ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis, Characterization and Antibacterial Studies of 8-[4-(4-Chlorocarbonyl-phenylimino)-buta-1,2,3-trienylideneamino]-2-oxo-2H-chromene-4-carbonyl chloride [Complex with Fe (II) , Co (II)].

Aziz Behrami[1]*, and Islam Krasnqi[2].

[1]Public University of Mitrovica , Kosovo.
[2] Faculty of Education, University of Prishtina.

ABSTRACT

This work reports the synthesese of some new derivatives from 8-Amino-4-methyl-chromen-2-one and their antibacterial activity. Compounds 4-Methyl-8-(4-p-tolylimino-buta-1,2,3-trienylideneamino)-chromen-2-one**1a**,8- [4-(4-Carboxy-phenylimino)- buta-1,2,3-trienylideneamino]- 2-oxo-2H-chromene-4-carboxylic acid **2a** , 8-[4-(4-Chlorocarbonyl-phenylimino)-buta-1,2,3-trienylideneamino]-2-oxo-2H-chromene-4-carbonyl chloride [Complex with Fe (II) , Co (II)] **3a,**. All Structures have been synthesized and characterized using melting points , IR spectra , ^{1}H-NMR and ^{13}C-NMR spectra.The purified synthesized compounds 1a,2a,3a,4a at contcentrations 2,3,5 mg/ml was subjected to test the antibacterial activity against the bacterial cultures ;Staphylococcus aureus, Escherchia coli and Bacillus cereus.The antibacterial activity of synthesized compounds were compared with antibacterial activity of standard antibiotics cephalexine and streeptomycine. The compounds show different bacteriostatic and bacteriocidal activity.

Keywords: 8-Amino-4-methyl-chromen-2-one derivatives ,antibacterial activity

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Starting from 8-Amino-4-methyl-chromen-2-one a); derivatives (1a,2a,3a) are synthesized.Coumarin derivatives are large group of heterocyclic with oxygen as heteroatom.Coumarin is a chemical compound (specifically, a benzo-α-pyrone) found in many plants [1-4] notably in high concentration in the tonka bean (Dipteryx odorata), vanilla grass (Anthoxanthum odoratum) , woodruff (Galium odoratum), mullein (Verbascum spp), and sweet grass (Hierochloe odorata).Coumarine and their derivatives have shown varius biological activities. Their fame has come mainly from their antithrombic, antiinflammatory, vasodilatory , and antiviral activities. Other several coumarin derivatives have antimicrobial properties [5-9] with reflux and condensation we have synthesize some new coumarine derivatives and to investigate their antibacterial activity against Staphylococcus aureus, E.coli and Bacillus cereus. The antibacterial activity of synthesized compounds is compared with antibacterial activity of Cefalexine and Streptomycine.

MATERIAL AND METHODS

Experimental Chemistry

Compounds 4-Methyl-8-(4-p-tolylimino-buta-1,2,3-trienylideneamino)-chromen-2-one **1a**, 8- [4- (4-Carboxy-phenylimino)-buta-1,2,3-trienylideneamino]-2-oxo-2H-chromene-4-carboxylic acid **2a**, 8- [4- (4-Chlorocarbonyl - phenylimino)- buta- 1,2,3-trienylideneamino]-2-oxo-2H-chromene-4-carbonyl chloride [Complex with Fe (II) , Co (II)] **3a** , are synthesized.

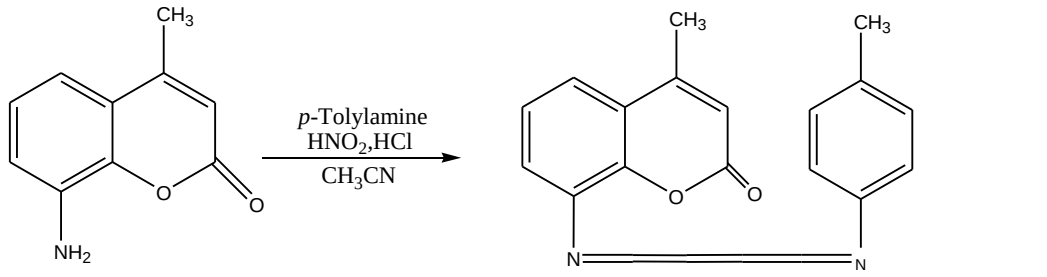
Measurement

The identification of 8-Amino-4-methyl-chromen-2-one derivatives **(1a,2a,3a)**, is made by using melting point , IR , 1H NMR , 13C NMR spectra and elemental analysis. Melting point was determinated on a Electrothermal apparatus (Fisher Scientific 2555) in a open capillary tube and are uncorrected.Infrared spectra were recorded in cm-1 for KBr pellts on a FT-IR Shimadzu 8400S spectrophotometer with resolution 4 cm-1 . ^{1}H NMR spectra were recorded on a Bruker UNITY plus-500 'NMR 1' spectrometer using DMSO-d6 as the solvent and TMS as the internal references standard (σ = 0,00 ppm).Chemical shifts are expressed in δ ppm.Mass spectra were taken on a LKB 9000 mass spectrometer. Element analysze was performed on a Perikin-Elmer 240 BCHN analyzer.The purity of the compounds (synthesized) was routinely checked by TLC using Merck Kieselgel-60 (F-254) and benzene,toluene,glacial acetic acid (80:10:10)as mobile phase. The spots were exposed in iodine vapour for visualization.

Preparation of 4-Methyl-8-(4-p-tolylimino-buta-1,2,3-trienylideneamino)-chromen-2-one (1a)

For this synthesis is used 4g 8-Amino-4-methyl-chromen-2-one as substrat in a 100 ml flask mixed 3ml HNO_2 , 1 ml HCl , 2g P-Tolylamine and 10 ml CH_3CN.

The mixture was refluxed at 90 ^{o}C for ca. 120 min. The obtained red crystals are filtred and rinsed with ethanol and dried at room temperature.Recrystallization form absolute ethanol gave a red product of 80% yield, melting point 326 ^{o}C.



8-Amino-4-methyl-chromen-2-one

4-Methyl-8-(4-*p*-tolylimino-buta-1,2,3-trienylideneamino)-chromen-2-one

Figure 1: 4-Methyl-8-(4-p-tolylimino-buta-1,2,3-trienylideneamino)-chromen-2-one (1a)

ISSN: 0975-8585

Preparation of 8-[4-(4-Carboxy-phenylimino)-buta-1,2,3-trienylideneamino]-2-oxo- 2H- chromene- 4-carboxylic acid (2a).

In a 100 ml flask were mixed 3g 4-Methyl-8-(4-p-tolylimino-buta-1,2,3-trienylideneamino)-chromen-2-one with 8ml CH_3CN and 2g $KMnO_4$ .The mixture was refluxed at 80 ^oC for ca. 20h .

The obtained yellow crystals are filtred and dried at room temperature . Recrystallization form CH_3CN gave yellow crystals product of 75 % yield,meltingpoint, 386^oC.

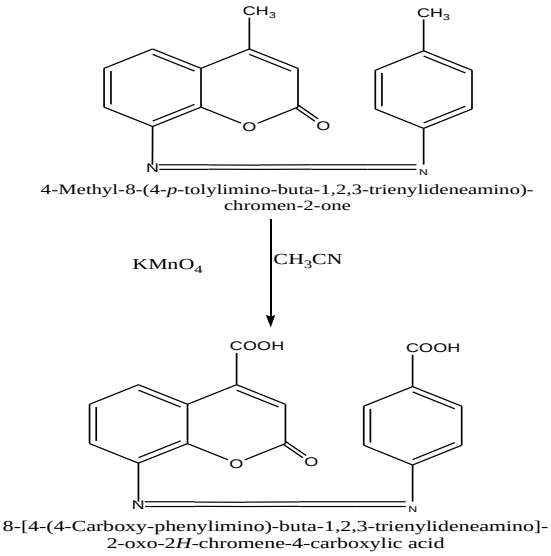


Figure 2: Preparation of 8-[4-(4-Carboxy-phenylimino)-buta-1,2,3-trienylideneamino]-2-oxo-2H-chromene-4-carboxylic acid (2a)

Preparation of 8-[4-(4-Chlorocarbonyl-phenylimino)-buta-1,2,3-trienylideneamino]-2-oxo-2H-chromene-4-carbonyl chloride [Complex with Fe (II) , Co (II)] (3a).

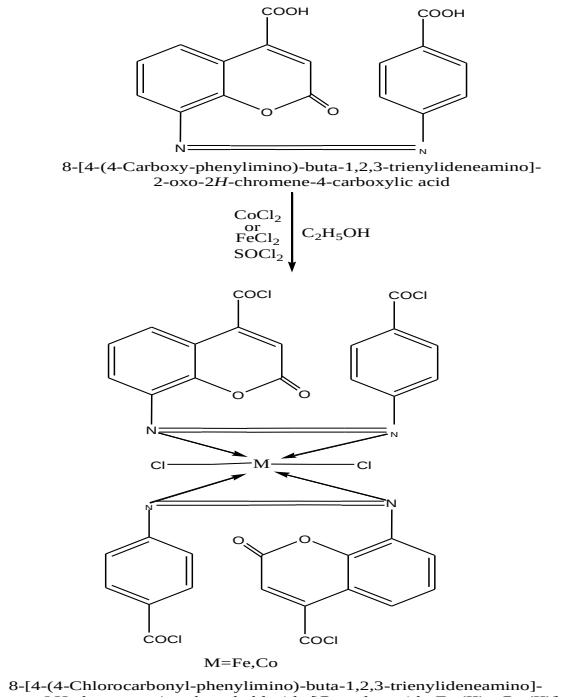


Figure 3: Preparation of 8-[4-(4-Chlorocarbonyl-phenylimino)-buta-1,2,3-trienylideneamino]-2-oxo-2H-chromene-4-carbonyl chloride [Complex with Fe (II) , Co (II)] (3a)

ISSN: 0975-8585

In a 100 ml flask were mixed 2.5g 8-[4-(4-Carboxy-phenylimino)-buta-1,2,3-trienylideneamino]-2-oxo-2H-chromene-4-carboxylic acid , with 1g $FeCl_2$ or $CoCl_2$, 10ml C_2H_5OH , 2ml $SOCl_2$.The mixture was refkuxed at 100^oC in water bath for ca.40 h.The flask was placed in an ice bath for 1h until yellow crystalline precipitate was formed. After filtration the product was recrystallized from CH_3CN .

The recrystallizacion gave a yellow product at 70% yield, meltingpoint 414 ^oC.

Table 1: characteristics and analytical data of the complexes

Comp	Yeld	m.p	M.F	Elemntal analysis , Calculate (Calc %)						
				C	H	N	O	Cl	Fe	Co
1a	83%	326^oC	$C_{21}H_{14}N_2O_2$	77.29 77.28	4.32 4.30	8.58 8.57	9.81 9.80			
2a	75%	386^oC	$C_{21}H_{10}N_2O_6$	65,29 65.28	21.61 21.60	7.25 7.23	24.85 24.85			
3a	70%	414^oC	$FeC_4H_{20}Cl_6N_4O_8$ $_{Co}C_4H_{20}Cl_6N_4O_8$	59.60 59.59	2.01 2.00	5.60 5.59	12.78 12.77	21.25 21.24	5.58 5.58	5.58 5.58

Antibacterial activity

The purified synthesized compounds (1a,2a,3a) was subjected to test in vitro its antibacterial activity against three bacterial cultures ; Staphylococcus aureus,E.Coli and B.cereus. Antibacterial activity of compounds was investigated applying the Kirby-Bayer method or disc method (d=5.5 mm max. capacity 10 µg)

Table 2: Antibacterial activity- Staphylococcus aureus

Inhibition zone (mm)

Compound	2mg/ml	3mg /ml	5mg/ml
1a	10	15	17
2a	10	16	18
3a	11	16	18
Cefalexine	9	9	9 10 µg
Streptomycine	20	20	20 10 µg

Table 3: Antibacterial activity – E.Coli

Inhibition zone (mm)

Compound	2mg/ml	3mg /ml	5mg/ml
1a	10	12	14
2a	11	12	15
3a	12	13	16
Cephalexine	9	9	9 10 µg
Streptomycine	23	23	23 10 µg

Table 4 Antibacterial activity – Bacillus cereus

Inhibition zone (mm)

Compound	2mg/ml	3mg /ml	5mg/ml
1a	12	16	23
2a	10	15	21
3a	13	19	24
Cephalexine	9	9	9 10 µg
Streptomycine	23	23	23 10 µg

ISSN: 0975-8585

RESULTS AND DISCUSSION

By reacting equimolar amounts of 8-Amino-4-methyl-chromen-2-one and correspomding reagents (according scheme 1) under reflux reaction condictions product **1a** is synthesized in 80 % yield.

By reacting equimolar amounts of 4-Methyl-8-(4-p-tolylimino-buta-1,2,3-trienylideneamino)-chromen-2-one and corresponding reagents (according scheme 2) under reflux reaction condictions product **2a** is synthesized in 70 % yield.

By reacting equimolar amounts of 8-[4-(4-Carboxy-phenylimino)-buta-1,2,3-trienylideneamino]-2-oxo-2H-chromene-4-carboxylic acid and corresponding reagents (according scheme 3) under reflux reaction condictions product **3a** is synthesized in 70% yield.

The structure of 8-Amino-4-methyl-chromen-2-one derivatives (1a,2a,3a)were determined fromtheir IR, ^{1}H NMR , ^{13}C NMR spectar and their melting points as follows.

For (1a); IR bands (KBr,cm-1) 3000cm^{-1} (C-H stretch.), 1720 cm^{-1} (C=O) , 1600 (C=C stretch.) , 1600 (C=C stretch)1280 cm^{-1} (N-H), 750 cm^{-1} (C-H bend.)

^{1}H NMR (DMSO-d6) δppm , 1.71ppm s(3H,CH_3), 2.35ppm s(3H,CH_3) , 6.627ppm ; 7.1ppm ; 7.2ppm ; 7.4ppm ; 7.6ppm ; m(8H aromatic)

^{13} C NMR (DMSO) δppm ; 20.9ppm ; 24.6ppm (2C,2CH_3) ; 122.9ppm ; 125.2ppm ; 126.5ppm 109.5ppm ; 123.2ppm ; 130.5ppm ; 129.1ppm (8C aromatic) ; 145.6ppm (C-O) ;133.6ppm (C,C-N) ; 137.8ppm (C,C-N) 162.0ppm (C,C=O)

For (2a) IR bands (KBr,cm -1) 2500cm^{-1} (O-H Stretch.), 1740 cm^{-1} (C=O) , 1710 (C=O stretch.) ,1600cm^{-1} (C=C Stretch) ,1280 cm^{-1} (N-H), 1210 cm^{-1} (O-H), 750 cm^{-1} (C-H bend.)

^{1}H NMR (DMSO-d6) δppm 7.2ppm; 7.4ppm; 7.5ppm ; 7.6ppm; 8.1ppm (8H aromatic)
11.0ppm d(2H,2COOH)

^{13}C NMR (DMSO) δppm 122.9ppm ; 123.2ppm ; 125.2ppm ; 126.5ppm ;126.7ppm ; 131.4ppm; (8C aromatic) ; 133.6ppm (C,C-N) ; 145.6ppm(C,C-O) ; 146.0ppm (C,C-N) 129.2ppm (C,COOH) 150.0ppm (C,C=O) 162.2 ppm (C,C=O) ; 170.0ppm (C,COOH) 172.0ppm (C,COOH)

For (3a) IR bands (KBr,cm -1) 2980cm-^{1}(C-H, stretch.), 3200cm^{-1}(C-NH,stretch.), 2565cm^{-1} (S-H) ,1720cm^{-1}(C=O,tretch.),1600cm^{-1}(C=C,stretch),1280cm^{-1}(N-O),1523cm^{-1} (N=O_2) ,1050cm^{-1}(C-O),1240 cm^{-1} (C=S) ,750cm^{-1}(C-S) 740cm^{-1} (C-H) , 1030cm^{-1} (C-S),650cm^{-1} (Me-O) , 600cm^{-1} (Me –S)

^{1}H NMR (DMSO-d6) δppm 7.2ppm ; 7.4ppm ; 7.5ppm ; 7.6ppm ; 7.9ppm ; 8.1ppm m(8H aromatic)

(**^{13}CNMR (DMSO) δppm** 122.9ppm ; 125.2ppm ; 123.6ppm ; 126.5ppm ; 129.1ppm ; 130.9ppm ; (12C aromatic) ; 162.0ppm (C,C=O) ; 163.0ppm (C-Cl) ; 145.6ppm (C,C-O) 189.2ppm (2C , 2C (C-N=N)

CONCLUSION

From the results the followin conclusion were drawn:The study provides the first evidence that compounds (1a,2a,3a) obviously inhibit the growth of S.auerus , E.coli and B.cereus.

The compounds (1a,2a,3a) compared with the antibacterial activity of Streptomycine in S.aureus, E.coli and B.cereus.

This study provided the first evidence that these compounds (1a,2a,3a) showed a significant antibacterial effect against S.aureus,E.coli and B.Cereus.

The chemical structures of synthesizen compounds were determined according to extensive NMR experiments and published data.

ACKNOWLEDGEMENTS

The authors thank Prof. Branko Stanovnik, University of Ljubljana and its laboratory staff for ^{1}H NMR spectrum and elemental analyses.

REFERENCES

[1] ABehrami, S Demaku, Bahrije Dobra, I Shehu. Int J Pharm Sci Rev Res 2013;20 (1):4-10.
[2] B Stanovnik, H Susachitzky and EF Scriven. Progr Heterocyclic Chem 1993;5:75-146.
[3] Vyas KB, Nimavat, KS Jani GR, Hathi MV. Orbital 2009;1:183-192.
[4] A Behrami, K Vaso, I Krasniqi. J Int Environ Appl Sci 2010;5:247.
[5] Mishra DK, Mishra AP. Int J Pharm Res Dev 2011;3(5):24-31.
[6] ZM Nofal, M El-Zahar, and S Abd El Karim. Mol 2000;5:99.
[7] Ali Mohammed Ashraf, and Sharayar Mohammed. Boorg Med Chem Lett 2009;17:3314.
[8] Nofal ZM, El-Zahar M, Abd El-Karim S. Mol 2000;5:99-113.
[9] Chandra S, and Kumar P. Spectrochimica Acta Part A 2005;6(1):219-224.