Synthesis spectral characterisation and biological activity of hetero-cyclic compound of 2-imidazolones

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Abstract:

2-imidazolones have gained immense significance in human life due to variety of their applications. Though there are several methods for the synthesis of 2-imidazolones, most of them required longer reflux time of 8 to 10 hours. Hence the proposed work was undertaken to workout simple methodology for the synthesis of 2-imidazolones and to improve the yield of the products, by employing Zeolite as a catalyst. The work presented here describes the synthesis of some substituted 2-imidazolones obtained from substituted benzoins and urea in CH_3COOH as a solvent in presence of Zeolite as a catalyst. Substituted benzoins in turn were obtained from aromatic aldehydes by their condensation in presence of aqueous NaCN. The characterisation of synthesized compounds was made on the basis of chemical properties, elemental and spectral analysis.

Keywords:

Substituted benzoins, Urea, Methyl urea, Phenyl urea, Zeolite catalyst, 2-imidazolones

INTRODUCTION

2-Imidazolones are the heterocyclic compounds containing nitrogen atoms at 1 and 3 position and C=O group at 2 position. Imidazolones are believed to be associated with several pharmacological activities. Many natural products are believed to contain imidazolones. For example Leucetta and the Oroidin families of alkaloids have been reported to contain either 2-aminoimidazole or 2-imidazolone moiety.

1,3 Azoles (e.g. 2-imidazolones) are found to exist in their carbonyl tautomeric forms. There is less aromatic character in such systems which can be illustrated by the acid catalyzed dimerization of 2–imidazolone which acts as an enamide in the process.The Leucetta and Oroidin families of alkaloids [1] have been identified which contain either 2-aminoimidazole or 2-imidazolone moiety[2-3]. Glass D et al.[4]reported 4-(4-Guanidinobenzoyl)-2-imidazolones and related compounds having phosphodiesterase inhibitors and novel cardio tonics with combined histamine H_2 receptor agonist and PDE 111 inhibitor activity.Stoffel and speziale[5] described the preparation of 2-imidazolones by a novel ring closure of propynylureas with phosphorous penta chloride 2-imidazolone was obtained via a stable isolable imidazolium chloride.Jie-Fei Cheng et al.[6] carried out A traceless solid phase synthesis of 2-imidazolones. Polymer-bound glycerol resin was reacted with bromo acetaldehyde diethyl acetal to give the cyclic acetal bromide on the solid support. Inas M AlNashef[7] described a novel method for the synthesis of 2-imidazolones. The superoxide ion electrochemically generated reduction of oxygen or chemically generated by dissolving potassium superoxide in ionic liquids, react with alkyl imidazoliumcations of imidazolium based ionic liquids at room temperature and atmospheric pressure to give the corresponding 2-imidazolones in excellent yield.Congiu et al.[8] reported in vitro antitumor activity of new 1,4-diarylimidazole-2-ones and their 2-thione analogues has been conceded by Compounds bearing a 3,4,5-trimethoxyphenyl ring linked to either N-1 or C-4 position of the imidazole core demonstrated an interesting profile of cyto toxicity with preferential activity against leukemic cell lines. Compound exhibited a potent antitumor activity against MOLT-4 (GI50 = 20 nM) and SR (GI50 = 32 nM) cell lines.

From the review of literature, it was observed that most of the methods of synthesis of 2-imidazolones required longer reflux time of 8-10 hours and the yield of the products was also quite low. Hence, in the context of the above observations, the proposed work was undertaken to reduce the reflux time and to improve the yield of the products by employing Zeolite as a catalyst.

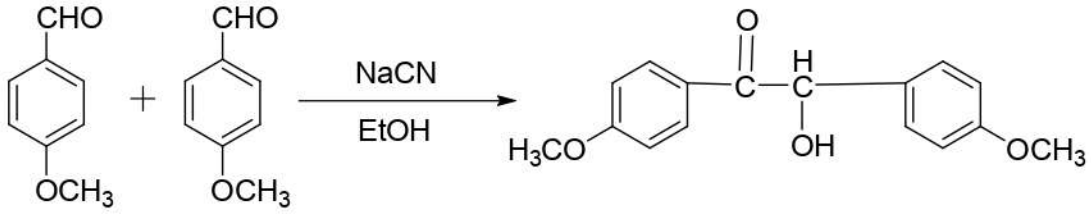
EXPERIMENTAL

Scheme-I :Synthesis of 4, 4'-dimethoxybenzoin.

In a round bottom flask, took 13.6 gms (0.1 mol) of anisaldehyde, added to it about 50 ml of ethyl alcohol. The mixture was shaken well. To this mixture added 4.9 gms aq. solution of sodium cyanide (0.1 mol). The reaction mixture was refluxed for 30-40 minutes. Cooled reaction mixture and poured it to ice cold water, obtained solid yellow product. Recrystallised it from water-ethanol mixture.

Yield: 65% Melting point: 113°C

Reaction:



(1a)

5. The IR spectrumof the compound (1a)(Spectrum No. 1) showed the following main absorption bands.

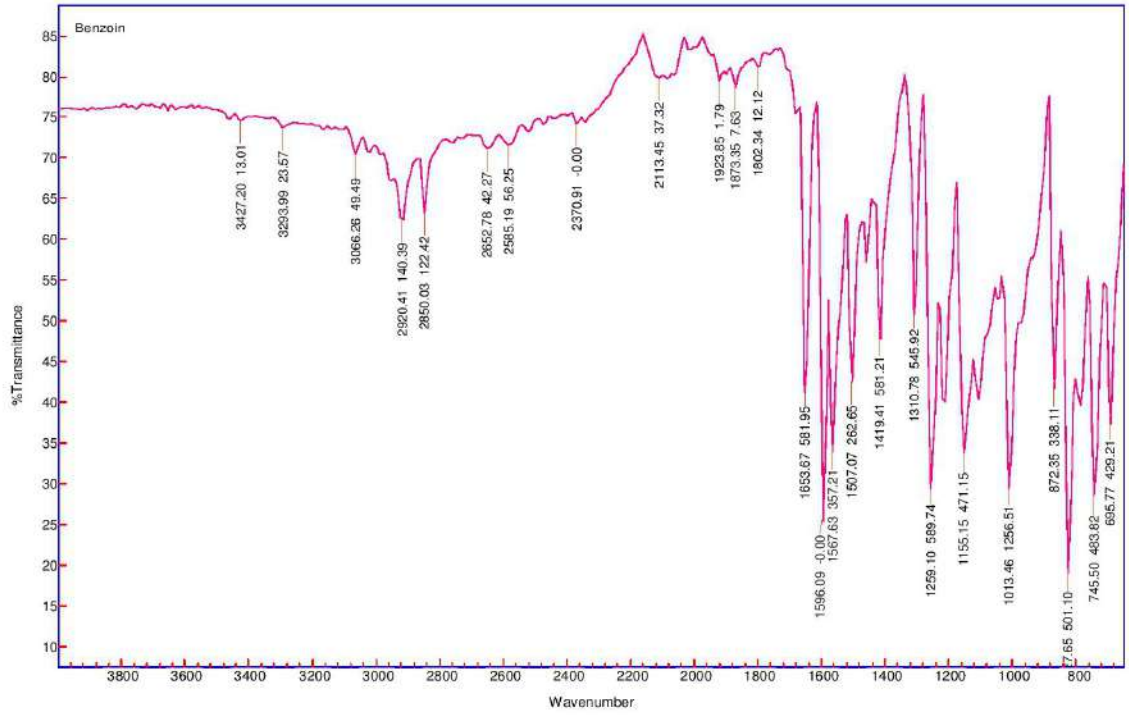
Absorption Observed (cm^{-1})	Assignment	Literature Value (cm^{-1})
3427	O–H Str	3570-3400
3066	Ar,C–H str	3100-3000
2920	Aliph, C–H	2980-2840
1653	C=O str	1850-1630
1507	Ar, C=C str	1500-1450
1310	C–O str	1350-1210

6. The ^{1}HNMR spectrumof the compound (1a) (Spectrum No. 2) showed the chemical shifts which can be correlated as given below.

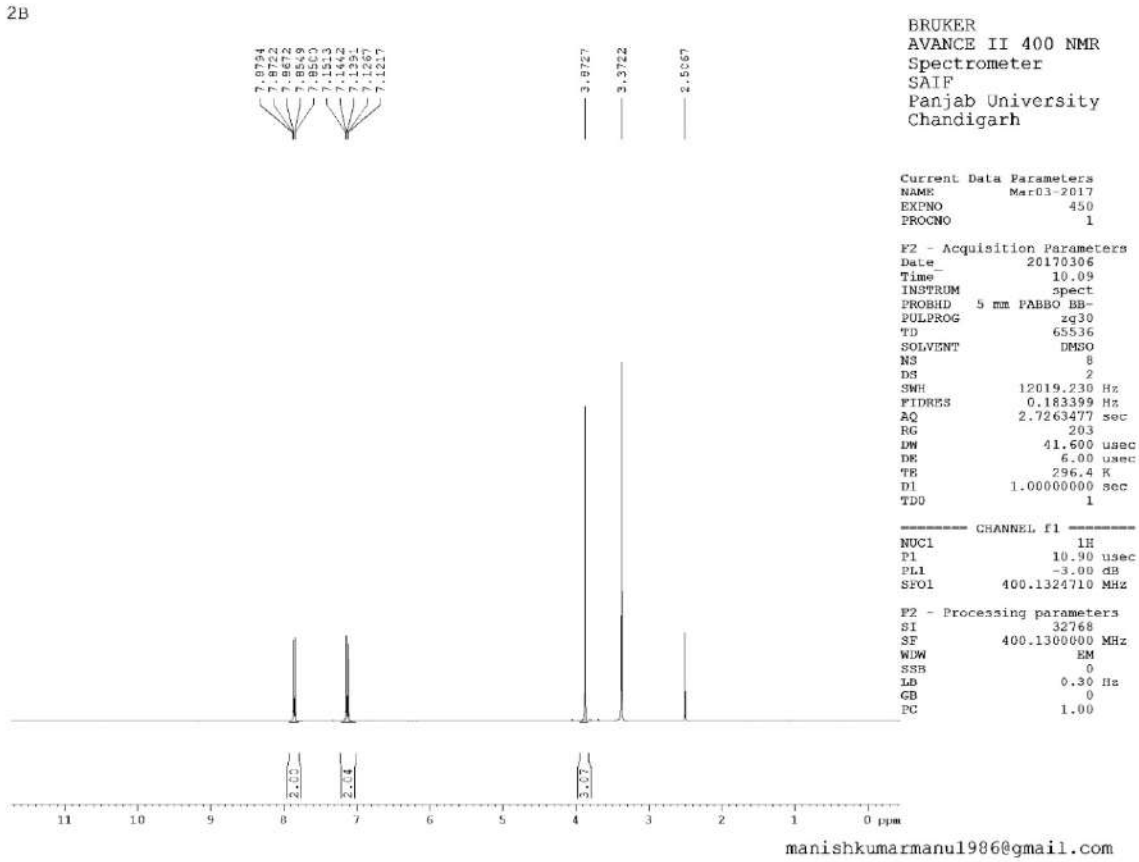
Chemical Shifts (δ)	Multiplicity	Assignment
7.86-7.85	d	4H,Ar–H
7.13-7.12	d	4H,Ar–H
3.87	s	1H, CH–OH
3.37	s	6H, $-OCH_3$
2.50	s	1H, Aliph, C–H

7. Elemental Analysis for $C_{16}H_{16}O_4$ (272.30)

Element (%)	C	H
Calculated	70.58	5.92
Found	70.55	5.90



SPECTRUM NO. 1



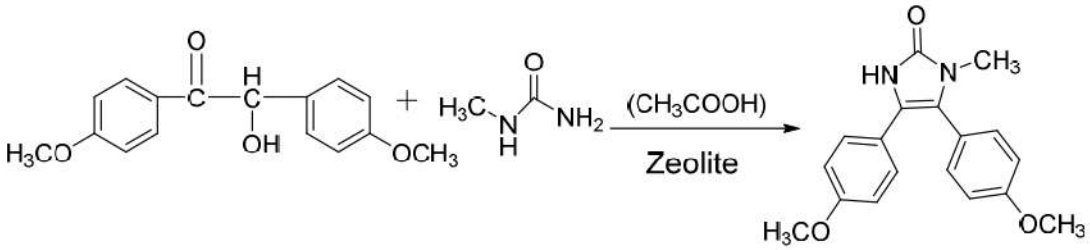
SPECTRUM NO. 2

Scheme-II: Synthesis of 1-H-3-methyl-4(4-methoxyphenyl)-5-(4-methoxyphenyl)-2-imidazolone

Took 4,4'-dimethoxybenzoin 2.72 gms (0.01 mol) in a round bottom flask, added to it glacial acetic acid (20ml). The mixture was warmed slightly to dissolve the solute. To this solution, added methyl urea 0.74 gm(0.01mol), followed by zeolite (1gm) as a catalyst. The reaction mixture was refluxed for three hours. Allowed it to cool and poured it to ice cold water. The solid yellow product formed was filtered, washed 2,3 times with cold water and recrystallized from water-ethanol mixture.

Yield: 62% Melting point: 180°C

Reaction:



(2a)

The IR spectrum of the compound (2a) (Spectrum No. 3) showed the following main absorption bands.

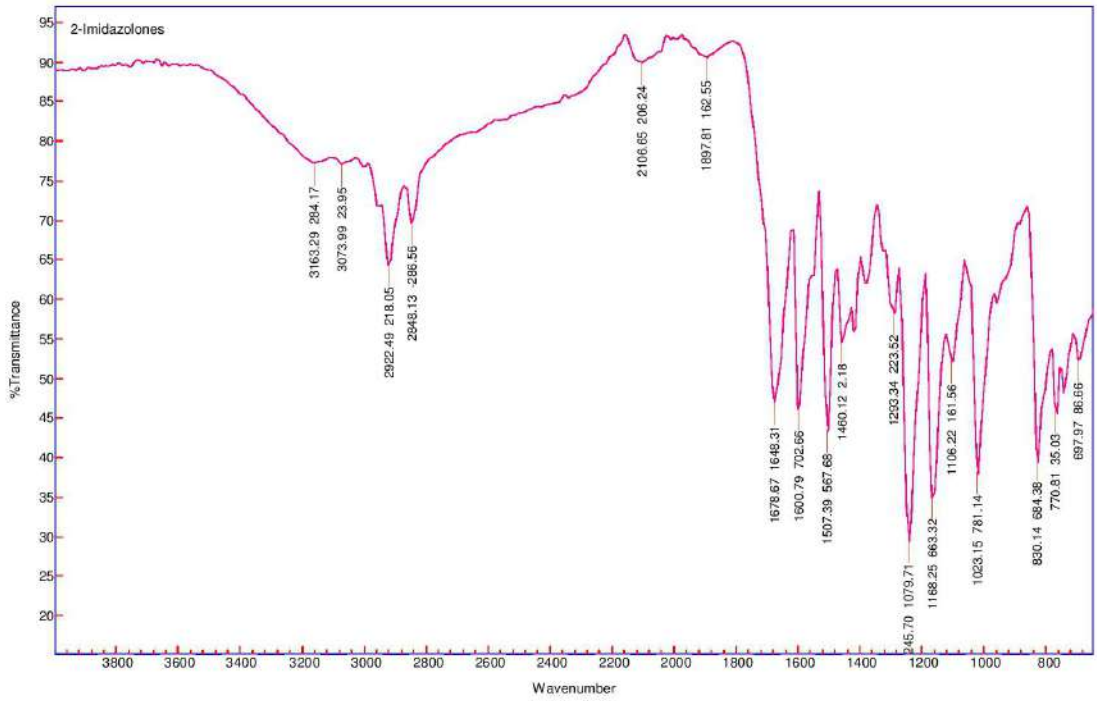
Absorption Observed (cm^{-1})	Assignment	Literature Value (cm^{-1})
3650	N–H str	3600-3200
3073	Ar, C–H str	3100-3000
2922	Aliph, C–H str	2980-2840
1678	C=O str	1850-1630
1600	C=N str	1690-1620
1507	Ar, C=C str	1500-1450
1293	C–N str	1360-1310
1245	C–O str	1350-1210

7. The ^{1}HNMR spectrum of the compound (2a) (Spectrum No. 4) showed the chemical shifts which can be correlated as given below.

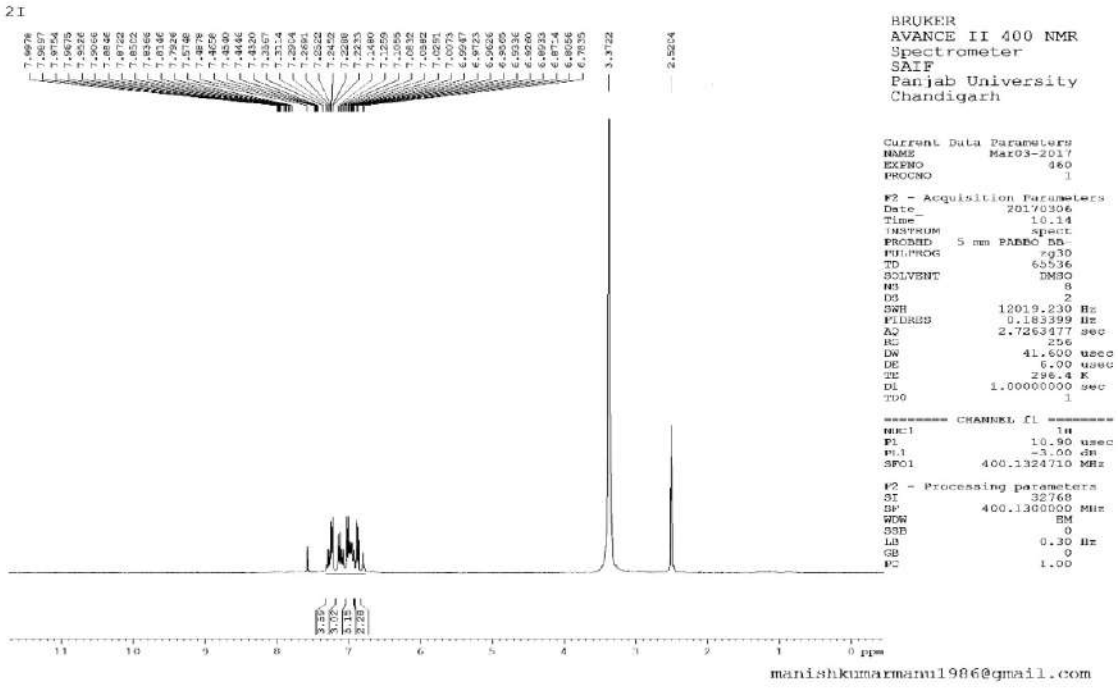
Chemical Shifts (δ)	Multiplicity	Assignment
7.57	s	1H, N–H
7.26-7.22	m	4H, Ar–H
7.17-7.05	m	4H, Ar–H
3.37	s	6H, $-OCH_3$
2.52	s	3H, $-CH_3$

8. Elemental Analysis for $C_{18}H_{18}N_2O_3$ (310.35)

Element (%)	C	H	N
Calculated	69.66	5.85	9.03
Found	69.62	5.44	9.00



SPECTRUM NO. 3



SPECTRUM NO. 4

Results and Discussion

We synthesized nine variedly substituted -2-imidzolones by the condensation of each of three substituted benzoins with urea, methyl urea and phenyl urea respectively. The target compounds gave positive tests for Nitrogen as well as for C=O linkage (red coloration with 1% solution of m-dinitrobenzene in ethanol)The IR spectrum showed sharp bands at 3650cm^{-1}(N-H

starching) and 1678cm^{-1} (C=O starching) and 1507 cm^{-1} (Ar, C=C starching) similarly, in ^{1}H-NMR spectrum chemical shifts at 7.97ppm (s,2H,-NH); 7.26ppm (d,4H,Ar-H); 7.05ppm (d,4H,Ar-H); 3.37 (S,6H,-OCH_3) with elemental analysis further confirmed the formation 2-imidazolones.

Table 1 :List of synthesized compounds, their % yield and melting points.

Sr. No.	Compound	Percent Yield (%)	Melting Point (°C)
1	1, 3-dihydro-4-phenyl-5-phenyl-2-imidazolone (2b)	70	120
2	1-H-3-methyl-4-phenyl-5-phenyl-2-imidazolone (2c)	65	130
3	1-H-3-phenyl-4-phenyl-5-phenyl-2-imidazolone (2d)	60	160
4	1,3-dihydro-4-(2-hydroxyphenyl)-5-(phenyl)-2-imidazolone (2e)	58	110
5	1-H-3-methyl-(2-hydroxyphenyl)-5-(phenyl)-2-imidazolone (2f)	70	125
6	1-H-3-phenyl-(2-hydroxyphenyl)-5-(phenyl)-2-imidazolone (2g)	60	148
7	1,3-dihydro-4-(4-dimethylaminophenyl)-5-(phenyl)-2-imidazolone (2h)	70	120
8	1-H-3-methyl-(4-dimethylaminophenyl)-5-(phenyl)-2-imidazolone (2i)	62	135
9	1-H-3-phenyl-(4-dimethylaminophenyl)-5-(phenyl)-2-imidazolone (2k)	60	160
10	1,3-dihydro-4-furfuryl-5-(furfuryl)-2-imidazolone (2l)	70	125
11	1-H-3-methyl-4-furfuryl-5-furfuryl -2-imidazolone (2m)	62	140
12	1-H-3-phenyl-4-furfuryl -5-furfuryl-2-imidazolone (2n)	60	175

Antimicrobial Activity

Method for the determination of antimicrobial activity

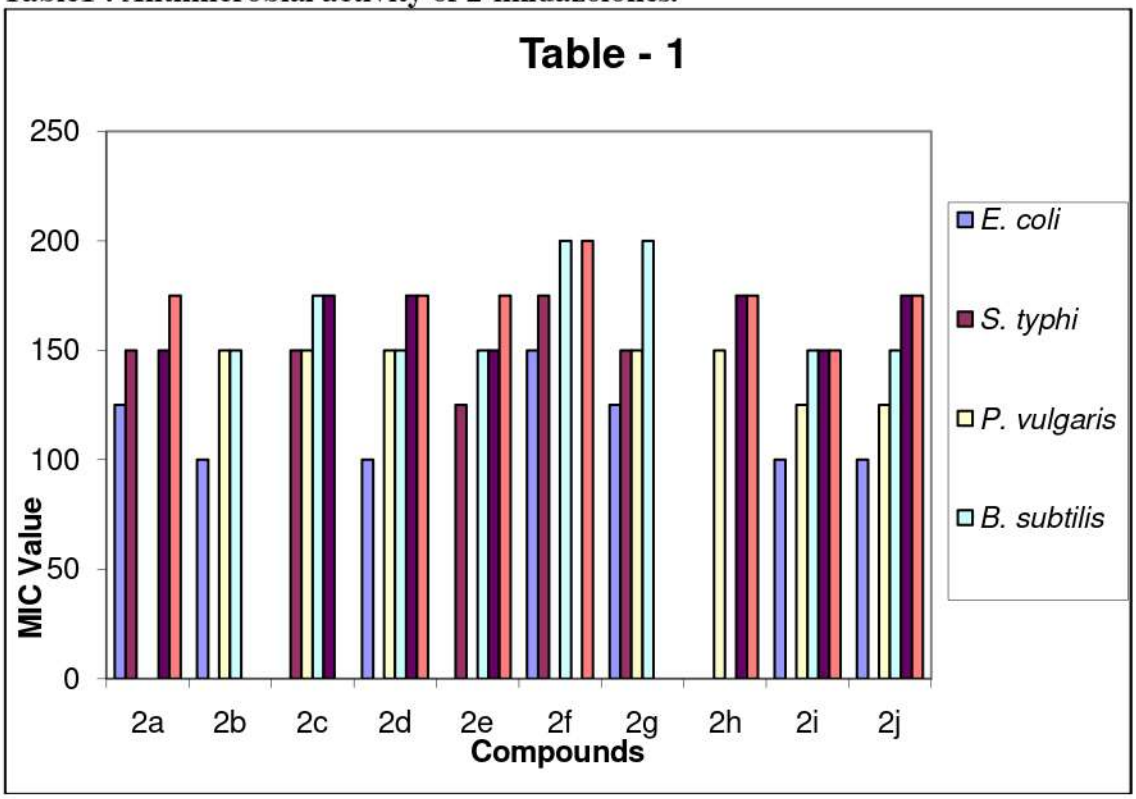
The newly synthesized eight compounds 2(a) were screened for their antimicrobial activity against the test organisms *E.coli, S.typhi, P.vulgaris, B.subtilis, S.aurus*and *S.penumoniae*by using agar disc diffusion method at concentration of 100 µgm/ml in DMF as a solvent. Each standardized test organism (0.1ml)was spread on the solidified sterile agar plates.

Conclusion

Thus we could succeed in synthesizing variedly substituted-2-imidazolone with simple and easy to workout methodology. Use of Zeolite as a catalyst enabled us rapid route for the synthesis of 2-imidazolones which could reduce reflux time to as low as two and half hours. The catalyst is insoluble in solvent due to which isolation of the product became much easy. The synthesized compounds were screened for antimicrobial activity against the test organisms *E.coli, S.typhi, P.vulgaris, B.subtilis, S.aurus and S.penumoniae*.

The compounds containing –NO2,-Cl and -OH group as a substituent showed antibacterial activity against maximum number of organisms .The compounds containing -OCH3,-N(CH3)2,-NO2 and -OH groups showed maximum activity against *S.typhiB.subtilis and E.coli* pathogens respectively.

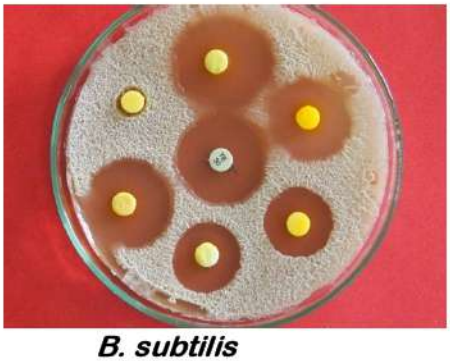
Table1 : Antimicrobial activity of 2-imidazolones.



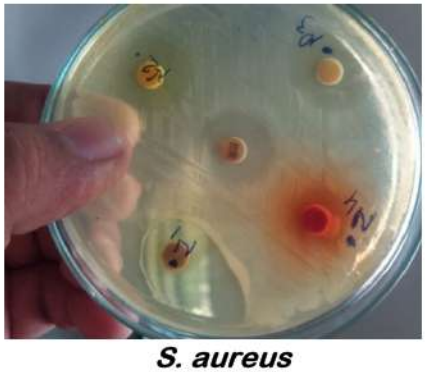
ANTIMICROBIAL ACTIVITY

E. coli

P. vulgaris



B. subtilis



S. aureus

S. pneumoniae

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