An Efficient Synthesis of Schiffs Base Containing Benzimidazole Moiety Catalyzed by Trichloro Salicylic Acid

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***Abstract*— An efficient method for the synthesis for a novel Schiff bases from 2-amino benzimidazoles with P-substituted aryl aldehyde by using Trichloro Salicylic Acid in organic solvent at room temperature. The intermediate moiety (2-amino Benzimidazole) can be synthesized from o-phenyl diamine with cyano bromide in the presence of acid medium. All the newly synthesized derivatives were evaluated by the advanced spectroscopic data (1HNMR, 13CNMR and LCMS) and also structural determination titled compounds were calculated by elemental analysis. In addition to all newly compounds were screened by their anti-microbial activity.**

***Index Terms*— O-phenyldiamine, CNBr, 2-aminobenzimidazole, Trichloro Salicylic Acid, substituted aryl aldehydes, Schiff bases, Bioevluation.**

I. INTRODUCTION

Schiff's base is synthesized by the condemnation between the primary amines and substituted aldehyde which is also important class in organic chemistry, medicinally chemistry and pharmaceutical compounds. Mostly, the synthetic organic moieties contains imines group and also very important role play in the class of organic synthesis due of their applications in many area such as biological, inorganic and also analytical chemistry.

The compounds of Schiff's base composed of the combination of part of heterocyclic rings which are responsible for exhibit the pharmacological properties and the compounds are containing five membered heterocyclic rings. The benzimidazoles is an important class of their significant biological properties showed against several virus like influenza, HIV, Herpes(HSV-1) and Epstein-barr[1-3] and benzimidazoles moiety present in Schiff bases which are show anti-cancer and anti-proliferate properties. Benzimidazole is being explored intermediate in the pharmaceutical industries and the benzimidazoles derivatives have also been found in the diverse therapeutic applications[4,5] .The versatile core contained in several substances of benzimidazoles derivatives are possess a broad spectrum of pharmacological activities [6-8] in particular and it has been important pharmacopoeia and privileged structure in medicinal chemistry [10,11],encompassing a diverse Schiff bases derived from aromatic primary amines and aryl aldehyde which are also important class of organic compounds. Mostly synthetic organic compounds possess imines group and also very important class of organic compounds because of their applications in many fields such as biological, inorganic and also analytical chemistry. Of biological activities including anti-microbial [12-14], antioxidant [15], anti-viral [16,14], antihypertensive [18], antiprotozoal [19], anti-inflammatory [20] and molluscicidal [21] agents. Further mode, benzimidazoles showed anticancer activity against DNA topoisomerase [22-23] and colon cancer cell lines [24].

In this investigation, we synthesized Schiff base from 2-amino benzimidazoles and various P-substituted aryl aldehyde using Trichloro Salicylic Acid as an acid catalyst. We aimed to the synthesis of new Schiff's bases using organic acid catalyst due to improved better yield as well as completion of the reaction time is less and also the intermediate of this reaction such as benzimidazoles can be synthesized O-phenyl diamine with cyan bromide..

II. METHODS & MATERIALS

2.1. EXPERIMENTAL

All the synthetic grade reagents and analytical chemicals were procured from Meric and Fine chemicals. Organic solvent used as absolute alcohol .The melting point of the all newly synthesized compounds were find out using an Aggarwal thermal apparatus and uncorrected. The NMR spectra of selective compounds were recorded on a Bruker for 400 1H NMR spectra and 100 MHz for 13C NMR spectra in CDCl3 solvent using TMS as internal standard.). The reaction was monitored by thin layer chromatography using silica gel as an adsorbent and ethyl acetate-hexane in different ratios as eluent. All the synthesized compounds find the molecular weight using LCMS.

2.2.1.PROCEDURE FOR THE SYNTHESIS OF 2-AMINOBENZIMIDAZOLE (2):

A mixture of O-phenyl diamine (1, 1 equiv) and cyano bromide (2, 1 equiv) are introduced 100ml RB flask and addition of an organic solvent acetonitrile to the above mixture. The reaction carried out on magnetic stirrer with reflux condition. After completion of the reaction, the mixture product extracted with ethyl acetate and washed with saturated solution of anhydrous sodium bicarbonate. The intermediate compound such as benzimidazole can be separated using column chromatography (4:6, ethyl acetate: n-hexane). The reaction was checked using TLC (4:6 ethyl acetate and n-hexane). The final compound obtained. .

2.2.2Synthesis of 2-aminobenzimidazole (2):

Orange red color, m.p-1550c, yield-94% ,1HNMR (400MHz, CDCl3) δ in ppm:12.154 (s,1H,NH),9.026(s,1H,CH), and 7.243-7.101(m,4H,A-r H), 6.160(s,2H,NH2). 13CNMR (100MHz, CDCl3) δ in ppm: 157.10, 135.91, 122.84, and 115.21. LCMS (m/z):132.54. Molecularformule: C7H7N3 Elemental analysis: Caliculated:C-63.14,H-5.30,N-31.56. Obtained:C-63.18,H-5.28,N-31.54.

GENERAL PROCEDURE FOR THE SYNTHESIS OF SCHIFF BASE:

2-aminobenimidazole (3,1 equiv)introduced in 100 ml RB flask in acetonitrile and P-substituted aryl aldehyde(4,1 equiv) added to the RB flask. The reaction carried on magnetic stirrer at RT. A catalytic amount of camphor sulphonic acid added to the above mixture. The reaction was monitored after all the reactants are consumed during the reaction time, after completion of the reaction, cold water added to the product. The product can be washed with brine solution and solid product was separated out. We desired compound can be recrystallized from ethanol.

2.2.1. N-benzylidene-1H-benzo[d]imidazol-2-amine (4a):
Brickred solid; yield-88%; m.p – 148-1500c ,1HNMR (400MHz, CDCl3) δ in ppm:12.138 (s,1H,NH),9.235(s,1H,CH), and 8.017-6.865(m,9H,A-r H). 13CNMR (100MHz, CDCl3) δ in ppm: 167.07, 156.44, 136.57, 135.84, 133.04, 129.61, 129.44, 122.45, 119.20, 111.45. LCMS (m/z):221.33. Molecular formula: C14H11N3. Elemental analysis: Caliculated:C-76.00,H-5.01,N-18.99. Obtained: C-76.02,H-5.00,N-18.98.

2.2.2. N-(4-hydroxybenzylidene)-1H-benzo[d]imidazol-2-amine (4b):
Red solid; yield-94%; m.p –217- 2190c, 1HNMR (400MHz, CDCl3) δ in ppm: 12.051(s,1H, NH), 9.235(s,1H,NH), 9.018(s,1H,-OH), 7.892-6.986(m,8H,Ar-H). 13CNMR (100MHz, CDCl3) δ in ppm: 160.41, 159.61, 157.91, 135.04, 129.08, 129.50, 122.66, 115.49, 11.28. LCMS (m/z):236.98. Molecular formula: C14H11N3O. Elemental analysis: calculated: C-70.87, H-4.67, N-17.71, 0-6.74. Obtained:C-70.90, H-4.66, N-4.16 O6.73.

2.2.3.N-(methoxybenzylidene)-1H-benzo[d]imidazol-2-amine (4c):
Orange red solid; yield-91%; m.p – 224-2260c ,1HNMR (400MHz, CDCl3) δ in ppm: 12.260(s,1H,NH), 9.035(s,1H,CH), 8.051-7.102(m,8H,Ar-H) & 3.722(s,3H,OMe). 13CNMR (100MHz, CDCl3) δ in ppm: 165.52, 163.55, 155.39, 131.58, 128.66, 122.82, 118.49, 114.77, 110.39 & 55.45(OMe). LCMS (m/z):258.35. Molecular formula: C15H13N3O. Elemental analysis: calculated: C-71.70, H-5.21, N-16.72, O-6.37. Obtained: C-71.75, H-5.20, N-16.70, O-6.35

2.2.4.N-(4-methylbenzylidene)-1H-benzo[d]imidazol-2-amine (4d):

Orange red solid; yield-92%; m.p – 223-2250c ,1HNMR (400MHz, CDCl3) δ in ppm:12.051(s,1H,NH), 9.039(s,1H.CH),7.950-7.012(m,8H,Ar-H) & 3.528(s,3H,Me). 13CNMR (100MHz, CDCl3) δ in ppm: 164.59, 155.08, 143.77, 132.08, 130.20, 122.34, 118.17, 111.08 & 32.35 (CH3). LCMS (m/z):235.08. Molecular formula: C15H13N3. Elemental analysis: calculated: C-76.57, H-5.57, N-17.86. Obtained: C-76.59, H-5.56, N-17.85.

2.2.5.N-(4-aminobenzylidene)-1H-benzo[d]imidazol-2-amine (4e):

Orange red solid; yield-90%; m.p – 218-2200c , 1HNMR (400MHz, CDCl3) δ in ppm:12.028(s,1H,NH), 9.385(s,1H,CH), 7.879-6.868(m,8H,Ar-H),5.120(s,2H,NH2). 13CNMR (100MHz, CDCl3) δ in ppm: 165.66, 156.64, 149.94, 136.67, 135.84, 133.51, 129.56, 129.24, 122.14, 118.09, 111.15. LCMS (m/z):236.46. Molecular formula: C14H12N4. Elemental analysis: calculated: C71.17, H-5.12, N23.71.Obtained: 71.20, H-5.10, N-23.70.

2.2.6.N-(4-chlorobenzylidene)-1H-benzo[d]imidazol-2-amine (4f):

Orange red solid; yield-89%; m.p –247-2490c, 1HNMR (400MHz, CDCl3) δ in ppm: 12.282(S, 1H, NH), 9.348(S, 1H, CH) and 8.089-7.188(m, 8H, Ar-H).13CNMR (100MHz, CDCl3) δ in ppm: 164.76, 155.87, 137.43, 133.29, 131.88, 129.54, 122.15, 117.79, & 112.51.LCMS (m/z): 255.39. Molecular formula: C14H10ClN3. Elemental analysis: calculated: C-65.76, H-3.94, Cl-13.86, N-16.43. Obtained: C-65.80, H-3.93, Cl-13.85,N-16.41.

2.2.7..N-(4-bromobenzylidene)-1H-benzo[d]imidazol-2-amine (4g):

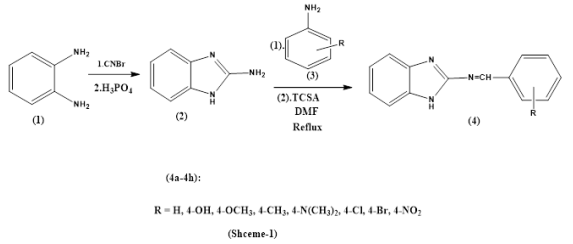
Brick red solid; yield-90%;M.P-250=2520c;1HNMR(400MHz,CDCl3) δ in ppm: 12.256(s,1H,NH), 9.136(s,1H,CH), and 7.989-7.118(M,8H,Ar-H). 13CNMR (100MHz, CDCl3) δ in ppm: 166.80, 155.33, 134.76, 132.51, 131.88, 126.87, 122.57, 119.35, 112.10. LCMS (m/z):298.95. Molecular formula: C14H10BrN3. Elemental analysis: calculated: C-56.02,H-3.36,Br-26.62, N-14.00 . Obtained: C-56.05,H-3.35,Br-26.61, N-13.99

2.2.8.N-(4-nitrobenzylidene)-1H-benzo[d]imidazol-2-amine (4h):

Brickredsolid; yield-87%; m.p–264-2650c ;1HNMR (400MHz, CDCl3) δ in ppm:12.483(s,1H,NH), 9.155(s,1H,CH), 8.235-8.016(m,4H,Ar-H) & 7.615-7.320(m,4H,Ar-H). 13CNMR (100MHz, CDCl3) δ in ppm: 164.01, 155.62, 149.59, 140.29, 130.55, 124.72, 118.19 & 112.40. LCMS (m/z):265.98. Molecular formula: C14H10N3O2; Elemental analysis: calculated: C-63.15, H-3.79, N-21.04, O-12.02. Obtained: C-63.18, H-3.78, N-21.03, O-12.01.

III. RESULT & DISCUSSION

All newly titled compounds can be synthesized at room temperature and also colored product. In this reaction, we got the percentage of the yield 87-94%.These titled compounds can be obtained, we used to organic acid catalyst is Trichloro Salicylic Acid. This organic catalyst can be used to develop the reaction conditions and reaction is completed maximum 3 hours. The rate of reaction was enhanced by using this catalyst. The catalyst used due to emerging as a powerful nature, inexpensive, ecofriendly, readily available, economical and water soluble compound. We used various substituted aromatic aldehydes such as electron donating group of aldehydes and electron withdrawing group of aldehydes. Hence ,electron donating group of aldehydes react with 2-aminobenzimidazole to give more yield and rate of reaction increases and completion of the reaction before 30 min compared to that of electron withdrawing group of aldehyde react with 2-aminobenzimidazole. We are using, Trichloro Salicylic Acid the reaction workup is easily. (Scheme-I)



Scheme-1: synthetic protocol of the compounds

CONCLUSION

The reaction condition carriedout at room temerature for all the newly synthesised compounds . The yield of the titled compounds obtained from 89-94%.The

compound possesses electron donating group gives maximum yeild than that of the compound possesses electron withdrawing group. The rate of reaction developed by using camphor sulphonic acid catalyst.

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