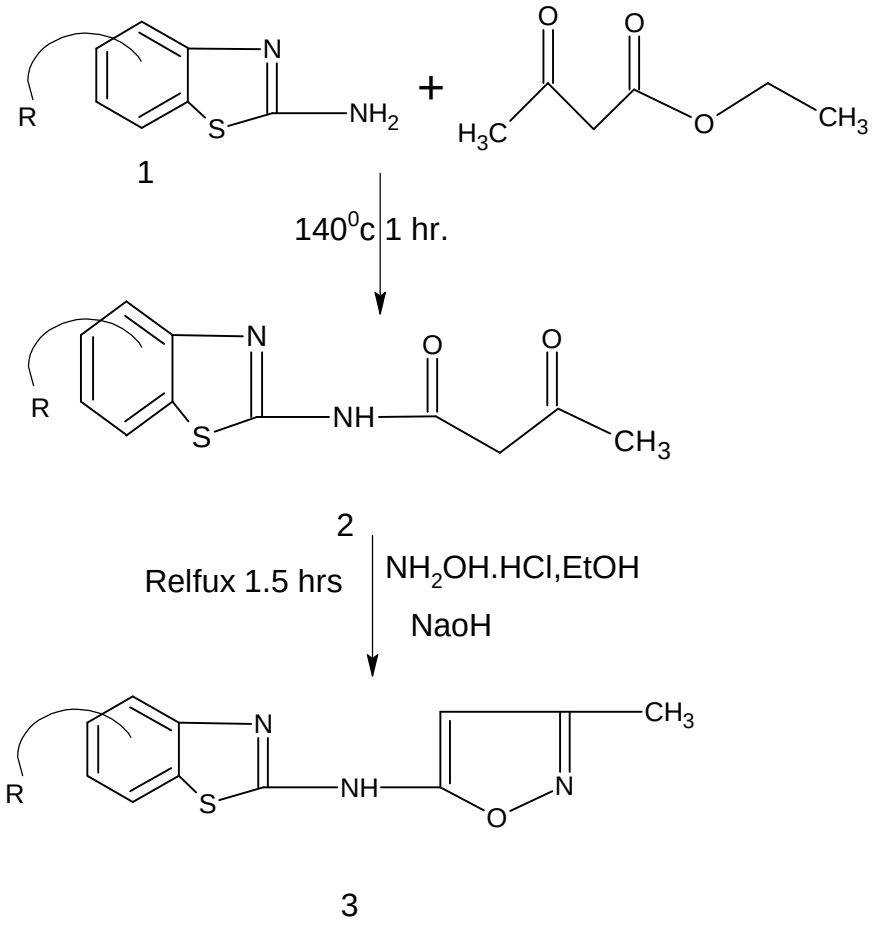
INTRODUCTION

Isoxazoles is a five member heterocyclic ring system containing oxygen and nitrogen atoms. In recent years the synthesis of novel isoxazoles derivatives remains a main focus of medicinal research. Isoxazoles shows antibacterial activity[1**].**Benzothiazole derivative[2,3] were prepared and known to exhibit biological activities as anti-tuberculosis [4], anti-allergic[5].Isoxazoles derivative have been reported to possess antibacterial[6], antitubercular [7], antiviral[8] and antifungal[9]activity. Isoxazoles [10-13] have played a crucial role in the history of heterocyclic chemistry and been used extensively important pharmacophores and synthons in the field of organic chemistry. Isoxazoles were inhibit the growth of gram positive bacteria and also gram negative bacteria [14]. A Novel Series of benzoxazole derivatives were prepared and studied for anti-inflammatory activity[15] The starting compound substituted 2-amino Benzothiazole 1 has been synthesized by oxidative cyclization of substituted phenyl thiocarbamides[16] with the help of molecular bromine.[17,19].

MATERIALS AND METHODS

Experimental

All melting points were determined in open capillary and are uncorrected. The purity of compounds was checked by TLC. The IR spectra were recorded with KBr on Schimadzu FTIR spectrophotometer, PMR spectra of the compounds was recorded in $CDCl_3$+DMSO using tetramethylsilane TMS) as an internal standard. The chemical shifts are quoted in parts per million (ppm) downfield from the internal standards and signals are quoted as *s* (single) and *m* (multiplate).Data of IR and PMR given for representative compound.



Scheme- 1

[R= H, 4 CH_3, 6 CH_3, 4 Cl, 5 Cl, 6 Cl]

Synthesis of 3-carboxamideo-(substituted-benzothizazole-2yl)-propane-2-one (2a)[20]

In a 250 ml round bottom flask mixture of 2-amino –Benzothiazole (0.01 mMol) and aceto-acetic ester (0.01 mMol) were taken. The reaction mixture was heated in oil-bath at 140^0c for 1 hr. The reaction mixture was cooled, diluted with water to get the crude product (2a). The solid product was filtered, dried and recrystalised from 50% ethanol.m.p.170^0c, yield 70%. The compounds (2b-f) were prepared by the same procedure .Their characterization data are shown in the Table 1.

Table 1. Characterization data of compounds (2a-f)

No	R	M.F.(M.W.)	Yield%	M.P^{0}c	% Analysis Cal.(Found)				
					C	H	N	S	Cl
2a	H	$C_{11}H_{10}N_2O_2S$	70	170	56.41 56.03	4.27 4.02	11.96 11.56	13.67 13.35	-
2b	4′-CH_3	$C_{12}H_{12}N_2O_2S$	70	160	58.06 58.06	4.83 4.55	11.29 11.01	12.90 11.29	-
2c	6′-CH_3	$C_{12}H_{12}N_2O_2S$	70	102	58.06 57.56	4.83 4.57	11.29 11.02	12.90 12.70	-
2d	4′-Cl	$C_{11}H_9N_2O_2SCl$	50	146	48.49 48.76	3.35 3.12	10.42 10.02	11.91 11.50	13.22 12.92
2e	5′-Cl	$C_{11}H_9N_2O_2SCl$	70	138	49.16 48.72	3.17 3.15	10.42 10.05	11.91 11.61	13.22 12.87
2f	6′-Cl	$C_{11}H_9N_2O_2SCl$	70	148	49.16 48.72	3.35 3.17	10.42 10.05	11.91 11.61	13.22 12.87

Synthesis of 5-(substituted-benzothizazole-2yl)-amino-3- methyl isoxazoles (3a):
In a 250 ml round bottom flask mixture of 3-carboxamideo-(benzothizazole-2yl)-propane-2one 2a (0.01 mMol) and Hydroxyl amine (0.01 mMol) were taken. About 15 ml ethanol and NaOH (0.01 mMol) was added to it and refluxed for 1.5 hrs. The reaction mixture was cooled, diluted with water to get the product 3a. The solid product was filtered, dried and recrystalised from 50% ethanol.m.p.110^{0}c, yield 60%.

The compounds (3b-f) were prepared by the same procedure .Their characterization data are shown in the Table 2.

Table 2.Characterization data of compounds (3a-f)

No	R	M.F.(M.W.)	Yield %	M.P^0 c	% Analysis Cal.(Found)				
					C	H	N	S	Cl
3a	H	$C_{11}H_9N_3SO$	60	110	57.14 57.05	3.89 3.70	18.18 17.82	13.85 13.62	-
3b	4′-CH_3	$C_{12}H_{11}N_3SO$	80	194	58.77 58.32	4.48 4.02	17.14 16.86	13.06 12.90	-
3c	6′-CH_3	$C_{12}H_{11}N_3SO$	75	180	58.77 58.46	4.48 4.05	17.14 16.88	13.06 12.75	-
3d	4′-Cl	$C_{11}H_8N_3SOCl$	70	210	49.71 49.40	3.01 3.00	15.42 15.12	12.05 11.80	13.37 12.92
3e	5′-Cl	$C_{11}H_8N_3SOCl$	60	110	49.71 48.72	3.01 2.98	15.42 15.08	12.05 11.65	13.37 12.87
3f	6′-Cl	$C_{11}H_8N_3SOCl$	65	185	49.71 48.72	3.01 3.00	15.42 15.10	12.05 11.70	13.37 12.90

Compound (3b): Yield 80% ,m.p.194^{0}c: IR (KBr, cm^{-1}): 3444, 3228 (N-H str.), 1645 (C=N str.), 1279 (C-N str.), 1580 (C=C str.), 736 (C-S str.);PMR($CDCl_3$,δ.ppm): 2.26 (3H, s, CH_3), 2,67 (3H,s,Ar-CH_3) , 6.26(1 H, b,N-H), 6.44-7.25(m, Ar-H).

Compound (3d): Yield 70% ,m.p.210^{0}c: IR (KBr, cm^{-1}): 3467, 3276 (N-H str.), 1635 (C=N str.), 1305 (C-N str.), 1537 (C=C str.), 725 (C-S str.)

RESULTS AND DISCUSSION

Antimicrobial activity

All the synthesized compounds were tested for their antimicrobial activity by measuring the inhabitation area on agar plates by method[21-22] with *Staphylococcus aureus, Escherichia coli,Proteus vulgaris,Pseudomonas areuginosa,Bacillus megatherium* and *Bacillus subtilis* as test germs.

The zones of inhibition were compared with standard Chloramphenicol. The result of antibacterial screening indicated that good activity was shown by compounds 3e, 3f against *Staphylococcus aureus* and compounds 3b, 3c shows good activity towards *Pseudomonas areuginosa.* Other compounds showed moderate activity against both bacterial strains. (Table 3)

Table 3- Antimicrobial activity of isoxazoles, zone of inhibition (mm)

Organism	Compounds						Standard Chloramphenicol
	3a	3b	3c	3d	3e	3f	
Staphylococcus aureus	18	18	12	12	25	25	32
Escherichia coli	16	18	14	-	-	16	30
Proteus vulgaris	14	-	-	-	13	14	32
Pseudomonas areuginosa	16	22	24	16	18	18	32
Bacillus megatherium	14	18	16	15	18	15	30
Bacillus subtilis	10	12	14	10	10	-	30

Acknowledgement

The authors are thankful to Dept.of Microbiology of Shri Shivaji Science College Amravati, for antimicrobial activity and NCL Pune for providing IR and PMR spectra.

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