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A HIGHLY EFFICIENT METHOD OF BIO ACTIVE SYNTHESIS OF 4-(1H-BENZO[D]IMIDAZOLE-2-YL)-N-PHENYLBENZAMIDE ANALOGOUS

A. Bhavani Verma[1], Y. Pavankumar[1], B. Priyank[1] and Dr. N. Krishnarao[1]*

Department of Organic Chemistry, PRISM PG&DG College, Visakhapatnam, AP, India.

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***Corresponding Author**
Dr. N. Krishnarao
Department of Organic Chemistry, PRISM PG&DG College, Visakhapatnam, AP, India.

ABSTRACT

The investigation of bioactive synthesis of five 4-(1H-benzo[d]imidazole-2-yl)-N-phenylbenzamide(7a-7b) derivatives can be obtained from the compound 4-(1 H-benzo [d] imidazole-2-yl) benzoyl chlorides (5) with substituted aromatic primary amines in the presence of strong base in DCM at reflux. The compound (5) can be obtained by the chlorination of compound (4) with thionyl chloride in dichloromethane as solvent at 10^0C which is also the compound (4) synthesized by benzil treated with substituted carboxybenzalde and ammonium acetate, acetic acid in the presence of transitionmetal copper acetate catalyst at reflux. All the synthesized compounds were evaluated for their antimicrobial activity. The structures of the newly synthesized compounds were confirmed by FTIR, ^{1}H NMR, ^{13}NMR and MASS spectral data and elemental analysis. The structural determination of desired compounds can be determined by elemental analysis. Compounds were screened for in-vitro antibacterial activity against the representative panel of one gram positive bacterial strains like *Staphylococcus aureus* and one gram negative bacterial strain like *Escherichia coli*. Hence, the new derivatives of the titled compounds have been continued to the development for the active potent of new drugs.

KEYWORDS: 4-(1H-benzo[d]imidazole-2-yl)-N-phenylbenzamideanalogous, Benzil, carboxy benzaldehyde, ammonium acetate, copper acetate, antibacterial activity.

1. INTRODUCTION

The legendary of German chemist, Paul Ehrlich invented the use of drugs for infectious diseases in 1900. He was developed a process for evaluating a series of chemicals for their potential activity against diseases. The use of chemicals to treat disease is called

chemotherapy, which was also coined by him.[1] The synthetic drugs were largely used in early twentieth century (1900-1930s). The microbial diseases minimsed by the use of synthetic drugs for the treating after the discovery and development of antibiotics. A paradigm shift in therapeutics for treating bacterial diseases took place after the industrial production of penicillin and consecutive improvement of other antibiotics. There was extraordinary decline in encumber of disease due to large-scale use of these antibiotics.[2] Therefore, a common opinion was generated among citizens and policy-makers that infectious diseases would not produce an important problem in the future. A great constraint arose with the emergence of antibiotic resistant variants of the earlier sensitive bacteria and the emergence vis-à-vis development of new infectious diseases. A timeline responding the discovery and improvement of antibiotics and also the emergence of antibiotic resistant bacteria is shown in Figure 1. It is reveals that the important focus currently imposed on pharmaceutical industry to release the novel antimicrobials more rapidly and at low price cost can be coerce innovation and discovery to enable much new process. In this context, heterocycles compounds are good targets and are also found abundantly in natural products. Heterocyclic compounds have already been provided a platform for the rapid development of research in the areas of organic, pharmaceutical, analytical, and medicinal chemistry. Hence we have attempted to review the implications of heterocycles with special emphasis on of 4-(1H-benzo[d]imidazole-2-yl)-N-phenylbenzamide analogous in medicinal chemistry and also hint upon the prospect of developing antibacterial compounds.

Heterocyclic compounds are played a vital in synthetic organic chemistry and medicinally. Analysis of scientific publication in the recent times revealed that thereis a general trend in research for new drugs involving modification of existing biologically potent active matrices and design of molecular the structures new derivatives. The derivatives of imidazoles nucleus is present an important synthetic strategy in drug discovery. An Imidazole derivative imposed vital properties such as antimicrobial, anti-inflammatory, analgesic, anti-tubercular and anticancer activity. One of the most important applications of imidazole derivatives are able to their use as material for treatment of denture stomatities.The high therapeutic activities of the imidazole and its related drugs have been encouraged the medicinal chemists to prepare large number of novel chemotherapeutic agents. Imidazole drugs have broadened scope in clinical medicines. Medicinal properties of imidazole include anticancer, anticoagulants, anti-inflammatory, antibacterial, antifungal, antiviral, antitubercular, antidiabetic and antimalarial.[1-7]

Now days, the imidazole nucleus has attracted to attention of the scientific community because its chemical and biological properties.[8,9] The essential amino-acid histidine or in alkaloids exhibiting anti-tumoral, anti-cancer (dacarbazine), antihistaminic (cimetidine), anti-parasitic (metronidazole), and antihypertensive (losartan) and anti-bacterial activities.[10-12] of the compounds containing imidazole nucleus is present in the structures of several natural products. A great numbers of medicines having the imidazole nucleus, including ketoconazole which are used to treat fungal infections, bacterial infections, and gastric ulcers, respectively.[13-14] Due to their importance; it has become an attractive target for the synthetic and medicinal chemist. There are many synthetic methodologies that have been developed for assembling and decorating the imidazole ring with diverse functional groups.

Various substituted imidazole and its derivatives are an important type of compounds in the field of synthetic organic chemistry as well as medicinally chemistry. They exhibit a broad range of biological activities such as, inhibitors of p38 MAP Kinase,[15] B-Raf kinase,[16] anti-HIV,[17] and anticonvulsant,[18] HIV-1 protease,[19] calcium antagonist and inhibitors of thromboxane A2 synthesize,[20] therapeutic agent,[21] antihistaminic,[22] tranquilizer,[23] antimuscarinic,[24] antiarthritic,[25] cardiotonic,[26] HMG CoA reductase(HMGR),[27] and antitumor agents.[28] In recent times substituted imidazoles are substantially used as Ionic liquids,[29] a new approach to "green chemistry Literature survey indicated that various methods have been developed for the synthesis of 2,4,5-triaryl-1H-imidazoles by three component cyclocondensation of 1,2-diketone, -hydroxy ketone with aldehydes and ammonium acetate, which comprises the use of ionic liquids,[30] silica sulphuricacid,[31] refluxing in acetic acid,[32] alum,[33] sulphanilic acid,[34] $NiCl_2.6H_2O$,[35] H_3PO_4,[36] CAN,[37] grinding with I_2,[38] from N-acylated -amino in presence of triphenyl phosphine followed by coupling with Pd catalyst.[39] Recently, Konwar, et al. reported the synthesis of imidazole using $InCl_3.H_2O$.[40]

The titled compound can be obtained from starting material 4-(1H-benzimidazol-2-yl) benzoic acid. Our continuous program is able to developing on the basis of synthesis of amides uses of various substituted aromatic primary amines. We reported the first time the synthesis of 4-(1H-benzo[d]imidazole-2-yl)-N-phenylbenzamide analogous employing from 4-(1H-benzo[d]imidazole-2-yl)-benzoyl chloride with various substituted aromatic primary amines strong base such as triethyl amines and also examined by antibacterial studies.

2. EXPERIMENTAL METHODS

The synthetic grade reagents, solvents, chemicals and desired raw materials are procured from Merck chemical PVLTd and also used for without purification. The melting points of the newly obtained derivatives were measured by a Thermo Scientific Fluke 51 II, melting point instrument and uncorrected was reported. The newly synthesized derivatives were interpreted by advanced spectroscopic methods such as ^{1}H NMR (400 MHz) and ^{13}C NMR (100MHz) spectra of the synthesized compounds were recorded values by an instrument Bruker Ultra Shield at room temperature Ultra Shield using tetramethylsilane (TMS) as the internal standard and deuterated chloroform ($CDCl_3$) as the solvent. Chemical shift values were recorded in δ (ppm) and multiplicities are expressed as s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). The molecular weights of the derivatives were measured by LCMS instrument were run on a Shimadzu spectrometer instrument, which was operating at 70 eV in positive mode. The progress of the reactions was examined by thin layer chromatography (TLC) analyses using Merck 60 F254 silica gel.

2.1.1. General Procedure for the Synthesis Preparation of 4-(1H-benzimidazol-2-yl) benzoic acid: (3)

The take clean and dry 50 mL four neck RBF. 25 mL ethanol was introduced into RBF and the mixture of benzil with carboxy benzaldehyde, ammonium acetate and acetic acid was dissolved in the above solvent. The catalyst is added gradually into RBF. The total arrangement fitted on the magnetic stirrer and reaction was continued for appropriate time at 70^{0}C. The reaction was checked by TLC as mobile phase (4:6 = EtOAc: petroleum ether). After completion of the reaction, we observed TLC and stop the reaction. The reaction mixture was cooled at room temperature and filtered the catalyst, poured in ethylacetae solvent. The organic layer is neutralized with saturated solution of sodium by carbonate and separated ethylacetae layer. This organic layer washed with water in TWO times and separated ethylacetae layer. The organic layer distilled of under vacuum and recrystallized from ethanol.

Characterization of the product

Pale red solid; Yield-84%, m.p-247-249^{0}C; R_f-0.40 (petroleum ether: EtOAc- 6:4); FTIR (cm^{-1}): 3612 (-OHstr), 3452 (NH-str), 3096 (Ar-CHstr), 1689 (COstr) 1584, 1557, 1519, 1498 (Ar-H, C=C),

1HNMR(400MHz,$CDCl_3$)ppm:10.982(acid,1H,s),9.664(N-Himidazole,1H,s,),8.182-8.095 (Ar-H,2H,m),7.857-7.718(Ar-H,4H,m),7.298-7.268(Ar-H,2H,m);^{13}CNMR(100MHz,$CDCl_3$) δppm:167.29,145.76,139.62,135.73,129.64,128.74,128.32,127.96,122.66,121.45,115.63; LCMS(m/z): 239.37(M^++H);Molecularformulae:$C_{14}H_{10}N_2O_2$:Elemental analysis: calculated: C- 70.58 , H-4.23 , N- 11.76 ; found : C- 70.52 , H- 4.22 ,N- 11.83.

2.1.2. General Procedure for the Synthesis 4-(1H-benzo[d]imidazole-2-yl)-benzoyl chloride (5)

The take clean and dry 50 mL four neck RBF. 25 mL DCM was introduced into RBF and the compound (4) was added with thionyl chloride slowly by using addition funnel into RBF. The total arrangement fitted on the magnetic stirrer and reaction was continued for appropriate time at 40^0C.The reaction was monitored by TLC as mobile phase (3:7 = EtOAc: petroleum ether).After completion of the reaction, we observed TLC and stop the reaction. The solvent was evaporated under heating at 40^0C. The crude was purified by ethyla acetate.

Characterization of the product

Paleredsolid: Yield-84%, m.p-221-223^{0}C; R_f-0.45(petroleum ether: EtOAc-5:5); FTIR (cm-1):3455(NH-str),3085(Ar-CHstr),1698(COstr),1591,1542,1509,1484(Ar-H,C=C),^{1}HNMR (400MHz,$CDCl_3$)ppm:9.574(N-Himidazole,1H,s,),8.216(Ar-H,2H,d,J=7.2Hz), 7.924 (Ar-H,2H,d,J=6.4Hz),7.638(Ar-H,2H,d,J=9.0Hz),7.294(Ar-H,2H,t,J=5.4Hz);^{13}CNMR(100MHz, $CDCl_3$)δppm:168.94,148.35,137.86,131.32,129.04,128.85,128.31,122.28,115.74.LCMS (m/z): 258.31(M+2); Molecular formulae: $C_{14}H_9ClN_2O$.Elemental analysis: calculated: C-65.51, H-3.53, N-10.91; found : C- 65.47, H- 3.51, N- 10.99.

2.1.3. General Procedure for the Synthesis 4-(1H-benzo[d]imidazole-2-yl)-N-phenylbenzamide analogues (7)

1).4-(1H-benzo[d]imidazole-2-yl)-N-phenylbenzamide (7a)

A mixture of the compound (5) (1mmol) and aniline (1mmol) dissolved in dichloromethane (50 mL) and added with strong base (5 mmol) such as triethylamine into dry and clean four necks RBF. The total arrangement fitted on the magnetic stirrer and reaction carried at 40^0C. The progress of the reaction was monitored by TLC as a mobile phase (4:6 = EtOAc: n-hexane). After completion of the reaction, evaporated the solvent, crude was dissolved in Ethyl acetate and followed by neutralized with saturated solution of sodium bi carbonate. Separated the organic layer and washed with water in two times. The layer was distilled off U/ vacuumed and compound recrystized from ethanol.

Pale red solid: Yield-89%, R_f-0.40 (petroleum ether: EtOAc-6:4); FTIR (cm-1): 3678 (CO NH), 3441 (NH-str), 3095 (Ar-CHstr), 1691 (COstr), 1590, 1539, 1510, (Ar-H, C=C),^{1}HNMR (400MHz, $CDCl_3$) ppm: 10.476 (s, 1H, NH-imidazole), 9.845 (s, 1H, -CONH), 7.914-7.723 (m, 8H, Ar-H), 7.318-7.729 (m, 4H, Ar-H); ^{13}CNMR (100MHz, CDCl3) ppm: 164.96, 147.66, 138.32, 136.45, 134.37, 130.95,129.68, 128.84,128.17, 127.83, 127.17, 122.35, 115.32 ; LCMS (m/z) : 312.54 (M-H); Molecular formulae : $C_{20}H_{15}N_3O$; Elemental analysis; Calculated: C-76.66 ,H- 4.83 ,N-13.41,Obtained:C- 76.60,H-4.81 ,N-13.48.

2).N-(4-acetylphenyl)-4-(1Hbenzo[d]imidazole-2-yl) benzamide (7b)

A mixture of the compound (5) (1 mmol) and 4-aminoacetophenone (1mmol) dissolved in dichloromethane (50 mL) and added with strong base (5 mmol) such as triethylamine into dry and clean four necks RBF.The total arrangement fitted on the magnetic stirrer and reaction carried at 40^{0}C . The progress of the reaction was monitored by TLC as a mobile phase (4:6 = EtOAc: n-hexane). After completion of the reaction, evaporated the solvent, crude was dissolved in Ethyl acetate and followed by neutralized with saturated solution of sodium bi carbonate. Separated the organic layer and washed with water in two times. The layer was distilled off U/ vacuumed and compound recrystized from ethanol.

Paleyellowsolid: Yield-92%, R_f-0.40 (petroleum ether: EtOAc-6:4); FTIR (cm-1): 3616(CONH), 3458 (NH-str),3072 (Ar-CHstr), 2952(C-Hstr), 1718 (COstr), 1583, 1532, 1490, (Ar-H, C=C), ^{1}HNMR (400MHz, $CDCl_3$) ppm:10.718 (s,1H,NH-imidazole), 9.913 (s, 1H,-CONH),7.950-7.697(m,10,Ar-H),7.297-7.271(m,2H,Ar-H),1.456(s,3H,CH^3);^{13}CNMR (100MHz,$CDCl_3$)ppm:190.12,165.84,148.15,139.07,138.36,136.61,134.37,132.08,130.95, 129.68,128.84,128.17,127.83,122.35,115.32,27.14;LCMS(m/z):356.25(M+H);Molecular formulae : $C_{22}H_{17}N_3O_2$; Elemental analysis;Calculated:C-74.35,H-4.81,N-11.82,Obtained:C-74.29,H-4.79, N- 11.89.

3). 4-(1Hbenzo[d]imidazole-2-yl)-(pyridine-2-yl) benzamide (7c)

A mixture of the compound (5)(1mmol) and 2-amino pyridine (1mmol) dissolved in dichloromethane (50 mL) and added with strong base (5 mmol) such as triethylamine into dry and clean four necks RBF.The total arrangement fitted on the magnetic stirrer and reaction carried at 40^{0}C . The progress of the reaction was monitored by TLC as a mobile phase (4:6 = EtOAc: n-hexane).After completion of the reaction, evaporated the solvent, crude was dissolved in Ethyl acetate and followed by neutralized with saturated solution of sodium bi

carbonate. Separated the organic layer and washed with water in two times. The layer was distilled off U/ vacuumed and compound recrystized from ethanol.

yellow solid: Yield-87%, R_f-0.45 (petroleum ether : EtOAc-5:5); FTIR (cm-1): 3678 (CONH),3441 (NH-str), 3095 (Ar-CHstr), 1691 (COstr), 1590, 1539, 1510, (Ar-H, C=C), ^{1}HNMR(400MHz,$CDCl_3$)ppm:10.094(s,1H,NH-imidazole),10.018(s,1H,-CONH),8.346(s, 1H,Ar-H),7.946-7.706(m,7H,Ar-H),7.394-7.292(m,4H,Ar-H);^{13}CNMR(100MHz,$CDCl_3$) ppm:166.38,148.71,146.46,138.38,137.23,136.61,135.65,134.22,130.98,128.73,128.16, 122.65,118.38,115.47,114.09;LCMS(m/z):314.37(M+);Molecularformulae:$C_{19}H_{14}N_4O$; Elemental analysis;Calculated:C-72.60 ,H-4.49 ,N-17.82,Obtained:C-72.55,H-4.47 ,N- 17.87.

4). 3-(4-(1-(Hbenzo[d]imidazole-2-yl) benzoic acid (7d)

A mixture of the compound (5) (1 mmol) and 3-aminobenzoicacid (6) (1mmol) dissolved in dichloromethane (50 mL) and added with strong base (5 mmol) such as triethylamine into dry and clean four necks RBF.The total arrangement fitted on the magnetic stirrer and reaction carried at 40^{0}C . The progress of the reaction was monitored by TLC as a mobile phase (4:6 = EtOAc: n-hexane). After completion of the reaction, evaporated the solvent, crude was dissolved in Ethyl acetate and followed by neutralized with saturated solution of sodium bi carbonate. Separated the organic layer and washed with water in two times. The layer was distilled off U/ vacuumed and compound recrystized from ethanol.

White solid: Yield-85%, R_f-0.45 (petroleum ether: EtOAc-5:5); FTIR (cm-1): 3762(-OHstr), 3616(CONH), 3456 (NH-str), 3063 (Ar-CHstr), 1686 (COstr), 1594, 1574, 1509, (Ar-H, C=C),^{1}HNMR(400MHz,$CDCl_3$)ppm:11.124(s,1H,COOH),10.346(s,1H,NH-imidazole), 10.024(s,1H,-CONH),8.146(s,1H,Ar-H),7.908-7.615(m,9H,Ar-H),7.299-7.281(m,2H,Ar-H);^{13}CNMR(100MHz,$CDCl_3$)ppm:166.85,163.35,148.38,138.52,136.47,133.42,131.26, 129.97,128.86,128.14,127.44,126.31,122.08,121.51,119.64,115.74;LCMS(m/z):358.22 (M+H);Molecularformulae:$C_{21}H_{15}N_2O_3$; Elemental analysis;Calculated:C-70.57,H-4.22,N-11.75,Obtained:C- 70.50,H-4.21 ,N- 11.83.

5).4-(1H-benzo[d]imidazole=2-yl)-N-(thiophene-2-yl) benzamide (7e)

A mixture of the compound (5) (1mmol) and 2-amino thiophene (1mmol) dissolved in dichloromethane (50 mL) and added with strong base (5 mmol) such as triethylamine into dry and clean four necks RBF.The total arrangement fitted on the magnetic stirrer and reaction carried at 40^{0}C . The progress of the reaction was monitored by TLC as a mobile phase(5:5 =

EtOAc: n-hexane). After completion of the reaction, evaporated the solvent, crude was dissolved in Ethyl acetate and followed by neutralized with saturated solution of sodium bi carbonate. Separated the organic layer and washed with water in two times. The layer was distilled off U/ vacuumed and compound recrystized from ethanol.

Pale yellow: Yield-88%, R_f-0.50 (petroleum ether : EtOAc-4:6); ^{1}HNMR (400MHz, $CDCl_3$) ppm:10.547(s,1H,NH-imidazole),10.102(s,1H,-CONH),7.918-7.646(m,6H,Ar-H),7.382-7.278(m,5H,Ar-H);13CNMR(100MHz,$CDCl_3$)ppm:163.89,147.44,139.05,138.51,136.24, 132.74,131.26,129.19,128.86,123.88,122.22,118.96,115.74,110.45;LCMS(m/z):319.39(M+); Molecularformulae:$C_{18}H_{13}N_3OS$;Elementalanalysis;Calculated:C-67.69,H-4.10,N-13.16, Obtained : C- 67.60,H-4.08 ,N- 13.23.

3. Biology

Antibacterial activity

The synthesized titled derivatives were evaluated for their antibacterial activity against two gram positive bacterial strains Staphylococcus aureus and Bacillus subtilis and two gram negative bacterial strains Escherichia coli and Pseudomonas aeruginosa by using modified paper disc diffusion method. The tube dilution technique is used for the determination of MIC values of test derivatives.[25] All the synthesized derivatives were dissolved separately to prepare a stock solution of 1 mg ml-1 using DMF. Stock solution was aseptically transferred and suitably diluted with sterile broth medium to have different concentrations of each test compound ranging from 100 µg ml-1, 250 µg ml-1 and 500µg ml-1 in different test tubes. All the tubes were inoculated with one loopful of one of the test bacteria. The process was continued with different test bacteria and different samples. Tubes inoculated with bacterial cultures were incubated at 37°C for 24 hrs. and the presence/absence of growth of the bacteria was observed. From these results reveals that MIC of each test compound was determined against each test bacterium. A spore suspension in sterile distilled water was prepared from five-days-old culture of the test bacteria growing on nutrient broth media. About 20 ml of the growth medium was transferred into sterilized Petri plates and inoculated with 1.5 ml of the spore suspension. In the paper disc-diffusion method, paper disc impregnated with compounds dissolved in DMSO at concentration 100, 250 and 500 µg ml-1 were used. Disc impregnated with DMSO were used as solvent control for antibacterial activity because of free solubility of test compounds. The microorganism culture was spread over nutrient agar media in petri dishes, and then the disc impregnated with the solution was

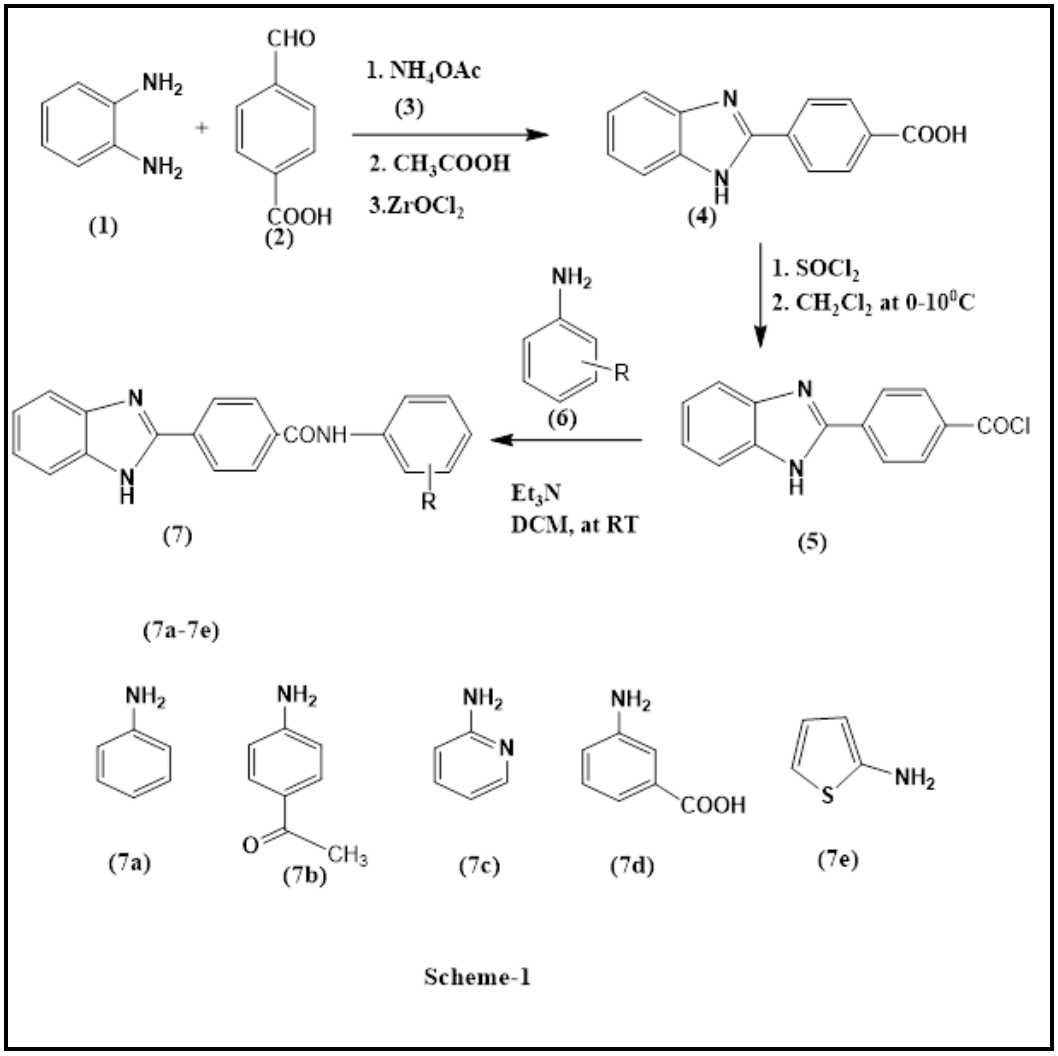
placed on the surface of the media inoculated with the bacterial strain. The plates were incubated at 35°C for 24 hrs. for bacterial cultures. After incubation, the zones of inhibition around the disc were observed. The zones of inhibition indicate that the compounds inhibit growth of microorganism. Each testing is done in triplicate. Ciprofloxacin at conc. 22 µg ml-1 and 25 µg ml- was used as standard drug for antibacterial activity.

4. RESULTS AND DISCUSSION

The key intermediate 4-(1H-benzo[d]imidazole-2-yl)-N-phenylbenzamide analogous **(7a-7e)** s can be obtained from the compound 4-(1 H-benzo [d] imidazole-2-yl) benzoyl chlorides (4) with substituted aromatic primary amines in the presence of strong base triethylamine at reflux. The compound (5) can be obtained by the chlorination of compound (4) with thionyl chloride in dichloromethane as solvent at 10^0C and also compound (4) synthesized by benzil treated with substituted carboxybenzalde and ammonium acetate, acetic acid in the presence of transitionmetal catalyst such as copper acetate at reflux.

In order to assess the efficiency of the present producer in comparison with the reported methods for the preparation of 4-(1H-benzimidazol-2-yl) benzoic acid (4) from benzil and carboxy benzaldehyde, the results of present method was compared with reported methods which used water as solvent (Table-II). As it is clear from Table-II, the present method is more efficient when all terms including yields, reaction times, conditions and catalyst are taken into account.

Table –II reveals that the compound (7) can be obtained from compound (5) with various suitable different substituted aromatic primary amines by strong base triethylamine in DCM as solvent. During in the synthesis, different bases are applied of same solvent, the conclusion of the data and finally observed triethyl amine is a perfect base for this preparation because excellent yield and short reaction time and also easy to evaporated the solvent.



Scheme-1

Table-I: Comparison of some other procedures with the present method for the synthesis of 4-(1H-benzimidazol-2-yl) benzoic acid:

Entry	Catalyst (mol)	Solvent	Yield (%)	Time(min)
1	Zinc acetate	Ethanol	58	270
2	**copper acetate**	**Ethanol**	**90**	**120**
3	Silver acetate	Ethanol	90	150
4	Mg(OAc)2	Ethanol	51	300
5	Mn $(OAc)_2$	Ethanol	63	250

We investigated the efficiency of copper acetate compared to other acid catalysts based on the synthesis of 4-(1H-benzimidazol-2-yl) benzoic acid (4). The results show that copper acetate is an efficient catalyst in terms of product yield and reaction time (Table-II). The catalyst was recovered after completion of the reaction; the catalyst was washed with dichloromethane, dried, and reused for subsequent reactions for additional five times. We observed a slight decrease in its activity in terms of product yield (Table- II). Copper acetate is the perfect suitable catalyst for this synthesis compound (4).

Table II: The different reagents for synthesis of derivatives (6a-6e).

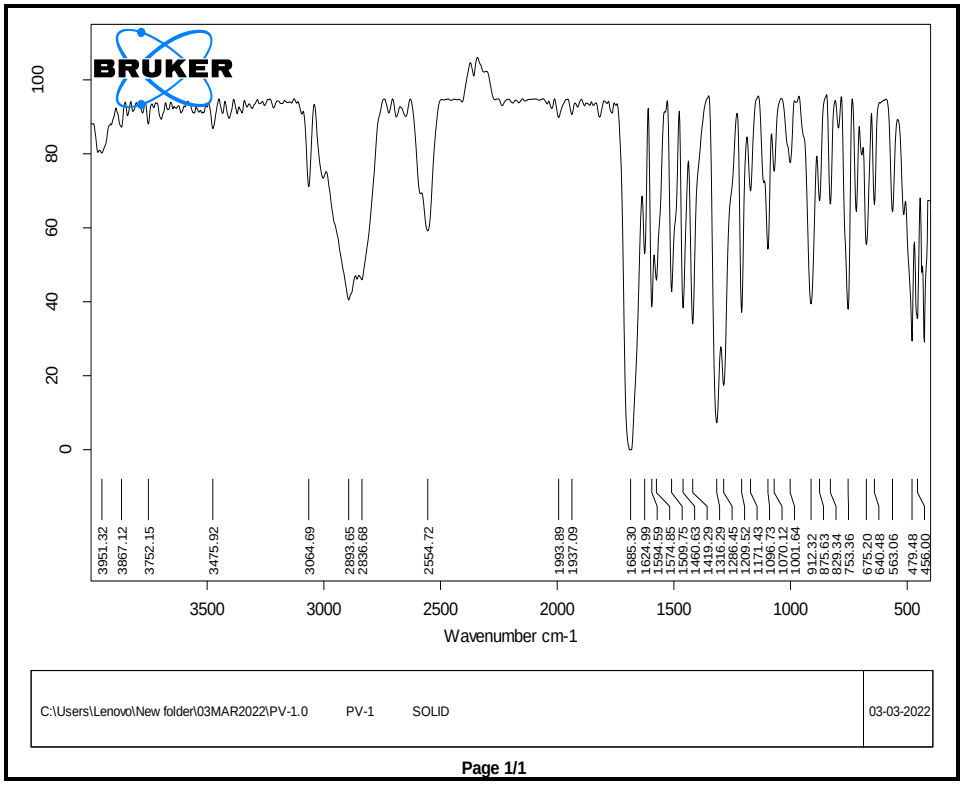
Entry	Reagent	Solvent	Yield (%)	Time(min)
1	K_2CO_3	MeOH	67	250
2	Et_3N	DCM	90	120
3	K_2CO_3	H_2O	64	180
4	KOH	H_2O	54	250
5	Et_3N	No solvent	31	5(hrs.)

Antibacterial Activity of the titled compound

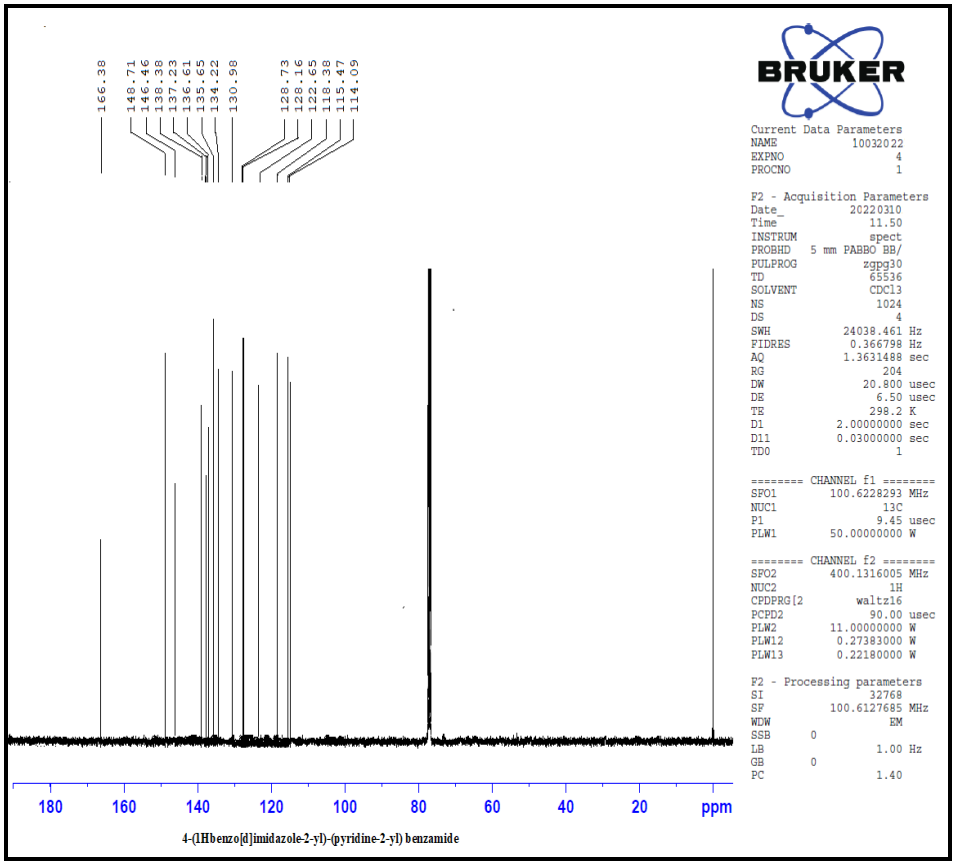
In the present investigation, we used various species on the bacterial strains like *Escherichia coli* and *Staphylococcus Aureus* to determined zone measure inhibitory of desired products. Results of anti-microbial screening of the analogues have been studied. All the five derivatives were evaluated for anti-microbial activity by cup-plate method at the concentration of 100 µg/ml, 250µg/ml and 500µg/ml using *Staphylococcus Aureus* and *Escherichia coli* bacteria. The results are represented Table III. Above observation all the synthesized compounds showed potent activity, among all the compounds "6e" exhibited excellent potent activity. The compound "6c" showed moderate to good active potential against bacterial strains. The compound "6a" and "6b" exhibited low active potential against the bacterial strains.

Table-III: Results were interpreted in terms of diameter (mm) of zone of inhibition of titled Derivatives.

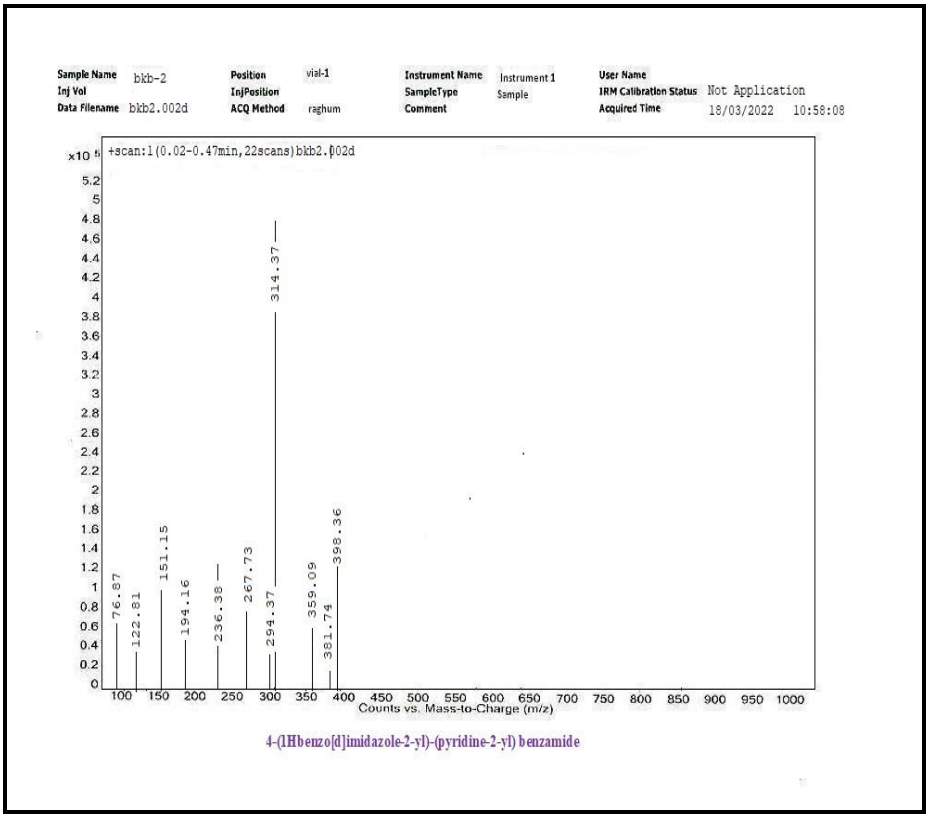
S.No	Compound code	Zone of Inhibition (mm)					
		Gram +ve			Gram –ve		
		S.aureus			E.coli		
		100µg/ml	250 µg/ml	500 µg/ml	100µg/ml	250 µg/ml	500 µg/ml
1	**6a**	10	12	11	13	11	11
2	**6b**	09	10	12	14	14	16
3	**6c**	12	14	16	11	12	15
4	**6d**	10	10	12	09	11	13
5	**6e**	15	18	19	18	21	22
Cont	**DMSO**	10			10		
STD	**Streptomycin**	22	22	22	25	25	25



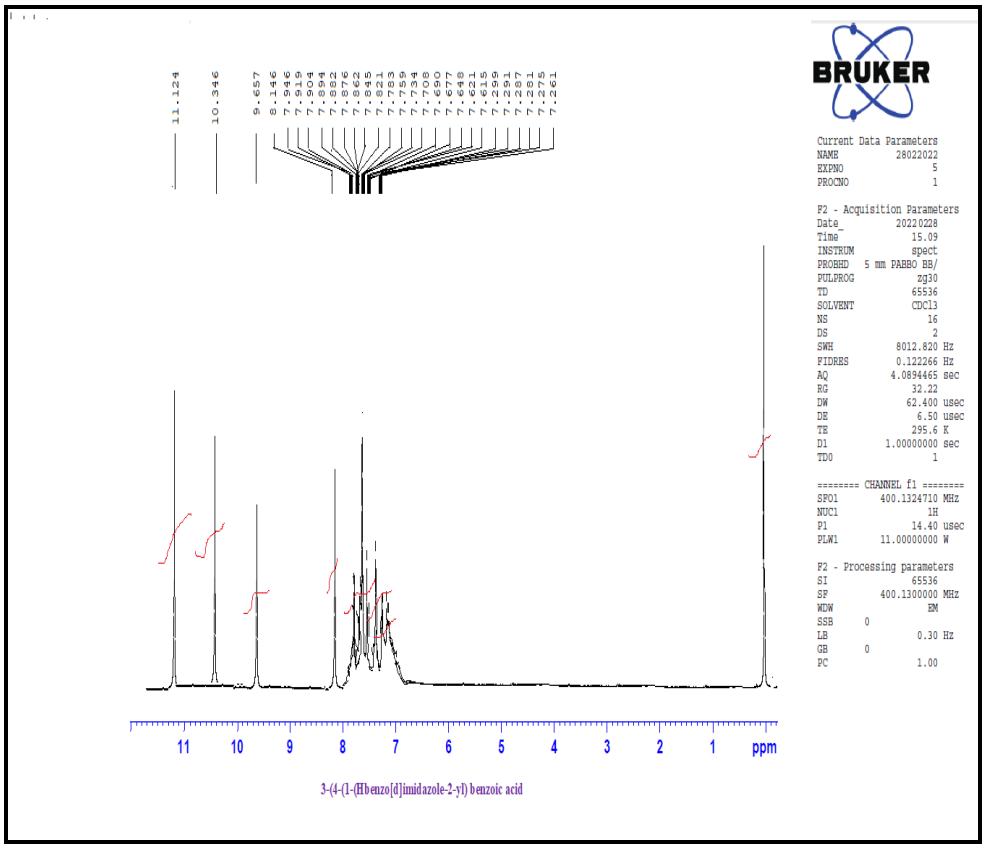
3-(4-(1-(Hbenzo[d]imidazole-2-yl) benzoic acid (7d)



4-(1Hbenzo[d]imidazole-2-yl)-(pyridine-2-yl) benzamide (7c)



4-(1Hbenzo[d]imidazole-2-yl)-(pyridine-2-yl) benzamide (7c)



3-(4-(1-(Hbenzo[d]imidazole-2-yl) benzoic acid (7d)

5. CONCLUSION

Imidazole compound (3) was synthesized in an excellent yield (91%) using a simple and an efficient synthetic producer and an easy purification procedure and also good catalytic activity. The compound was characterized by the usual FT-IR, ^{1}HNMR, ^{13}CNMR and LCMS spectroscopic techniques. The synthesized derivatives showed antibacterial activity against S.aureus as well as E.coli at low concentrations, and the diameter of the inhibition zone appears to depend on the concentration of the compound used. Imidazole derivative presents a substitution on all carbons of the imidazole ring, revealing it to be a novel molecule to use as a potential antibiotic against S. aureus.

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7. REFERENCES

1. Congiu C, Cocco MT, Onnis V. BioorgMed Chem Lett, 2008; 18: 989–993.
2. Siddiqui IR, Singh PK, Srivastava V, Singh J. Indian Journal of Chemistry, 2010; 49: 512-520.
3. Lin YI, Peterson PJ, Yang Y, Weiss WJ, Shales DM, et al. Bioorg Med Chem Lett, 2008; 16: 1890–1902.
4. Nakamura T, Kakinuma H, Umemiya H, Amada H, Miyata N, et al. Bioorg Med Chem Lett, 2004; 14: 333–336.
5. Roman G, Riley JG, Vlahakis JZ, Kinobe RT, Brien JF, et al. Bioorg MedChem, 2007; 15: 3225-3234.
6. Babizhayev MA. Life Sci, 2006; 78: 2343-2357.
7. Nantermet PG, Barrow JC, Lindsley SR, Young M, Mao S, et al.. Bioorg Med Chem Lett, 2004; 14: 2141-2145.
8. Narasimhan B, Deepika S, Kumar P,. Med Chem Research, 2011; 20: 1119–1140.
9. Botta M, Corelli F, Gasparrini F, Messina F, Mugnaini CJ et al. Organic Chemistry, 2000; 65: 4736–4739.
10. Jin Z, Imidazole, oxazole and thiazole alkaloids. Nat Prod Rep, 2006; 23: 464-496.
11. Molina P, Tárraga A, Otón F, Org Biomol Chem, 2012; 10: 1711-1724.
12. Jin Z (2013) Muscarine, imidaozle, oxazole and thiazole alkaloids. Nat ProdRep, 2013; 30: 869-915.

13. Kumar JR, Pharamacophores, 2010; 1: 167–177.
14. Bendaha H, Yu L, Touzani R, Souane R, Giaever G., Eur J Med Chem, 2011; 46: 4117-4124.
15. Priya, B.; Nanjunda Swamy, S.; Tejesvi, M.; Sarala, G.; Gaonkar, S.; Naveen, S.; Shashidhara Prasad, J.; Rangappa, K.,),. European Journal of Medicinal Chemistry, 2006; 41(11): 1262-1270.
16. Zanatta, N.; Alves, S. H.; Coelho, H. S.; Borchhardt, D. M.; Machado, P.; Flores, K. M.; da Silva, F. M.; Spader, T. B.; Santurio, J. M.; Bonacorso, H. G.; Martins,Lee.M. A., Bioorganic Medicinal. Chemistry, 2007; 15(5): 1947-58.
17. Sener, E. A.; Bingol, K. K.; Oren, I.; Arpaci, O. T.; Yacin, I.; Altanlar, N., Farmaco, 2000; 55(6-7): 469-76.
18. Temiz-Arpaci, O.; Aki-Sener, E.; Yalcin, I.; Altanlar, N.,, Arch. Pharm. (Weinheim), 2002; 335(6): 283-8.
19. Ertan, T.; Yildiz, I.; Ozkan, S.; Temiz-Arpaci, O.; Kaynak, F.; Yalcin, I.; Aki-Sener, E.; Abbasoglu, U., Bioorganic Medicinal. Chemistry, 2007; 15(5): 2032-44.
20. J. Lundstrom and A. Brossi, The Alkaloids, Ed. Academic Press: New York, USA, 1983; 21: 255.
21. M.A. Collins and A. Bross, The Alkaloids, Ed. Academic Press: New York, USA, 1983; 21: 329.
22. M. Chrzanowska, B.V. Schonenberg, A. Brossi and J. L. Flippen-Anderson, Helv. Chim. Acta, 1987; 70: 1721-1731.
23. Z. Czarnocki, D. Suh, D.B. MacLean, P.G. Hultin and W.A. Szarek,, Canada Journal of Chemistry, 1992; 70: 1555-1561.
24. E.H. Corey and D.A., Gin Tetrahedron Letters, 1996; 37: 7163-7166.
25. B. Zhou, J. Guo and S.J. Danishefsky, Organic Letters, 2002; 4: 43-46.
26. J.D. Scott and R.M. Williams, Chemical Review, 2002; 102: 1669-1730.
27. R. Mechaca, V. Martinez, A. Todriguez, N. Rodriguez, M. Flores, P. Gallego, I. Manzanares and C. Cuevas, Journal of Organic Chemistry, 2003; 68: 8859-8866.
28. G. Blasko and A. Brossi,, The Alkaloids, Ed. Academic Press: New York, USA, 1990; 48: 249.
29. J. Sousek, G. Guedon, T. Adam, H. Bochorakova, E. Taborska, I. Valka and V. Simanek, ,Photochemcal Analysis., 1999; 10: 6-11.
30. Z. Kaluza, D. Mostowicz, G. Doleca and R. Wojcik, Tetrahedron, 2008; 64: 2321-2328.

31. K. Funabashi, H. Ratni, M. Kanai and M. Shibasaki., Journal of American Chemical Soceity, 2001; 123: 10784-10785.
32. J. Houston and I. Rodger., Clinical Experimental Pharmacology, 1974; 1: 401-413.
33. M. Ohkubom, A. Kuno, K. Katsuta, Y. Ueda, K. Shirakawa, H. Nakanishi, I. Nakanishi, T. Kinoshita and H. Takasugi., Chemical Pharma. Bull., 1996; 44: 95-102.
34. W. J. Thompson, P.S. Anderson, S.F. Britcher, T.A. Lyle, J.E. Thies, C.A. Magill, S.L. Varga, J.W. Schwering, P.A. Lyle, and M.E. Christry., Journal Medicinal Chemistry, 1990; 33; 789-808.
35. J. Olney, M. Price, K.S. Salles, J. Labruyere and G. Friedrich., European Journal Pharmacology, 1987; 141: 357-361.
36. J.W. McDonald, F.S. Silverstein and M.V. Johnston. European Journal Pharmacology, 1987; 14: 359-361.
37. H. Kubota, T. Watanabe, A. Kakefuda, N. Masuda and K. Wada. Dioorg., Journal Medicinal Chemistry, 2004; 12: 871-882.
38. Rahbari, R.; Sheahan, T.; Modes, V.; Collier, P.; Macfarlane, C.; Badge, R.M.; BioTechniques, 2009; 46: 277.
39. Scherer, W. F.; Syverton, J. T.; Gey, G.O.Journal Experimental Medicine, 1953; 97: 695.