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SYNTHESIS OF BROMO BENZYL AMINE SUBSTITUTED CHROMENE AND THEIR ANTIMICROBIAL ACTIVITY

Mr. Mejo joseph*, Dr. S. Alaxander, Dr. D, Sudhahar
* Faculty of pharmacy Nehru College of pharmacy, Kerala. India
Faculty of pharmacy Vinayaka Mission College of pharmacy, Salem, Tamil nadu, India

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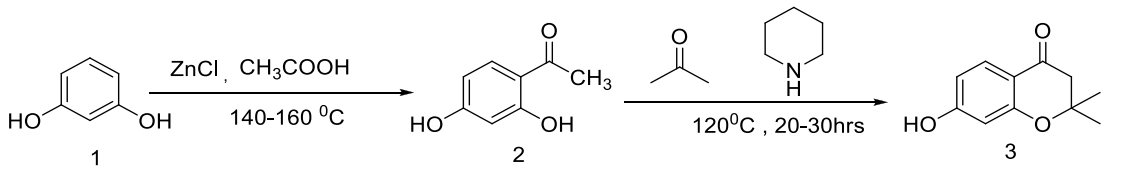
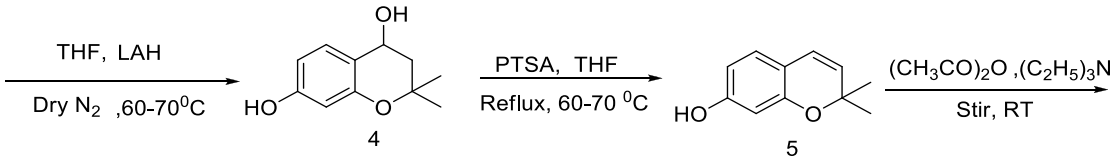
ABSTRACT
The benzopyran derivatives are present many of biological sources and having wide variety of pharmacological activities .They act as antitumor agents and have photochromic effects.Pharmacological study of these derivatives showed antispasmodic activity and possess a higher level of coronary dilatory action.Benzopyran derivatives also have a benificial effects in preventing some type of naphylaxis in animals and anti-allergic or anti asthmatic action in human.chromene also possess antimicrobial activities against gram positive and gram negative microorganisms.

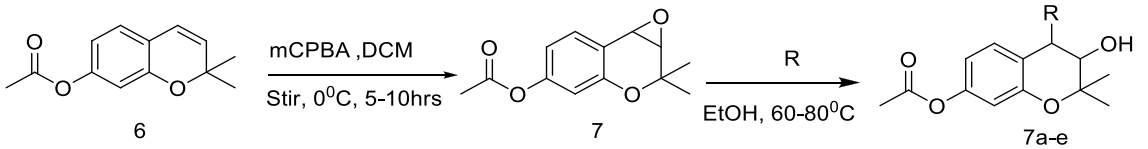
INTRODUCTION
Medicinal chemistry is the branch of science, which has remarkable value for synthesis of novel drugs with intense therapeutic activity. Compounds with benzene and a pyran ring are fused together are called chromene. The major classes of these compounds are 1-benzopyran and 2-benzopyran.It concerns with discovery, development, identification and interpretation of mode of action of biologically active compounds at molecular level. These developments have provided new challenges and opportunities for drug research in general and drug design in particular. The major objectives of the medicinal chemists are transformation of patho biochemical and physiological data into a`chemical language' with the aim of designing molecules interacting specifically with the derailed or degenerating processes in the diseased organisms. Benzopyran compounds are important because many of them occurs naturally and shows many activities .The discovery of benzopyran is in the 19th century, their naming has changed several times. Examples are the cyclic system of chromene lacked uniformily in the early literature.3-aryloxy propionic acid has been cyclised to 4-chromanones using acetyl chloride and sulphuric acid. The yield was 27%.almost all benzopyran derivatives having marked anti-microbial activity

EXPERIMENTAL
MATERIALS AND METHODS: An anti-microbal activity was carried out at Nehru College of pharmacy, Kerala, Department of microbiology. Suitable media were prepared. Details about media preparation described in methodology part. Melting point of each step products are carried out by using Gallenkamp melting point apparatus. The purity of the compounds was checked by TLC, Merck Silica Gel 60f 254 .using Hexane and Ethyl acetate 6:4 ratio solution as mobile phase.

SCHEME OF SYNTHESIS





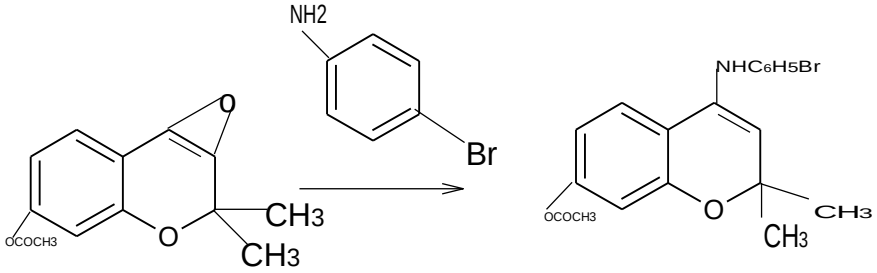


R= benzylamine, 4-F benzylamine,4-methoxy benzylamine,
4-methyl benzylamine, 4-F aniline

4-chloro aniline

SYNTHESIS OF DERIVATIVES

To a 50 ml of RBF 250mg (1.066 mmol) of compound 7a-e was taken in 30ml of ethanol. After that 0.271ml (2.136 mmol, 2 equivalents) of 4-bromo aniline was added, reaction was refluxed at 80⁰C for 4hours. After completion of reaction the solvent was evaporated.



M+1 Peak: 313

The anti-bacterial screening was carried out in the pharmaceutical biotechnology laboratory, Nehru College of Pharmacy, Pampady, Thrissur.

MEDIA USED IN THE STUDY

Nutrient agar

Nutrient agar at concentration of 2%.(Bacteriological grade)

Ingredients

Peptic digest of animal tissue	: 5g/Ltr
Sodium chloride	: 5g/Ltr
Beef extract	: 1.5g/Ltr
Yeast extract	: 1.5g/Ltr
Agar	: 50g/Ltr
Final PH (at 25^0c)	: 7.4

Preparation

The ingredients dissolved in distilled water and heated to maintain.PH to 7.2-7.6 using alkali diluted acid.15-20ml of Nutrient Agar was then autoclaved at a pressure of 15psi(120 ^{0}c) for 20 min. and the organisms used are *S.aureus* MTCC 405,*Pseudomonas aeroginosa* ,were collected from Institute of Microbial Technology, Chandigarh. The strain was confirmed for their purity and identity by Gram's staining method and characteristic biochemical reactions. The selected strains were preserved by sub-culturing them periodically on other slants and storing them under frozen conditions .For the study, fresh 24 hrs broth cultures were used after standardization of the culture. The entire work was done using horizontal laminar flow hood at Nehru College. So as to provide aseptic conditions in absence of bacterial growth. Confirmed by aseptic working condition. The medium for the experiments were prepared fresh in Nutrient agar from preserved frozen slant culture. It as kept incubated at 37^0 c for one day.

Drug used: t_1 (1000mcg/100ml)

Standard used: Levofloxacin (5mcg/disc)

Vehicle used: Ethanol

ANTIBACTERIAL SCREENING

Two Nutrient agar plates were prepared aseptically to get a thickness of 5-6 mm. The plates were allowed to solidify and inverted to prevent the condensate falling on the agar surface. The plates were dried at 37^0 c before inoculation. The organisms were inoculated in the plates prepared by spread plate method. i.e, using a micropipette, the culture place randomly on the agar plate and it is spread by using L-shaped glass rod where it is just touch the surface of the agar and rotating it to to and fro direction.

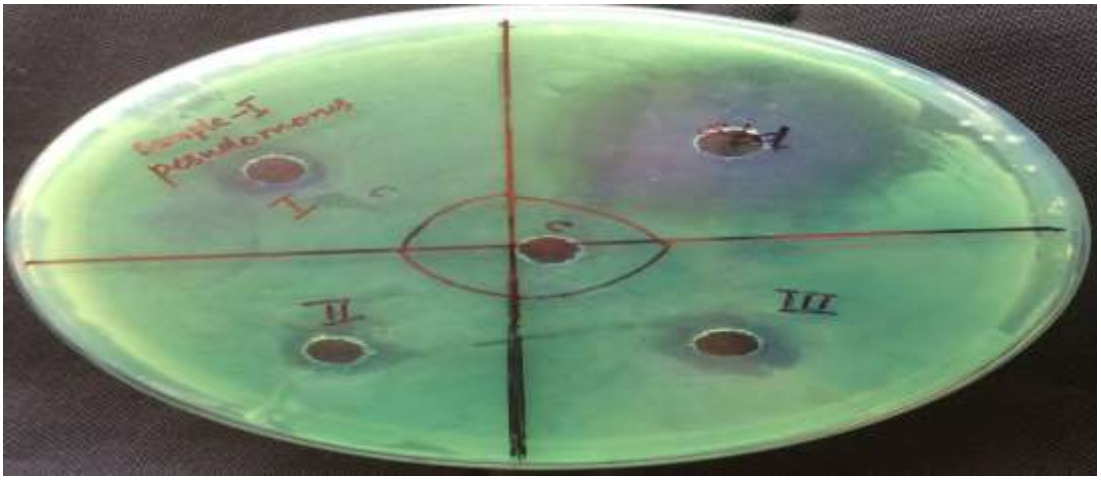
The organism used were Gram positive S.*aureus* and Gram negative *Pseudomonas aeroginosa*

The standard and test drugs were introduced in two agar plates by using **cup plate method.**

- By using the tips of borer, the four agar wells were made at each quadrant and central well for control.

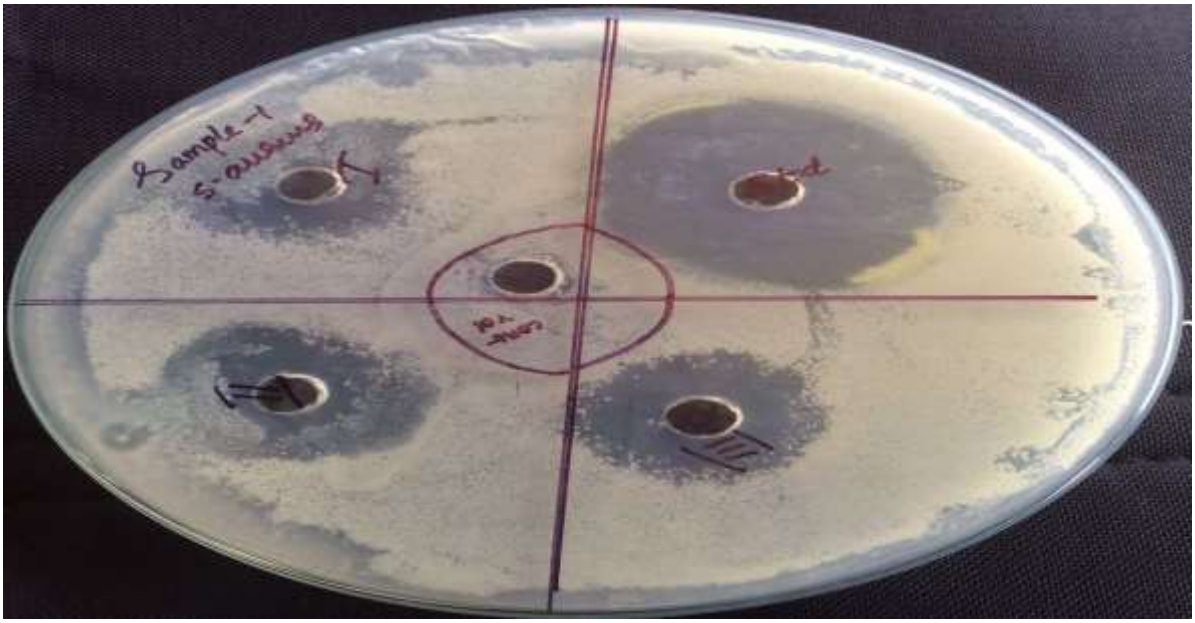
- Add three different dilution of test drug which has been prepared from previously prepared stock solution of 1g test drug per 100mL ethanol.
- The different dilutions are prepared by taking 1ML stock solution and dilute with 4ML solvent(ethanol) similarly two more dilutions were prepared in the ratio 2:3 and 3:2.
- Also add the standard drug to one well, which has prepared in the ratio 1:4 and ethanol was added as control at the centre.
- By kept in the refrigerator for one hour to make uniform diffusion of drugs.
- Two plates prepared were then incubated for one day..
- The zone of inhibition around the drug and compared with of standard. The compound synthesized was tested for antibacterial activity against gram positive and gram negative bacteria.

Zone of inhibition of the compound against Gram negative *Pseudomonas aeroginosa*
Drug used: Test sample (1000mcg/100ml) of different dilution in the ratio 1:4, 2:3 & 3:2
Standard: Levofloxacin (1mL/4ml)
Solvent: Ethanol



Name of organism	Compounds	Dilutions (compound: Solvent)	Total Diametre (T) (cm)	Well Diametre(W)	Zone of Inhibition (T-D)*10 mm
Pseudomonas aeroginosa	Standrad	1:5	4:3	0.6	34
	Solvent	_	_	0.6	_
	Sample	1:4	1.5	0.6	12
		2:3	1.8	0.6	14
		3:2	1.9	0.6	14

Zone of inhibition of the compound against Gram positive *S.aureus*
Drug used: Test sample (1000mcg/100ml) of different dilution in the ratio 1:4, 2:3 & 3:2
Standard: Levofloxacin (1mL/4ml)
Solvent: Ethanol



Name of organism	Compounds	Dilutions (compound : Solvent)	Total Diametre (T) (cm)	Well Diametre (W)	Zone of Inhibition (T-D)*10 mm
S.aureus	Standrad	1:4	4.1	0.6	35
	Solvent	–	–	0.6	–
	Sample	1:4	2.2	0.6	16
		2:3	2.6	0.6	23
		3:2	3.1	0.6	26

RESULT AND DISCUSSION

The antibacterial activity of newly synthesized compound was evaluated by using both gram positive and gram negative organisms..*S.aureus*, *Pseudomonas aeroginosa*

Various dilution of 1000mcg/100ml has been for the test compound, results were compared with the standard Levofloxacin 1mL\4mL concentration and ethanol .The results were interpreted as the KB method The test organism *Pseudomonas aeroginosa* was found to be moderately sensitive at given concentration of test compound. And the organism *S.aureus* was found to be highly sensitive at given concentration of test compound

CONCLUSION

From these findings, the results concluded that the selected compound possess promising antimicrobial activity against selected pathogenic microorganism. The investigation of the selected compound and it possible mechanism of action due to the presence of bromine atom in para position is crucial for significant activity. This is an useful approach to develop new synthetic agents for antimicrobial activity.

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CONFLICT OF INTEEST

Authors have no conflict of interest.

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