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Research

Design, Synthesis, Characterisation and Biological Study of Pyrimidine Based Heterocycles

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Abstract:
A series of novel 4-(2-amino-6-(substituted phenyl)pyrimidine-4-yl)-2,6-dibromobenzene-1,3-diol, were synthesized from different substituted 2,3-dibromo-1-(3,5-dibromo-2,4-dihydroxyphenyl)-3-(substitutedphenyl)propane-1-one and guanidine hydrochloride were dissolved in ethanol. Double the quantity of sodium hydroxide was dissolved in minimum amount of water and added to reaction mixture. After 6Hrs. reflux, it was poured into 250 ml of water and recrystalized the structures of the compounds were elucidated by elemental and spectral (IR, 1H NMR,) analysis. The synthesized compounds were checked for biological evaluation i.e. antimicrobial study.

Keywords: Chalcone, Pyrimidine, biological evaluation.

Introduction

The chemistry of heterocyclic compounds is as logical as that of aliphatic or aromatic compounds[1-5]. Their study is of great interest both from the theoretical as well as practical importance. Various compounds such as alkaloids, essential amino acids, vitamins, haemoglobin, hormones, large number of synthetic drugs and dyes contain heterocyclic ring systems[6-16]. There are large number of synthetic heterocyclic compounds, like pyrrole, pyrrolidine, furan, thiophene, piperidine, pyridine and thiazole having important application and many are important intermediates in synthesis[17-20]. Fused pyrimidines continue to attract considerable attention because of their great practical usefulness, primarily due to very wide spectrum of biological activities[21-22]. This is evident in particular from publications of regular reviews on the chemistry of systems where the pyrimidine ring is fused to various heterocycles such as purines, pteridines, quinazolines, pyridopyrimidines, triazolopyrimidines, pyrazolopyrimidines, pyrimidoazepines, furopyrimidines and pyralopyrimidines.

Materials& Methods

Step I - Synthesis of 1-(3,5-dibromo-2,4-dihydroxyphenyl)ethanone

In hot glacial acetic acid, fused zinc chloride was added and refluxed till solid was dissolved. Then powdered 2,4-dibromobenzene-1,3-diol was added and refluxed for eight hours. The reaction mixture was cooled and then poured in acidulated water. The solid obtained was filtered, washed with water and recrystallized from rectified spirit to obtain titled compound. Thus following compounds were synthesized.

Step II - Synthesis of (E)-1-(3,5-dibromo-2,4-dihydroxyphenyl)-3-(subsitutedphenyl)prop-2-en-1-one (3a-d)

In ethanol solvent, 2,4-dibromobenzene-1,3-diol and Substituted aromatic aldehyde were added. To this mixture, drop wise added 10 % of KOH solution with constant stirring. The reaction mixture was kept overnight. Then this mixture was poured over HCl and crushed ice. The product (E)-1-(3,5-dibromo-2,4-dihydroxyphenyl)-3-(subsitutedphenyl)prop-2-en-1-

one (3a-d) was filtered and recrystalized from ethanol.

Step III – Synthesis of 2,3-dibromo-1-(3,5-dibromo-2,4- dihydroxyphenyl)-3-(substituted phenyl)propane-1-one (4a-d)

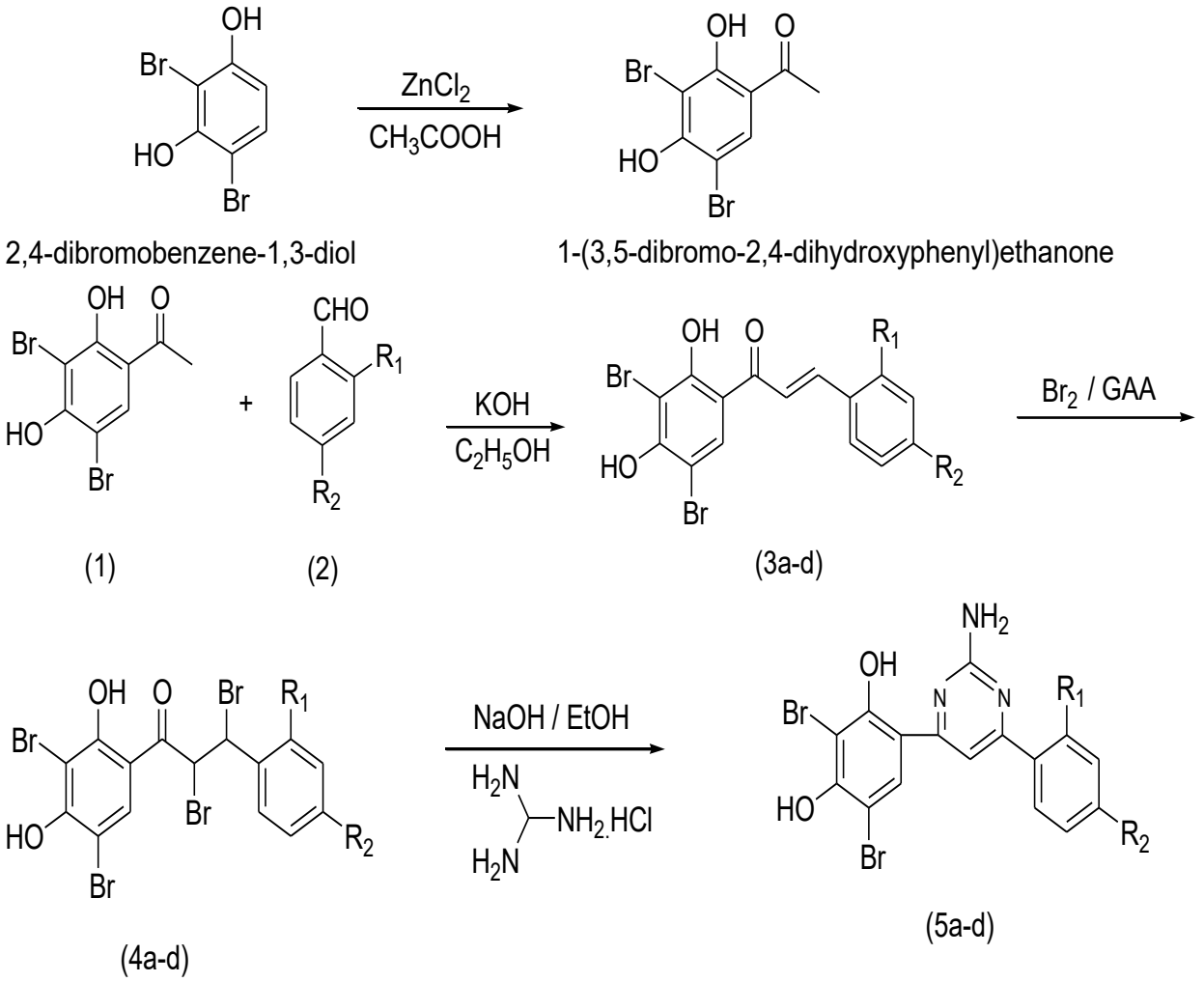
An equimolar quantity of (E)-1-(3,5-dibromo-2,4-dihydroxyphenyl)-3- (substituted phenyl)prop-2-en-1-one (3a-d) were dissolved in glacial acetic acid by warming. The solution was cooled at room temperature and treated with the solution of bromine in glacial acetic acid till the yellow color of bromine of persisted. The solution was allow to stand overnight, when crystal of 2,3-dibromo-1-(3,5-dibromo-2,4- dihydroxyphenyl)-3-(substituted phenyl)propane-1-one (4a-d) separated out.

Step IV - SYNTHESIS OF PYRIMIDINE DERIVATIVES (5a-d)

An equimolar quantity of 2,3-dibromo-1-(3,5-dibromo-2,4- dihydroxyphenyl)-3-(substituted phenyl)propane-1-one (4a-d) and guanidine hydrochloride were dissolved in ehhanolic sodium hydroxide solution and stirred for about 5-6 hours. This was then poured into cold dilute hydrochloric acid with continuous stirring for an hour and kept in refrigerator overnight and participate obtained was filtered and dried. It was then recrystalized using petroleum ethanol.

Result &discussion:

SCHEME



The structure of synthesized compound has been elucidated by IR and H^1 NMR analysis. IR spectra shows absorption band at expected values. H^1 NMR showed the proton of aromatic ring at excepted chemical shift and integral value. The probable mechanism has been suggested for the formation of Pyrimidine derivatives.

Table1: Physical property of compounds

Spectral Analysis (Compound No. 5d):

Compounds	R_1	R_2	Molecular Formula	MP◦C	%Yield	R.F. Value	% Nitrogen	
							Found	Calculated
5a	OMe	OMe	$C_{18}H_{15}O_4N_3Br_2$	170	42%	0.65	10.89	10.85
5b	H	NO_2	$C_{16}H_{10}O_4N_4Br_2$	187	36%	0.61	11.19	11.91
5c	H	OMe	$C_{17}H_{13}O_3N_3Br_2$	150	39%	0.68	10.32	11.40
5d	OMe	H	$C_{17}H_{13}O_3N_3Br_2$	151	52%	0.62	09.68	10.71

IR analysis (wave number in cm^{-1}) 3100-3000 (Ar-H stret.), 3200-3300(-OH stret), 3200-3250(-NH_2stret), 1675-1575(-NH stret), 1610-1620 (C=N stret), 1550-1475(N-O stret), 2815-2832(O-CH3 stret).

NMR analysis (δ ppm): 4.00 (-NH_2, 2H),5.35 (-OH,1H) ,6.8-8.0 (Ar-H , 7H), 3.73(-OCH3, 3H).

Biological evaluation:

Antimicrobial agents, sometimes known as medicines, are substances that stop microorganisms such as bacteria, fungus and viruses from growing. The primary physiological issues that negatively impact an individual's body are infections. Bacteria are the source of many infectious illnesses. Antibiotics are medications used to treat bacterial infections. Two different kinds of techniques can be used to track the development of such alien germs. Additionally classified into two categories, antibiotics are based on how they influence bacteria. The antibacterial activity of the molecule synthesised is examined against both gram-ve and gram+ve bacteria, with gram-ve bacteria being *E. coli, S. typhi* and *A. aerogenes* and gram+ve bacteria being *S. aureus, B. subtilis* and *B. megatherium*, which cause illness.

Disc diffusion method

To use the disc diffusion technique for screening each sample, fresh, sterilized nutrient agar medium was created. All of the apparatus, equipment and glassware were sanitized before to the experiment's start. Each sterile petri plate was filled with 10–25 cc of melted liquid. A diluted organism culture of 0.05–0.1 mL (about 2-3 drops) was added to each petri dish that was being observed. At room temperature, the solidified nutrient agar medium was equally covered with the nutrient broth culture. Next, the prepared compound sample was gently wet onto 6 mm diameter, sterile Whatman filter paper No. 1 discs on the plate. Concurrently, a disk that had been wet with 70% methanol was used as a control. After dispersing the filter paper across the plates, they were incubated at 37 °C for 24 hours. It was measured and noted how big the zone of inhibition that the specific medication created was.

The potato dextrose plate was utilized instead of the standard method to assess antibacterial.

Result and Discussion

From result it is very clear that some of the compounds are against gram positive and gram negative bacterial and exhibited good antimicrobial activity. On the basis of screening data it was observed that these heterocyclic compounds can be easily used against treatment of disease caused by test microbes.

Antibacterial Activity of Compounds

Sr. No.	Compound code	Gram positive			Gram negative		
		S. aureus	*B. subtilis*	*B. megatherium*	*S. typhi*	*E. Coli*	*A. aerogenes*
1	Ia	Inactive	Active	Active	Active	Active	Inactive
2	Ib	Active	Active	Active	Active	Inactive	Inactive
3	Ic	Active	Active	Active	Active	Inactive	Inactive
4	Id	Active	Inactive	Active	Inactive	Inactive	Inactive
5	Ie	Active	Active	Active	Active	Inactive	Active
6	Ethanol (Con)	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive
7	Standard (Ciprofloxacin)	Active	Active	Active	Active	Active	Active

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