Available online at www.ilcpa.pl

International Letters of Chemistry, Physics and Astronomy

12 (2014) 1-6 ISSN 2299-3843

Synthesis, characterization and antimicrobial activity of some new dihydropyrano[c]chromenes

Ankita Bhalu[1], Pooja Moteriya[2], Sumitra Chanda[2], Shipra Baluja[1,*]

[1]Department of Chemistry, Saurashtra University, Rajkot 360005, India

[2]Department of Bioscience, Saurashtra University, Rajkot 360005, India

*E-mail address: shipra_baluja@rediffmail.com

ABSTRACT

Some new dihydropyrano[c]chromenes derivatives are synthesized from 4-hydroxycoumarin. The structure of newly synthesized compounds was confirmed by mass, ^{1}H NMR and IR spectroscopy. Further, antimicrobial screening of these synthesized compounds was done against some bacterial (Gram positive as well as Gram negative) and fungal strains in N,N-dimethylformamide. It is observed that some of synthesized compounds exhibited significant antibacterial activity against Gram positive bacterial strains. The selected fungal strains were most resistant for the studied compounds as none of the synthesized compounds showed activity against any of the fungal strain studied. The best antibacterial activity was shown by ABR-10.

***Keywords*:** Dihydropyrano[c]chromenes; Antibacterial activity; Gram positive bacteria; Gram negative bacteria; N,N-Dimethylformamide

1. INTRODUCTION

Coumarin constitutes one of the major classes of naturally occurring compounds and interest in its chemistry continues unabated because of its usefulness as biologically active agents. It also represents the core structure of several molecules of pharmaceutical importance. This class of compounds are known to exhibit a wide spectrum of biological activities such as antioxidant [1-2], anti-inflammatory [3-4], anticoagulant [4], antibacterial [5-6], antitumour [7-8], etc. These pharmacological properties aroused our interest in synthesizing some new coumarin derivatives with the aim of testing their microbial efficacy.

Thus, in the present work, some new dihydropyrano[c]chromenes are synthesized. The structure of newly synthesized compounds was confirmed by mass, 1H NMR and IR spectroscopy. Further, antimicrobial screening of these synthesized compounds was done against some bacterial (Gram positive as well as Gram negative) and fungal strains in N,N-dimethylformamide (DMF).

2. EXPERIMENTAL

2. 1. Materials

Reagent grade chemicals were used without further purification. The purity of the synthesized compounds was checked by Thin Layer Chromatography.

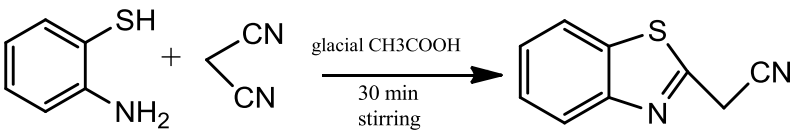
Synthesis of 2-(benzo[d]thiazol-2-yl)acetonitrile

In an equimolar solution of 2-aminothiophenol and malano nitrile in ethanol, 0.5 ml glacial acetic acid was added drop wise. The solution was stirred for 30 min. Light yellow colored solid was formed which was filtered and dried.

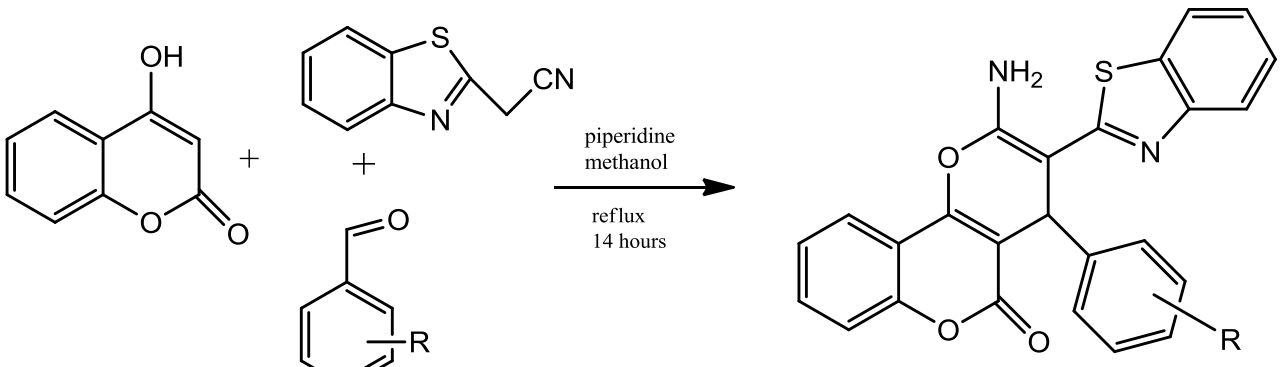
Synthesis of dihydropyrano[c]chromene derivatives

In an equimolar methanolic solution of 2-(benzo[d]thiazol-2-yl)acetonitrile and 4-hydroxycoumarin, different substitutes aldehydes were added in the presence of piperidine as a catalyst. The reaction mixture was refluxed for 8-9 hours. The product was filtered and recrystallized with ethanol.

Step-1.



Step-2



ABR-1to10

The physical constants of synthesized compounds (ABR-1 to ABR-10) are given in Table 1. IR spectra were recorded by SHIMADZU-FTIR-8400 spectrophotometer in frequency range of 4000-400 cm^{-1} by KBr powder method.

^{1}H NMR spectra were recorded by BRUCKER spectrometer (400 MHZ) using internal refences TMS and DMSO – d6. The Mass spectra were recorded by GCMS- SHIMADZU-QP 2010.

3. ANTIMICROBIAL ACTIVITY

3. 1. Microorganisms tested

The studied microorganisms were obtained from National Chemical Laboratory (NCL), Pune, India. The microorganisms were maintained at 4 °C. The Gram positive bacteria studied were *Staphylococcus aureus* ATCC29737 (SA), *Corynebacterium rubrum* ATCC14898 (CR), *Listeria monocytogenes* ATCC19112 (LM), *Bacillus cereus* ATCC11778 (BC); Gram negative bacteria were *Pseudomonas aeruginosa* ATCC27853 (PA), *Escherichia coli* NCIM2931 (EC), *Klebsiella pneumoniae* NCIM2719 (KP), *Salmonella typhimurium* ATCC23564 (ST) and Fungi were *Candida albicans* ATCC2091 (CA), *Cryptococcus neoformans* NCIM3542 (CN), *Candida glabrata* NCIM3448 (CG), *Candida epicola* NCIM3367 (CE).

The organisms were maintained on nutrient agar and MGYP medium (Hi Media, India) for bacteria and fungi respectively, at 4 °C and sub-cultured before use. The microorganisms studied are clinically important ones causing several infections and food spoilage.

3. 2. Agar well diffusion method

In vitro antimicrobial activity of the new dihydropyrano[c]chromenes derivatives were studied against pathogenic microbial strains by the agar well diffusion method [9]. Mueller Hinton No. 2 / Sabouraud dextrose agar (Hi-media) was used for the antibacterial and antifungal susceptibility test respectively.

The new dihydropyrano[c]chromenes derivatives were dissolved in 100 % DMF to give a concentration of 20 $mg \cdot ml^{-1}$.

The Mueller Hinton agar / Sabouraud dextrose agar was melted and cooled to 48-50 °C and a standardized inoculum (1.5 × 108 CFU/ ml, 0.5 McFarland) was then added aseptically to the molten agar and poured into sterile Petri dishes; wells (8.5 mm) were prepared in the seeded agar plates.

The test compound (100 µl) was introduced into the well.

The plates were incubated overnight at 37 °C and 28 °C for 24 h and 48 h respectively, for bacteria and fungi. DMF were used as negative control. The microbial growth was determined by measuring the diameter of the zone of inhibition and the mean values are presented with ± SEM.

4. RESULTS AND DISCUSSION

4. 1. Characterization

IR, ^{1}H NMR and Mass spectral data of 2-amino-3-(benzo[*d*]thiazol-2-yl)-4-(3-methoxyphenyl)pyrano[3,2-*c*]chromen-5(4H)-one (ABR-8)

IR: 3439.19 (N-H str.), 1746.60 (C=O), 1306.82 (C-N str.), 1271.13 (C-O-C str. assymetrical), 1114.89 (C-O-C str. sym.), 1586.50 (C=C str. aromatic), 3042.81 (C-H str. aromatic), ^{1}H NMR (δ ppm): 3.698 (3H, s, $-OCH_3$), 4.766 (1H, s, -CH), 8.670 (2H, s, $-NH_2$), 6.755-8.670 (12H, multiplate, aromatic); Mass: (M/Z) 454, 410, 347, 291, 279, 265, 249, 174.

Table 1. Physical constants of synthesized compounds.

Sr.No.	Compound Code	R	M.F.	M.W. (gm/mol)	% Yield
1	ABR-1	-H	$C_{25}H_{15}N_2O_3S$	424	76
2	ABR-2	4-CH_3	$C_{26}H_{15}N_2O_3S$	438	73
3	ABR-3	3,4-di-OCH_3	$C_{27}H_{20}N_2O_5S$	484	72
4	ABR-4	4-F	$C_{25}H_{15}N_2O_3SF$	442	75
5	ABR-5	4-OCH_3	$C_{26}H_{18}N_2O_4S$	454	74
6	ABR-6	4-Br	$C_{25}H_{15}N_2O_3SBr$	502	70
7	ABR-7	3-Br	$C_{25}H_{15}N_2O_3SBr$	502	77
8	ABR-8	3-OCH_3	$C_{26}H_{18}N_2O_4S$	454	69
9	ABR-9	2,5-di-OCH_3	$C_{27}H_{20}N_2O_5S$	484	74
10	ABR-10	3-Cl	$C_{25}H_{15}N_2O_3SCl$	453	73

4. 2. Antimicrobial activity

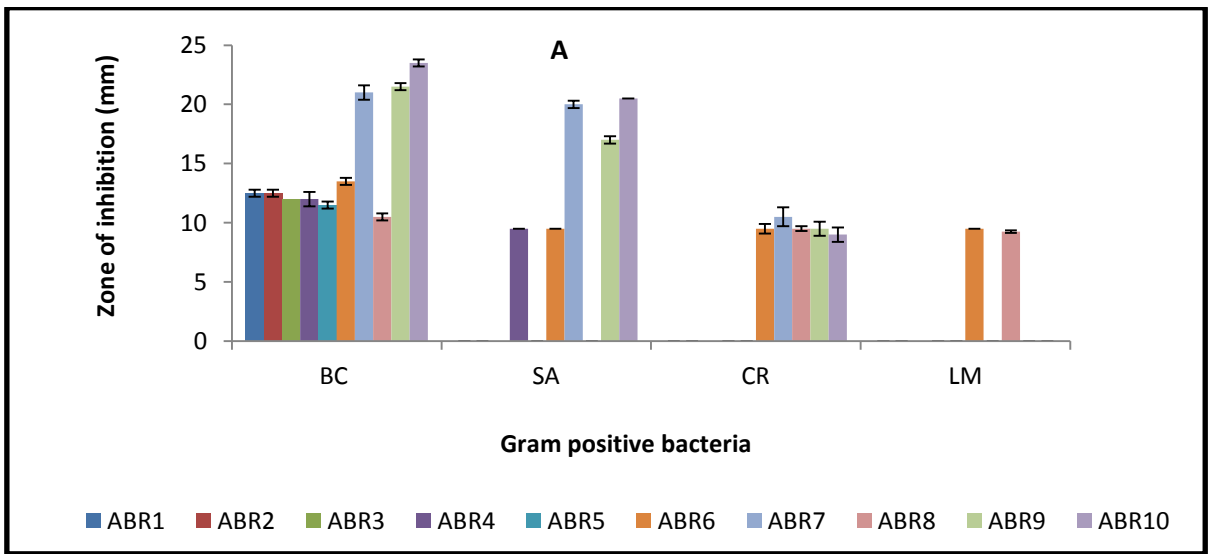


Fig. 1. Antibacterial activity of dihydropyrano[c]chromenes in DMF against (A) Gram positive and (B) Gram negative bacteria.

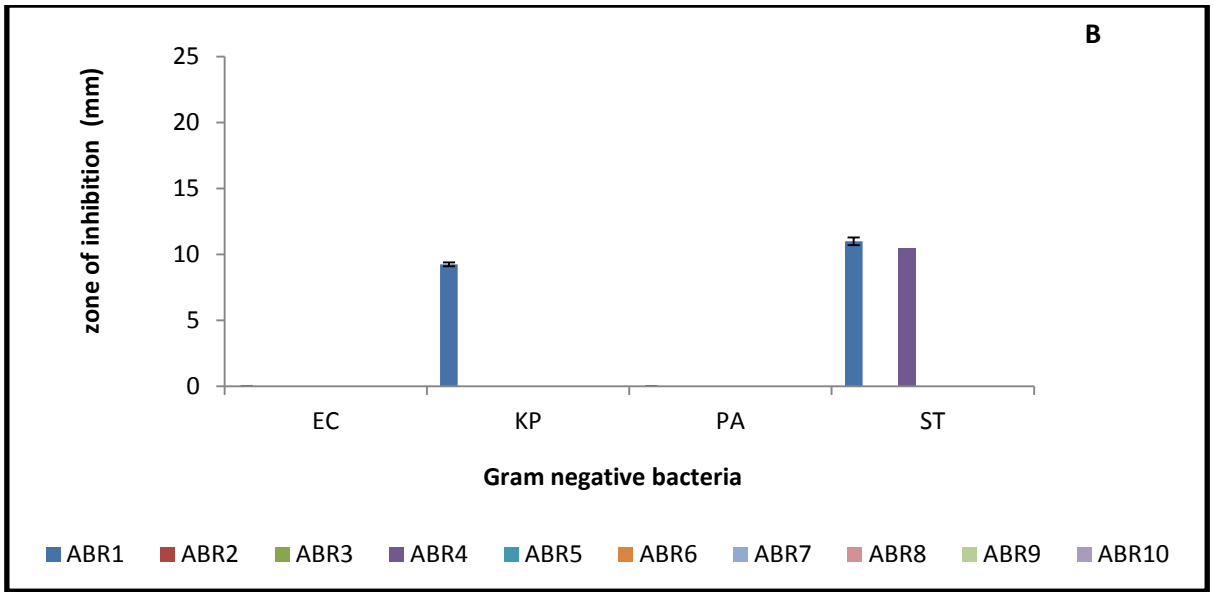


Fig. 1 (continue). Antibacterial activity of dihydropyrano[c]chromenes in DMF against (A) Gram positive and (B) Gram negative bacteria.

The 10 synthetic compounds and their respective controls produced different inhibition zones against the tested bacterial strains. The in vitro antibacterial activity of the ten compound in DMF against medically important Gram positive and Gram negative bacteria is shown in Fig. 1.

All the 10 compounds showed inhibitory activity against B. cereus but ABR-9 and ABR- 10 showed highest activity than all other strains studied. ABR-7, ABR9, ABR-10 showed higher activity than ABR-4 and ABR-6 against *S. typhimurium.* ABR-6, ABR-7, ABR-8, ABR-9, ABR- 10 showed lesser activity against *C. rubrum*, *L. monocytogenes* and *B. cereus* was the most susceptible bacteria, getting inhibited by all the 10 synthesized compounds.

None of the compounds in DMF showed antibacterial activity against *E. coli* and *P. aeruginosa*. ABR 1 showed some inhibitory activity against *K. pneumonia* compound and *S. typhimurium*. *E. coli* and *P. aeruginosa* were the most resistant bacterial strains not getting inhibited by any of the tested compounds. Different antibacterial activity with different side chains but same central moiety is already reported from work on Schiff bases from our group [10].

5. CONCLUTION

In the present study, the central moiety in all the compounds is dihydropyrano [c]chromenes with different side chains and because of this differential antibacterial activity was observed.

The best activity was with side chain 3-Cl (ABR-10). It can be concluded that different response of the synthesized compounds is because of their structural differences and the polarity of solvent used.

ACKNOWLEDGEMENT

Authors are thankful to Department of Chemistry for providing laboratory facilities. The authors are also thankful for the facilities and grants given under UGC-SAP for Department Research Support (DRS) and Department of Science and Technology (DST) New Delhi for Fund for Improvement of Science and Technology (FIST).

References

[1] Trapkov VA, Parfenov EA, Smirnov LD. *Pharm. Chem. J.* 30 (1996) 445-447.

[2] Vukovic N, Sukdolak S, Solujic S, Niciforovic N. *Arch. Pharm. Res.* 33 (2010) 5-15.

[3] Emmanuel-Giota AA, Fylaktakidou KC, Hadjipavlou-Litina DJ, Litinas KE, Nicolaides DN., *J. Heterocyclic Chem.* 38 (2001) 717-722.

[4] Hamdi N, Dixneuf PH. Topics in Heterocyclic Chemistry, Springer-Verlag, BerlinHeidelberg, 2007.

[5] Basanagouda M, Kulkarni MV, Sharma D, Gupta VK, Sandhyarani P, Sasal VP. *J. Chem. Sci.* 121 (2009) 485-495.

[6] Liu X, Dong M, Chen X, Jiang M, Lv X, Zhou J., *Appl Microbiol Biotechnol.* 78 (2008) 241-247.

[7] Wang M, Wang L, Li Y, Li Q., *Trans. Met. Chem.* 26 (2001) 307-310.

[8] Marchenko MM, Kopyl'chuk GP, Shmarakov IA, Ketsa OV, Kushnir VN, *Pharm. Chem. J.* 40 (2006) 296-297.

[9] Perez C, Paul M, Bazerque P., *Acta Biol Med Exp* 15 (1990) 113-115.

[10] Baluja S, Parekh J, Chanda S, Vaishnani KP, *J Indian Chem Soc* 86 (2009) 1338-1342.

(Received 12 March 2014; accepted 18 March 2014)