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Synthesis, characterization and antibacterial screening of some novel biphenyl-4-carboxylic acid (4-benzylidene-5-oxo-2-subsituted phenyl-4,5-dihydro-imidazol-1-yl)-amide

VIJAY TRIVEDI[1]* and SHAILESH H. SHAH[2]

[1]Department of Chemistry, Arts, Commerce and Science College, Khambhat Dist.Anand, Gujarat (India).
[2]Department of Chemistry, Arts, Commerce and Science college Borsad, Dist: Anand, Gujarat (India).

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ABSTRACT

Imidazolinone derivatives of 4a-l have been prepared by the condensation of biphenyl-4-carboxylic acid hydrazide 2 with 5-oxazolone derivatives, which were prepared by Erlenmeyer condensation of benzoyl glycine with different aldehydes in the presence of sodium acetate and acetic anhydride. The compounds 3a-l was further reacted with biphenyl-4-carboxylic acid hydrazide 2 to give 4a-l in basic condition. The constitution of the products has been supported by IR, ^{1}H-NMR, ^{13}C-NMR Mass spectra and Elemental analysis data.

Key words: Imidazolinone derivatives, synthesis, antibacterial screening.

INTRODUCTION

Oxazolone is a class of small heterocycles which are important intermediates in the synthesis of several small molecules, including amino acids, peptides[1-3] antimicrobial or antitumor compounds[4,5] heterocyclic precursors[6,7,8] as well as biosensors coupling and photosensitive composition devices for proteins[9]. Some oxazolones have shown a wide range of pharmaceutical properties[1]). 5-oxazolones are synthesized by the Erylenmeyer condensation as reported in the literature[11]

Literature survey reveals that various imidazolinone derivatives possess a broad spectrum of activities which are reflected by their use as anticonvulsant[12] and anti-Parkinsonian agents[13]. Some novel imidazolinones have been synthesized by using different oxazolones and condensing them with aliphatic and aromatic amines[14, 15] and with sulphonamide as anticonvulsant agents[16].

Numbers of biphenyl acids are marketed as anti-inflammatory drugs such as (1,1'-biphenyl)-4-aceticacid[17], g-oxo(1,1'-biphenyl)-4-butanoicacid[18], a-ethyl-(1,1'-biphenyl)-4-aceticacid[19]. Anti-inflammatory activity of biphenyl acid (20) such as 2-fluoro biphenyl acid derivatives, which were useful intermediates for many analgesics and anti-inflammatory agents.

Similarly, 3-aryl-2-(1,1'-biphenyl-4yl)-3-hydroxy-propionic acid[21]) having anti-inflammatory activity were synthesised by reacting substituted benzaldehyde with biphenyl acetic acid dianion. Heteroaroyl biphenyl amides compound are also reported as agrochemical and Industrial fungicides[22]. Several anti-hypertensive agents having biphenyl moiety incorporated with imidazole[23, 24], pyrrole[25], triazole[26] and other compounds have been reported.

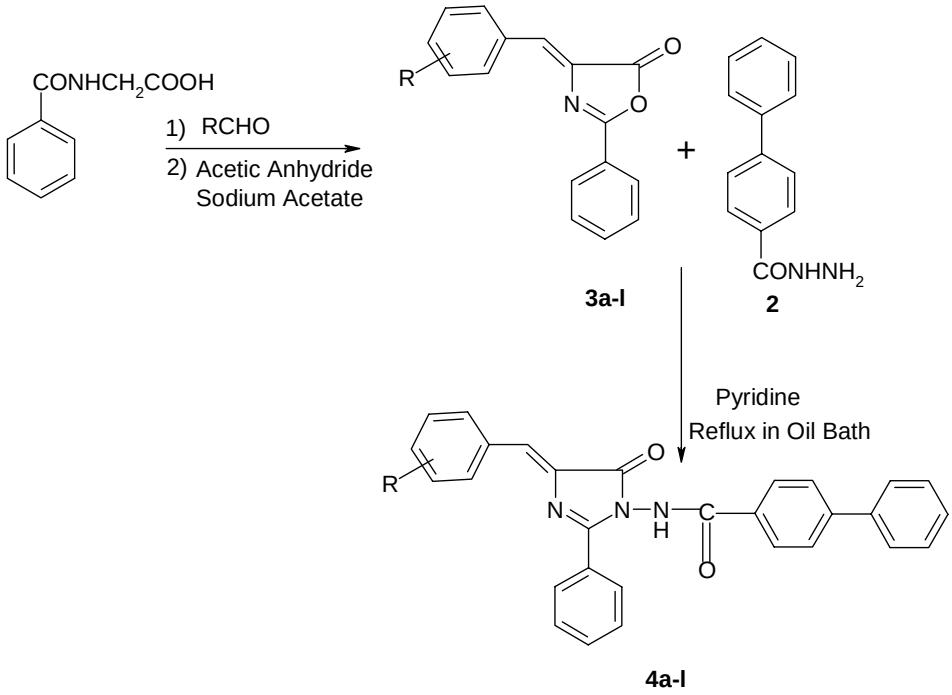
In this paper the author reports the

synthesis of the key intermediate biphenyl carboxylic acid hydrazide has been synthesized from ester by the method of Bernstein[27]. The author have also shown the synthesis of biphenyl-4-carboxylic acid hydrazide 2 and various 5-oxazolones 3a-l to give novel imidazolinones 4a-l.

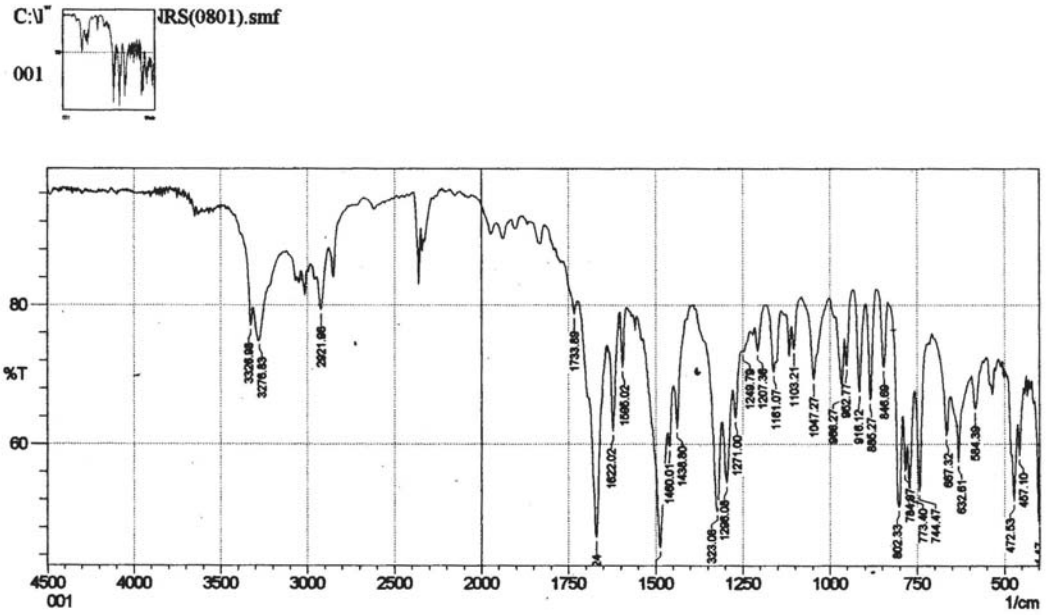
Commercially available biphenyl was heated with acetic anhydride in CS_2 in the presence of anhydrous $AlCl_3$ at 45-50°C (Friedel Craft acylation). This yielded p-phenyl acetophenone. p-Phenylacetophenone for the preparation of biphenyl carboxylic acid from Hechenbleikner (28) method was somewhat modified. Powdered p-phenyl acetophenone was directly added to sodium hypobromite solution in portions with in 15 minutes and stirred vigorously for ½ hr then 70 ml dioxane was added. Stirring was continued for further 4 hrs. Temperature of the reaction mixture increases up to 45°C due to exothermic reaction. After completion of reaction, sodium dithionate or sodium metabisulphite solution was added to remove the excess hypobromite then water was added. About 70% of added water was distilled off, then the solution was acidified with concentrated HCl and purified with acetic acid**.**

EXPERIMENTAL

All the recorded melting points were determined in open capillary tubes and are uncovered. All the chemicals and solvents used are of Laboratory Grade and solvents were purified. Completion of the reaction was monitored by TLC (silica gel GF254 (E. Merck), Toluene: Methanol= 8:2). The final products were purified by column chromatography using silica gel in increasing percentage of ethyl acetate in carbon tetrachloride. I.R (Infrared Spectrum) (KBr, cm^{-1}) were recorded on a Shimadzu-8400 FT-IR spectrometer, ^1H NMR spectra on a Brucker spectrometer (300MHz) using TMS as a internal standard (chemical shift in ä, ppm) in $CDCl_3$ and DMSO d6 and mass spectrum was recorded on Hewlett-Packard 5989, a Quadrapole Mass Spectrum and LC-MS on Perkin Elmer API 165. All the synthesized compounds gave satisfactory C, H, N analyses on Perkin Elmer (U.S.A) 2400 Series.



Scheme 1



No.	Peak	Height	Corr. Height	Base (H)	Base (L)	Area	Corr. Area
1	401.17	51.588	4.122	412.74	399.24	3.417	0.131
2	457.1	41.605	5.696	460.96	445.53	3.078	0.263
3	472.53	48.169	8.283	478.31	462.88	3.805	0.48
4	815.83	34.893	5.359	594.03	563.18	5.117	0.513
5	632.61	42.532	10.419	653.82	595.96	10.739	1.16
6	667.32	38.774	7.667	700.97	655.75	7.24	0.562
7	744.47	46.727	16.975	757.97	723.26	6.566	1.427
8	773.4	46.772	7.484	777.26	759.9	3.905	0.474
9	784.97	43.777	5.663	790.76	779.19	2.688	0.244
10	802.33	48.973	16.791	833.19	792.69	7.319	1.564
11	846.69	26.965	10.074	865.96	835.12	3.511	0.735
12	885.27	33.638	14.594	896.84	867.91	3.644	1.034
13	916.12	32.508	13.965	933.48	898.77	4.183	1.029
14	952.77	28.722	5.604	958.56	935.41	2.621	0.262
15	966.27	32.444	7.649	983.63	960.48	3.217	0.514
16	1047.27	30.666	11.738	1061.99	1002.92	9.049	1.839
17	1103.21	26.33	4.065	1081.99	1063.92	2.7	0.164
18	1161.07	29.628	2.722	1108.99	1157.21	3.105	0.119
19	1207.36	26.623	4.099	1182.28	1184.21	3.501	0.255
20	1249.79	26.706	0.32	1215.07	1230.5	2.717	0.052
21	1271	36.243	5.736	1251.72	1253.64	4.105	0.346
22	1296.08	45.543	10.791	1309.58	1280.65	6.413	1.096
23	1323.08	49.705	15.597	1357.79	1311.5	9.672	2.024
24	1438.8	37.773	8.628	1448.44	1413.72	5.267	0.585
25	1460.01	40.32	4.454	1465.6	1450.37	3.053	0.205
26	1487.01	54.889	20.027	1535.23	1467.73	15.52	4
27	1595.02	28.975	8.212	1602.74	1585.38	2.104	0.355
28	1622.02	38.121	14.652	1639.38	1604.66	5.251	1.237
29	1670.24	53.421	23.182	1691.46	1641.31	11.006	3.356
30	1733.89	21.274	3.18	1764.75	1724.24	3.497	0.267
31	2921.96	20.627	6.182	2947.03	2879.52	5.321	0.94
32	3276.83	25.116	0.202	3278.76	3161.11	9.912	0.003
33	3326.96	23.003	4.47	3380.98	3315.41	4.611	0.299

Fig. 1: 2 acid hydrazide IR

Preparation of 4-Arylidene-2-phenyl-5-(4H)-oxazolones 3a-l

4-Arylidene-2-phenyl-5-(4H)-oxazolones were prepared according to the reported method [11].

Preparation of biphenyl-4-carboxylic acid hydrazide 2

Hydrazine hydrate (80%) (0.4 mol) and 20 ml methanol were taken in a three necked flask,

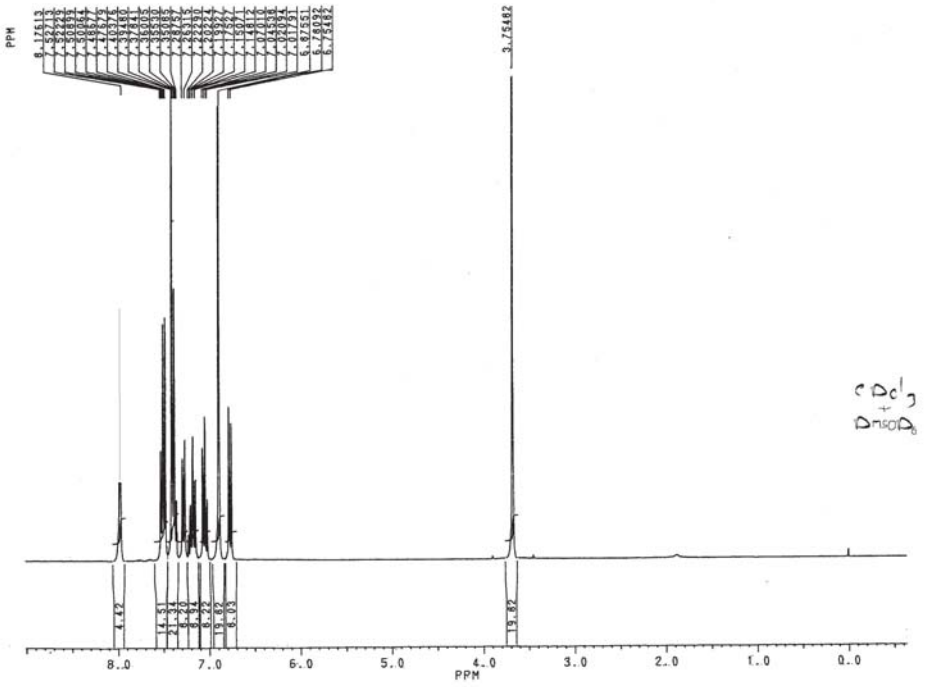


Fig. 2: 4a-White

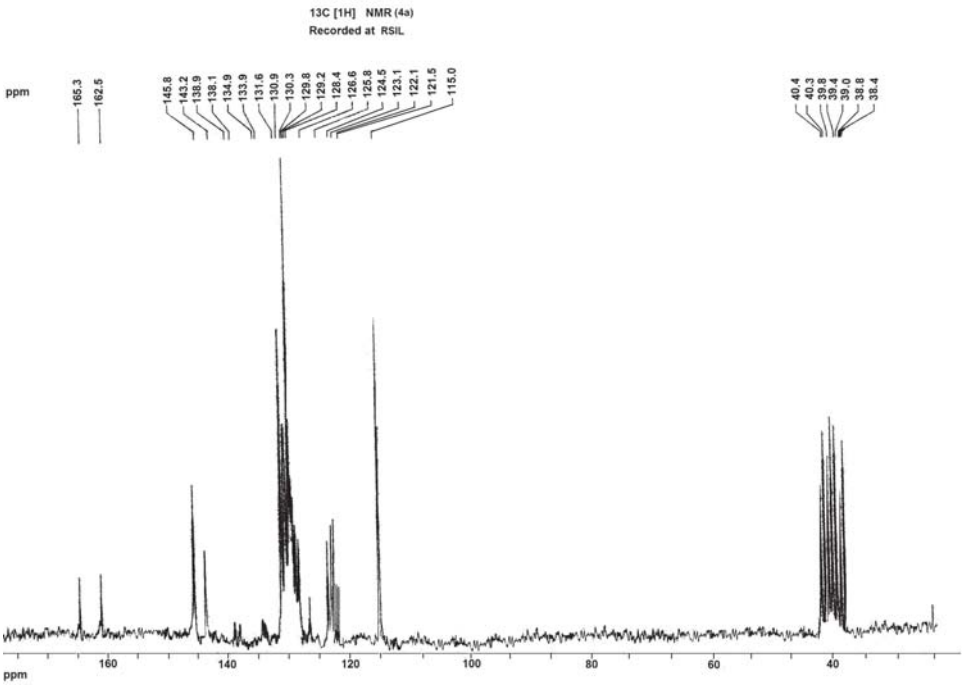


Fig. 3.

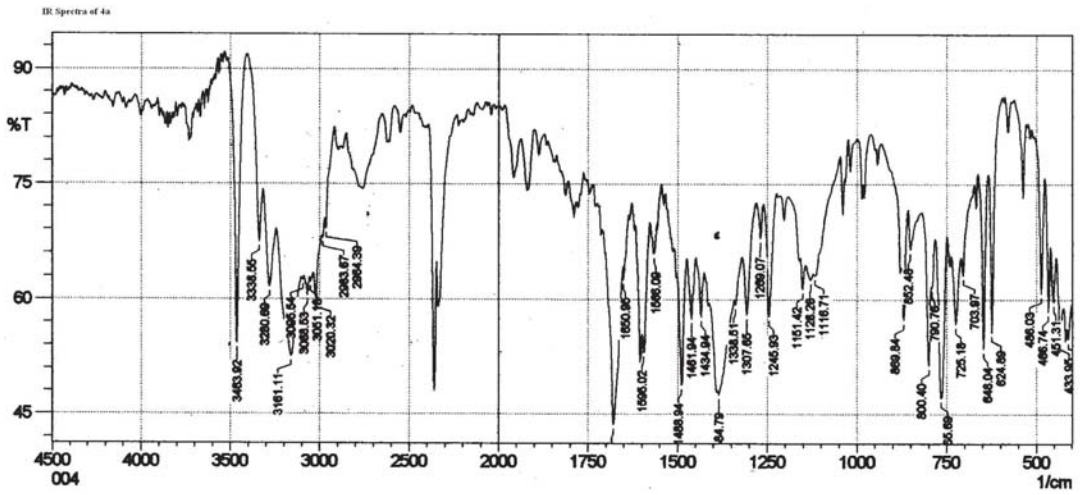


Fig. 4: IR SPectra of 4a

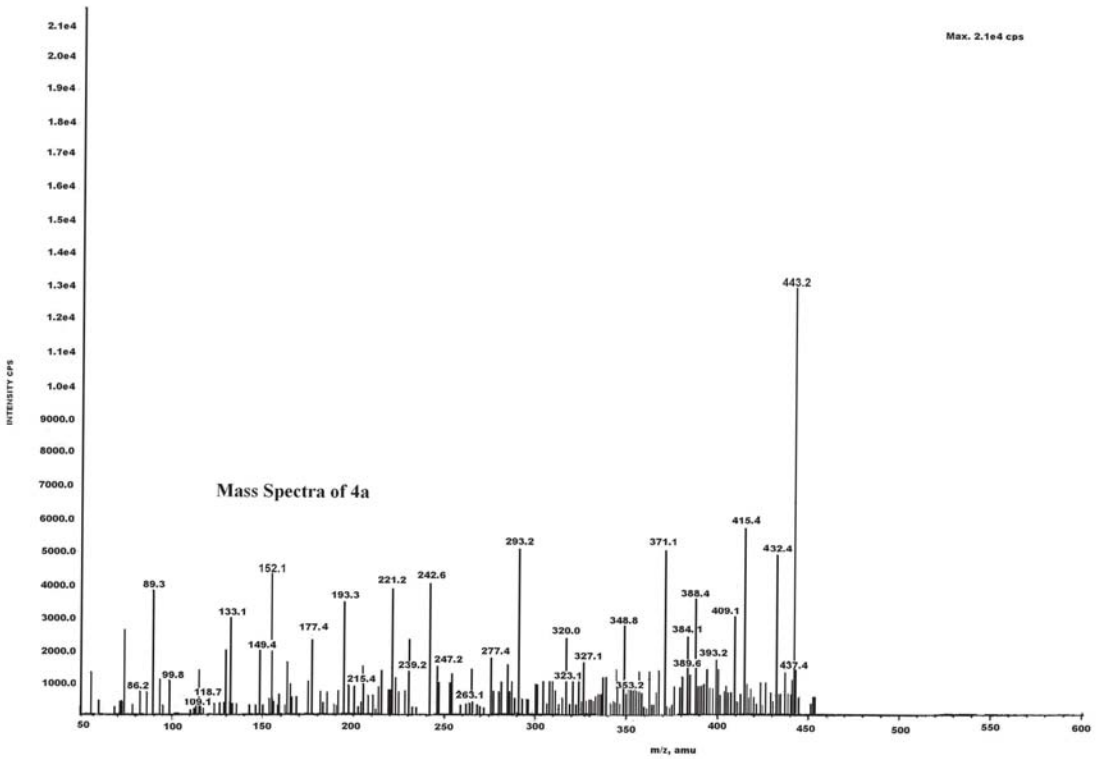


Fig. 5: Mass Spectra of 4a- Final

fitted with mechanical stirrer and reflux condenser. The methyl 1,1'-biphenyl-4-carboxylate (0.2 mol) was added slowly in portions with in 15 min. Refluxing was continued for 3 hrs. Excess methanol was distilled off. Reaction mixture was cooled and solid mass obtained was isolated by filtration, dried and recrystallized from ethanol. Purity of white crystals of biphenyl-4-carboxylic acid hydrazide having MP 185-190°C was checked by TLC.

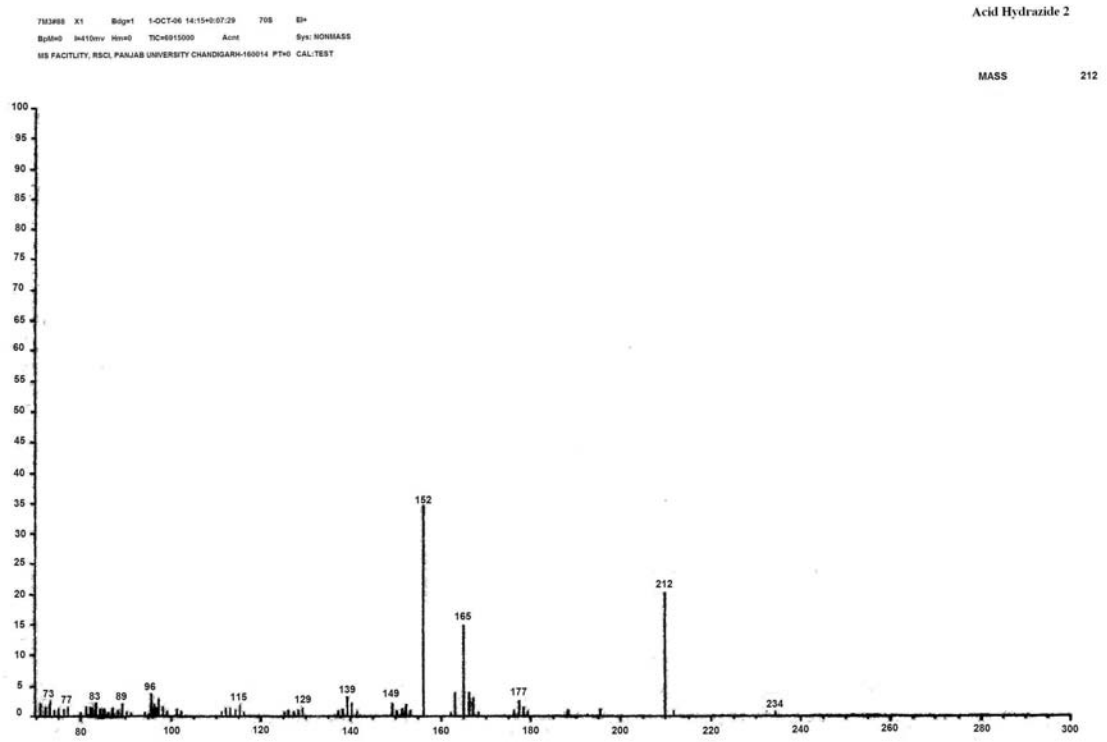


Fig. 6: Mass Spectra of Acid hydrazide 2

General procedure for the preparation of Biphenyl -4-carboxylic acid (4-benzylidene-5-oxo-2-subsituted phenyl-4,5-dihydro-imidazol-1-yl)-amide (4a-l)

2-Phenyl-4-benzylidene-5-oxazolone (2.49 g, 0.01 mol) was heated with an equimolar quantity of biphenyl-4-carboxylic acid hydrazide 2 (0.01 mole) in pyridine on oil bath at 140 °C for 4 hours. The resulting jelly-like mass was taken in an organic solvent and refluxed for 6 hours with continuous removal of water, cooled, excess solvent removed under vacuum and the resultant solid was worked up and purified over a column of silica gel, and the solid recrystallised from light petroleum to get 5-imidazolinone and was found chromatographically homogeneous.

RESULTS AND DISCUSSION

Imidizoline derivatives are useful intermediates in the heterocyclic chemistry. The synthesis of the compound is performed by the literature and the novel biphenyl derivative prepared is having good stability. The C NMR Signal is also supporting the presence of group attached. IR Spectra is also absolute clear and showing the condensation successfully. Activity photographs is quite clear and it shows good antibacterial activities. Thus the route and the molecules is right and it is having further scope to develop.

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