"ONE POT SYNTHESIS OF BENZOTHIAZAOLE DERIVATIES AND THEIR CHARACTERIZATION"

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ABSTRACT–

Benzothiazole ring made from thiazole ring fused with benzene ring. Thiazole ring is a five-member ring consists of one nitrogen and one sulphur atom in the ring. A number of 2-aminobenzothiazoles have been studied as central muscles relaxants and found to interfere with glutamate neurotransmission in biochemical, electrophysiological and behavioral experiments. Various 2-Substituted benzothiazole derivatives in moderate to good yield have been prepared in a one-pot reaction by condensation of 2-aminobenzene thiol and different aromatic aldehyde in the present of ammonium chloride as a catalyst and ethanol as solvent 80^0-90^0C. The reaction is green and economically viable. The characterization of newly synthesized compounds was made by chemical properties, elemental analysis and FT-IR,^{1}H-NMR and Mass Spectra. The advantage of this method is extremely mild reaction conditions, short reaction time, high yield, simple experimental technique and compliance with green chemistry protocols.

KEY WORDS- One pot, synthesis and characterization.

1. INTRODUCTION

The development of simple, efficient, environmentally-bengin and economically viable chemicalprocess or methodologies for widely used organic compounds is in great demand [1]. Benzothiazole is a heterocyclic compound, weak base having varied biological activities and still of great scientific interest now a days. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. Benzothiazole moites are part of compounds showing numerous biological activities such as antimicrobial[2-6], anticancer[7-9,10], anthelmintic[11], anti-diabetic[12] activities.Antimicrobial agents, since their discovery have substantially reduced the threats posed by infectious diseases. The use of these 'wonder drugs' has led to a dramatic drop in deaths from diseases that were previously widespread, untreatable and frequently fatal. Over the years, antimicrobial have saved the lives and eased the suffering of millions of people. But today's main concern is the emergence and spreads of microbes those are resistant to economical and effective first-line drugs. The bacterial infections which contribute most to human diseases are also those in which emerging and microbial resistance is most evident. Some important examples include diarrhoeal diseases, respiratory tract infections, meningitis, penicillin-resistant Streptococcus Pneumoniae, vancomycin-resistant enterococci, and multi-resistant Mycobacterium Tuberculosis. When infections become resistant to first line antimicrobials, treatment has to be switched to second or third line drugs which are nearly always much more expensive and more toxic as well e.g. the drug needed tontrat multi drug-resistant form of tuberculosis are over 100 times more expensive than the first line drugs used to treat non-resistant forms[13].Cancer is currently second leading cause of death aftercardiovascular disease. Consequently, there is greatunmet medical need for new anticancer small moleculetherapeutics. A tumour is an abnormal mass of tissue,the growth of which exceeds and uncoordinated withthat of normal tissue and continues in the same mannerafter cessation of the stimuli which have initiated it[14].Wealth of basic knowledge with regard to molecularand cellular biology, better understanding ofmechanism of cellular division, tumourimmunologyand detailed information of fundamental factorsinvolved in both viral and chemical carcinogenesis andthe improved investigative techniques have ultimatelyled to the introduction of a substantial number ofnewer antineoplastic agents[15].Benzothiazole is a privileged bicyclic ring system. It contains a benzene ring fused to a thiazole ring. The small and simple benzothiazole nucleus is present in compounds involed in research aimed at evaluating new products that possess interesting biological activities like- antimicrobial,antitubercular, antitumour, antimalarial, anticonvulsant,anthelmintic, analgesic and anti-inflammatory activity[16].2-aminobenzothiazole derivatives were prepared from the substituted aromaticamines, in the presence of ammonium thiocyanateformsubstituted 1-phenylthiourea in acidic medium. Thissubstituted 1-phenylthiourea in the presence of oxidizing agent like bromine is cyclised into substituted 2-aminobenzothiazoles. The titled compounds wereevaluated for anti-inflammatory property by λ-Carrageenan-induced paw edema method in rats[17]. Several synthetic methodologies were available for the synthesis of benzothiazole .Generally the condensation of 2-aminobenzene thiol with aldehyde and their nitrile,imide and orthoesters derivatives have been widely used for benzothiazole.

2.EXPERIMENTAL DETAILS

2.1The melting points of all synthesized compound were recorded using hot paraffin bath and are uncorrected. ^{1}H NMR spectra ($CDCl_3$) were recorded on Bruker Advance II 400 NMR spectrophotometer using TMS as internal standard. IR spectra were recorded on Perkin-Elmer-1800 FTIR spectrophotometer in the frequency range 4000-450 cm^{-1} in Nujol mull and as KBr pellets. Mass spectra were recorded on a LC-MS Q-Tof Micro, Mass analyzer (Shimadzu). Chemicals used were of AR grade. The purity of the compound was checked on silica gel-G plates by TLC.

2.2General procedure for the synthesis of 2-(4-methoxyphenyl-2,3-dihydrobenzo thiazole(3c)

2-aminobenzene thiol (1) (0.01 mole) and anisaldehyde (2c) (0.01 mole) both instoichiometric proportion was taken in ethanol as solvent in presence of NH_4Cl as a catalyst. The reaction mixture was stirred for 4hrs at 90^0C on hot plate. After completion reaction, the reaction mixture was cooled and poured in the ice cold water. The granular solid was obtained. It was crystallized from the alcohol, yield 88.00%, m.p.120^0C.

IR(KBr) ν = 3190 (-NH), ν = 1591 (C=N), ν =1424 (C=C),ν = 1321 (C-N), ν =852 1,4-disub Aromatic ring & ν =762 1,2-disub Aromatic ring cm^{-1}.
^1H NMR ($CDCl_3$) 8.19 ppm (2H, d, Ar-H), δ7.64 ppm (2H, d, Ar-H), δ7.54 ppm (2H, d, Ar-H), δ7.12ppm (2H, d, Ar-H).Mass (m/z) 229 (M^+).

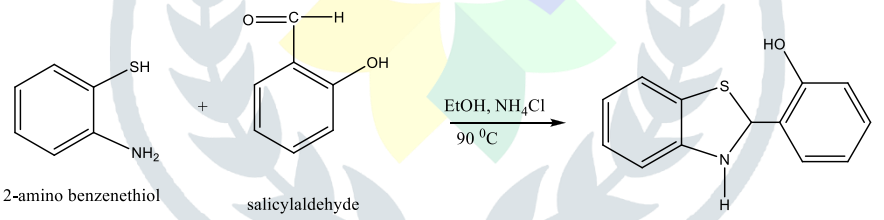
2.2Preparation of 2-(2,3-dihydrobenzo thiazole2yl)-phenol (3e).

2-Aminobenzene thiol (1) (0.01 mole) and salicyladehyde (2e) (0.01 mole) both instiochiometric proportion was taken in ethanol as solvent in presence of NH_4Cl as a catalyst.The reaction mixture was stirred for 5hrs at 90 ^{0}c on hot plate.After completion of reaction, the reaction mixture was cooled and poured in the ice cold water. The granular solid was obtained. It was crystallized from the alcohol. yield 89.18%, m.p.115^{0}C.
IR(KBr) ν = 3190 (-NH), ν = 1591 (C=N), ν =1424 (C=C),ν = 1321 (C-N), ν =852 1,4-disub Aromatic ring & ν =762 1,2-disub Aromatic ring cm^{-1}.^1H NMR ($CDCl_3$) 8.19 ppm (2H, d, Ar-H), δ7.64 ppm (2H, d, Ar-H), δ7.54 ppm (2H, d, Ar-H), δ7.12ppm (2H, d, Ar-H).Mass (m/z) 229 (M^+).
All other compounds (3c-e) were synthesized in similar manner by treatment of (1) with substituted aromatic acids (2c- e) respectively **Table No.1.**

Table No.1: Reaction of o-phenylene diamine (1) (0.01 mole) with different aromatic acids (2) (0.01 mole) :

Sr. No	Product (3)	-R (2a-e)	Yield (%)	Melting Point^{0}C	Molecular Formula	Elemental analysis of N Found (Calcd.) (%)		
						C	H	N
1	3a	p-chlorobenzoic acid	78.88	260	$C_{13}H_9ClN_2$	68.15 (68.28)	3.79 (3.97)	12.22 (12.25)
2	3b	Salicylic acid	79.18	120	$C_{13}H_{10}N_2O$	73.80 (74.27)	4.21 (4.79)	13.00 (13.33)
3	3c	Benzoic acid	75.08	90	$C_{13}H_{10}N_2$	80.11 (80.39)	5.01 (5.19)	14.30 (14.42)
4	3d	o-chloro benzoic acid	90.08	200	$C_{13}H_9ClN_2$	68.15 (68.28)	3.79 (3.97)	12.22 (12.25)
5	3e	Cinnamic acid	72.15	170	$C_{15}H_{12}N_2$	81.60 (81.79)	5.40 (5.49)	12.68 (12.72)
6	3f	p- hydroxy benzoic acid	78.88	190	$C_{13}H_{10}N_2O$	73.95 (74.27)	4.21 (4.79)	13.00 (13.33)

REACTION SCHEME – Synthesis of be derivatives**.**



2-amino benzenethiol salicylaldehyde 2-(2,3-dihydrobenzo (d) thiazole 2-yl phenol

3.RESULTS AND DISCUSSION

In order to synthesized substituted Benzimidazole derivatives (3), a relatively more versatile yet simplified procedure was perceived. Our argument have been that an instantaneous condensation of o- phenelene diamine and aromatic acid at 80- 90 ºC to affords substituted Benzimidazole with the use of NH_4Cl as catalyst. The strategy worked well affording the desired product in respectable yields. (Table No.1), the present reaction have been relatively faster, as anticipated, comp aired to those in conventional solution phase synthesis. It is necessary to mention that in all cases the conversion was never 100 %. Some amount of starting material recovered after each reaction.

4.CONCLUSION

In conclusion we have developed a simple methodology for the preparation of substituted Benzimidazole derivatives (3).The advantage of this method are extremely mild reaction conditions , short reaction time , high yield , simple experimental technique and compliance with green chemistry protocols.

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