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Synthesis of novel Tetrazole derivatives and their biological evaluation

Sumalatha P[1], Ravi Kumar G[2*]
[1]Department of Chemistry, Government Degree College, Husnabad 505467, Telangana.
[2]Department of Chemistry, Kakatiya Government College, Hanamkonda 506001, Telangana.
***Corresponding author**: E-mail:ravig333@gmail.com

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ABSTRACT

Tetrazole have very important biological activity. We have synthesized the 10 novel tetrazole derivatives characterized by 1H NMR 13C NMR HRMS and evaluated antibacterial and antifungal activity. Among the compounds compound 6g shows prominent activity.

1. INTRODUCTION

Tetrazole chemistry has very much importance in the drugs discovery. The current drugs which are having tetrazole pharmcore group are losartan. This losartan compound is used in the salt form as losartan potassium. The terazole pharmacore group shows antibacterial, antifungal, antiplatelet, antifungal, anticancer, anti HIV, anti-inflammatory activities.

Now a days Antibiotics has much importance. Latest antibiotics which we are currently using oflaxcin was invented in the 1985. From that year onwards no new antibiotics were synthesized. As the days goes on the bacteria is developing the much resistance to the latest drugs. So the bacterial devolving multidrug resistance, finally our human beings are the victims. So the world is looking for new antibiotic which is very strong to fight against the all types of bacteria gram positive and gram negative.

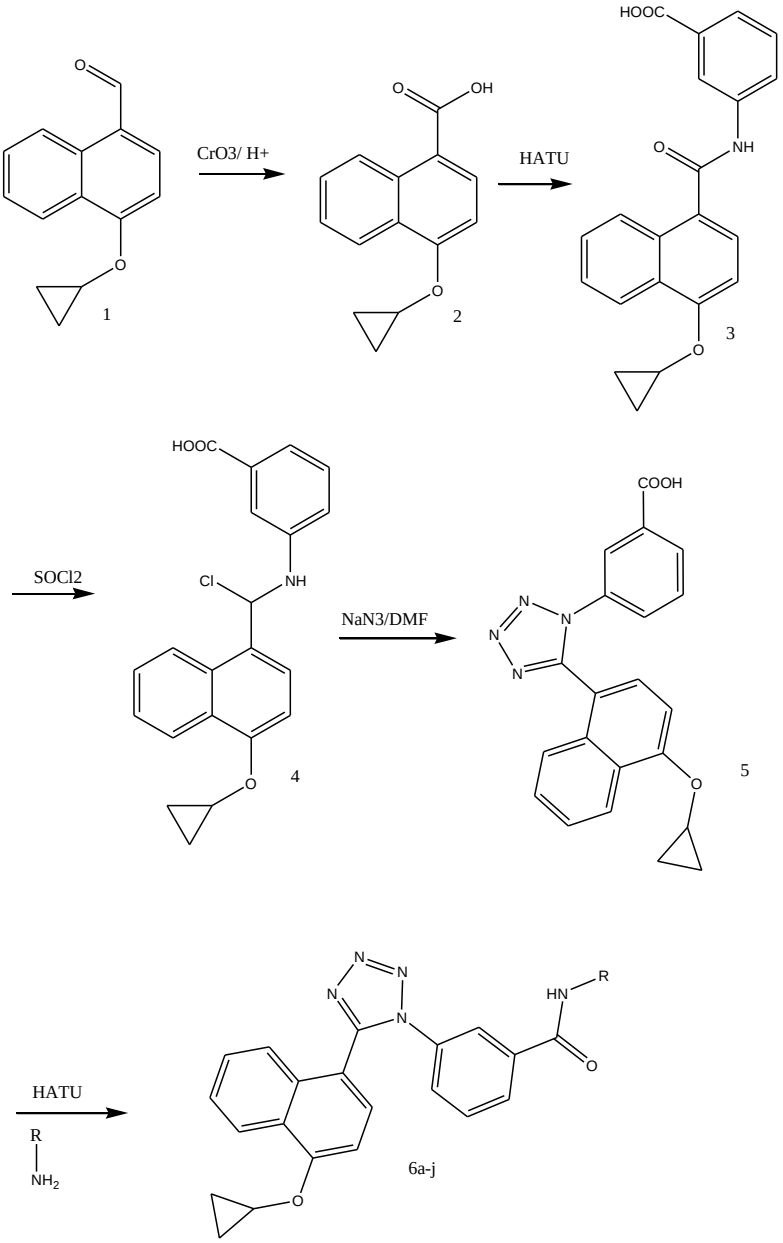
2. MATERIALS AND METHODS

Compound 1 on oxidation reaction with chromium trioxide in acidic medium, aldehyde is converted into carboxylic acid. The obtained carboxylic acid on reaction with meta amino benzoic acid the amide derivative compound 3 was obtained. The acid to amide conversion was completed by using HATU reagent. The obtained compound with excellent yields. The formed compound 3 on reaction with thionyl chloride chloro derivative was obtained as compound 4.

Compound 4 on reaction with sodium azide in DMF tetrazole derivative was obtained. The terazole derivative on reaction with different types of amines respective amide derivatives obtained.

3. RESULTS AND DISCUSSION:

The final 10 derivatives of tetrazole were subjected to the antibacterial activity through agar diffusion method different types of bacteria were used for evaluations. The used bacteria were *Bacillus subtilis*, Streptomyces, *Escherichia coli*, *Streptococcus lactis* and Pseudomonas species and antifungal activity against various fungi viz. (*Aspergillus niger*, Penicillium species) and yeast (*Candida albican* and *Rhodotorula ingeniosa*). Compound 2 was obtained in average yield. The acid amine coupling was done by different types of coupling reagents like EDC.HCL, T_3P, HATU, amomg the coupling reagents the HATU coupling reagent gives excellent yield. The compound 4 was obtained in good yiled with thionyl chloride. For this OH to Cl conversion we had tried with $POCl_3$ and thionyl chloride, but the thinly chloride gives better results than with $POCl_3$. Compound 5 was obtained with good results and final targets were obtained in good results.



Scheme 1

Table.1.Antimicrobial activity of final derivatives IC_{50} (µg ml^{-1})

Compound no	Fungi			Bacteria			
	Rhodotorula ingeniosa	***Candida albican***	**Penicillium species**	***Escherichia coli***	**Pseudomonas species**	***Streptococcus lactis***	***Bacillus subtilis***
6a	125	100	105	85	95	90	85
6b	85	89	95	68	87	88	56
6c	95	>200	>200	>200	>200	>200	>200
6d	>200	>200	>200	>200	>200	>200	>200
6e	>200	>200	>200	>200	>200	>200	>200
6f	>200	>200	>200	>200	>200	>200	>200
6g	25	20	30	40	12	10	8
6h	100	145	150	145	144	156	147
6i	95	99	78	45	85	88	84
6j	>200	>200	>200	>200	>200	>200	>200
Amoxcilin	-	-	-	15	20	20	25
Fusidic acid	15	17	18	-	-	-	-

4. CONCLUSION

Compounds 6b, 6g, 6h, 6i, show prominent activities than the rest of the compounds. The compounds 6c 6d, 6e, 6f show very poor activity against both fungi and bacteria. Finally the compound 6g shows better results among the all the compounds against both bacteria and fungi. Tetrazole had excellent antimicrobial activities, but in the case of present scheme only 6g show better activity. So by changing the groups around it may give better biological activity.

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