Punyashlok Ahilyadevi Holkar Solapur University Solapur

“Synthesis of some pyrazinobenzimidazole derivatives”

Submitted by

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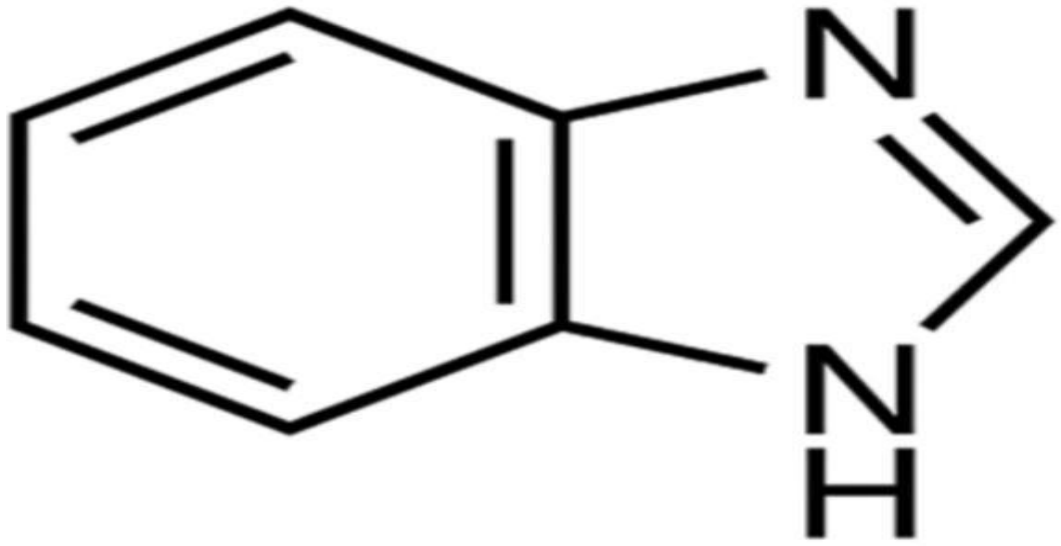
Content:

- Introduction of Benzimidazole
- Pyrazine
- Present work
- Procedure
- Spectral data

Benzimidazole:

- Benzimidazole is an aromatic heterocyclic organic compound.
- Basically benzimidazole is a bicyclic compound consisting of the fusion of benzene with imidazole which ultimately gives previleged structure.
- This magical moiety posseses many pharmacological properties.
- Benzimidazole posseses many biological activities such as antimicrobial, antifungal,antihistaminic, anti-inflammatory, antiviral, antioxidant,antiulcer property,etc.
- Thats why benzimidazole derivatives are considered as an important moiety for development of molecules of pharmaceutical interest.

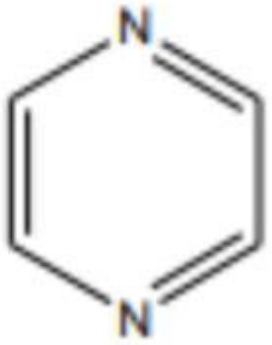
Benzimidazole structure:



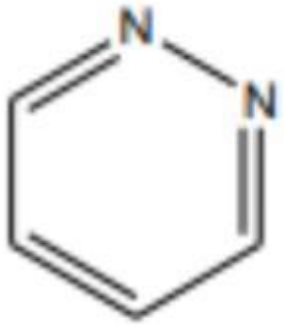
Benzimidazole

Pyrazine:

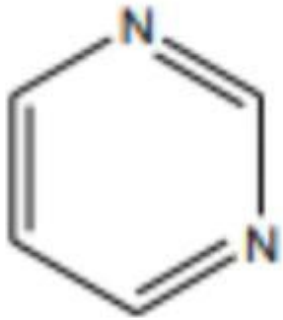
- Pyrazine is a kind of natural product which can be found in plants, animals, insects, marine organisms and microorganisms.
- Pyrazine and its derivatives were also produced in industries mainly for fragrance, flavor and pharmaceutical applications.
- Diazine is described as a compound with monocyclic aromatic ring that contains two nitrogen atoms with a molecular formula of C4H4N2.
- Pyrazine, or more commonly known as 1,4- diazine, refers to the 6 membered heterocyclic compounds with two nitrogen atoms in para position.
- Naturally occurring pyrazine is regarded as an important component that contributes greatly to the flavor of raw and processed food.
- Synthetic pyrazine derivatives are actively utilized not only in fragrance and flavor industry, but also in pharmaceutical industry.



Pyrazine



Pyridazine



Pyrimidine

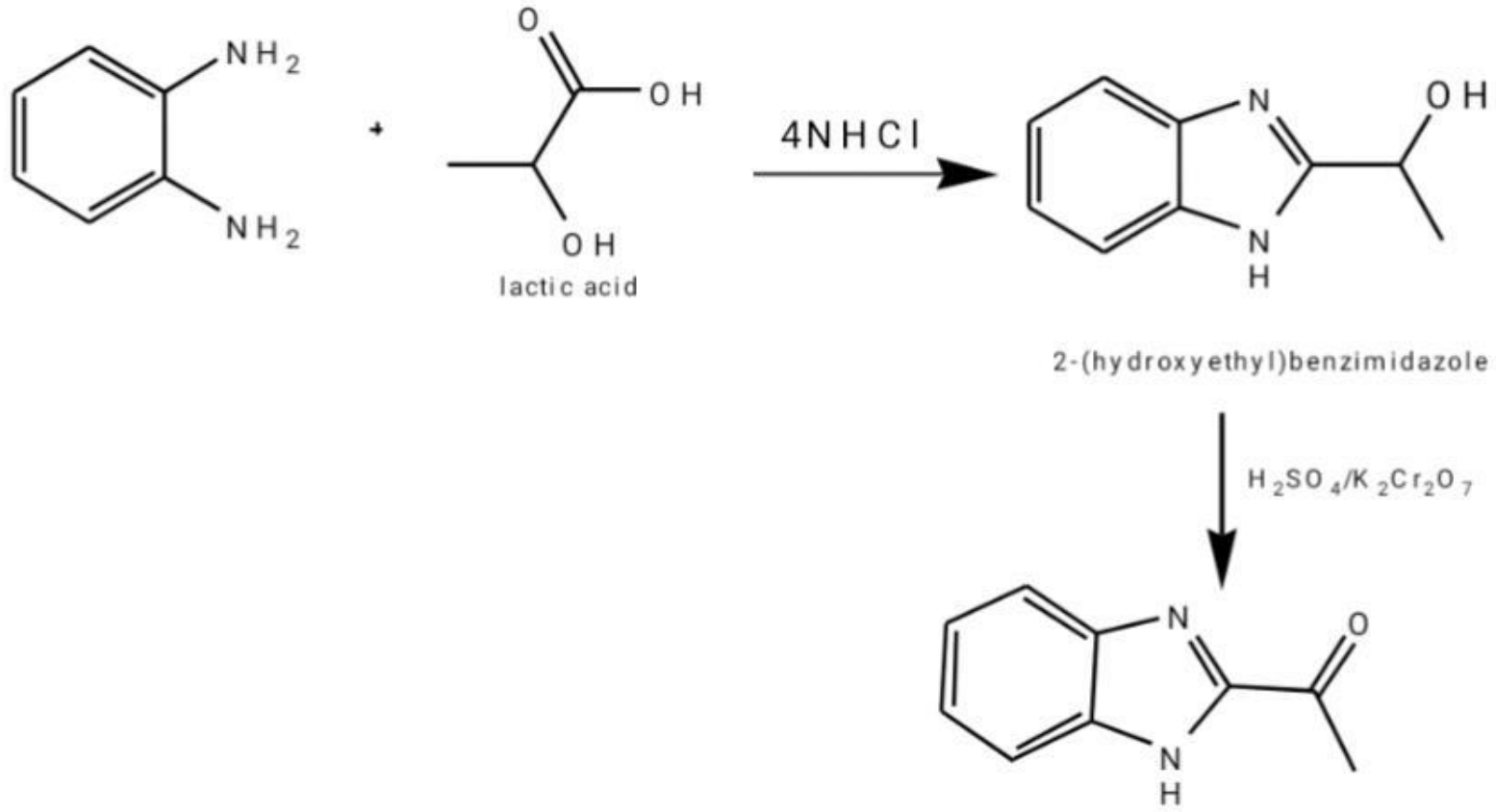
Isomers of diazine

Pyrazinobenzimidazole:

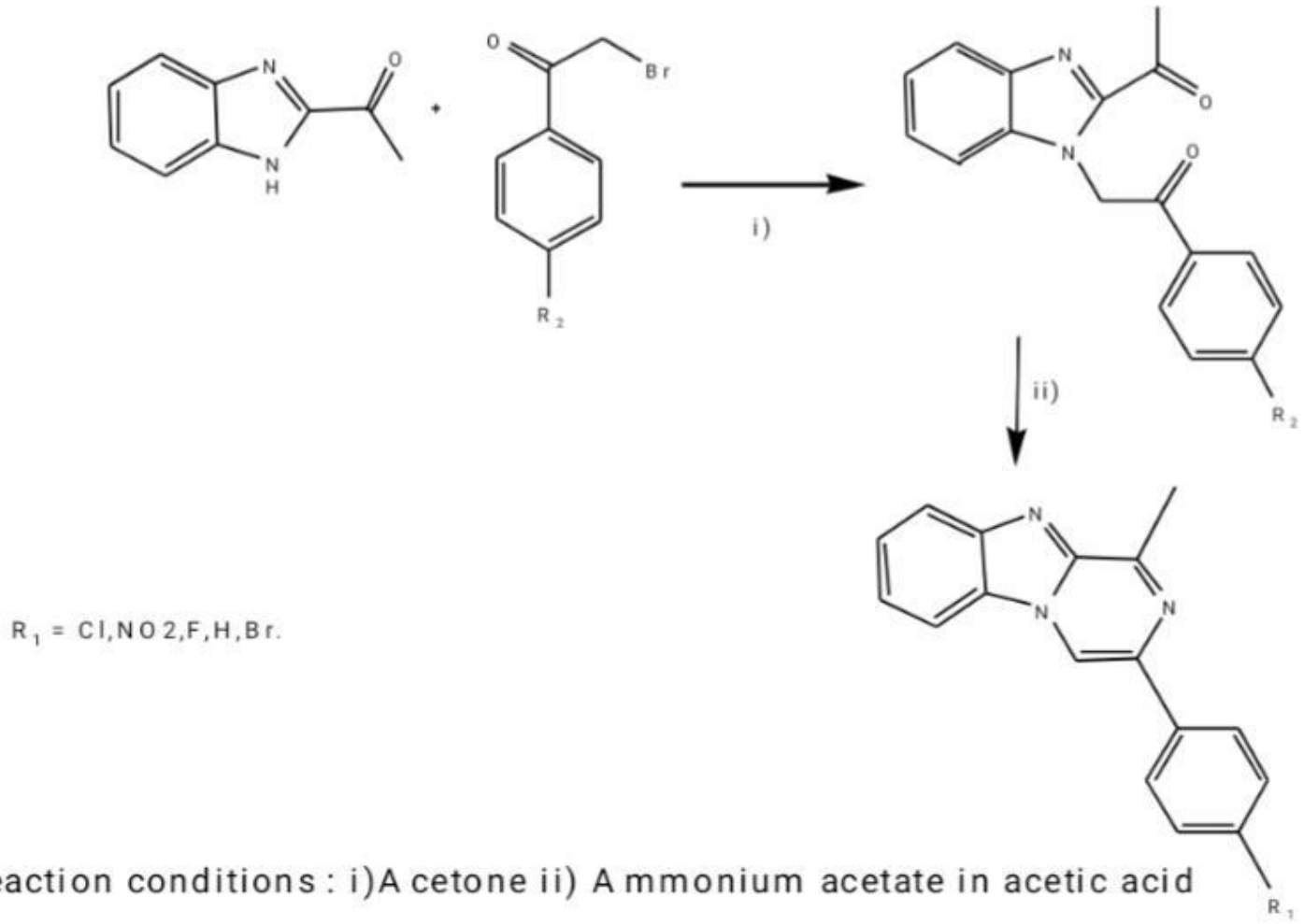
As Benzimidazole and pyrazine both have varied biological activities it inspired us to integrate both the nucleous for enhanced biological activity,to achieve this The synthesis of some new pyrazino[1,2-a]benzimidazole derivatives aimed in this work.

Present work:

A) Preparation of 2-Acetylbenzimidazoles:

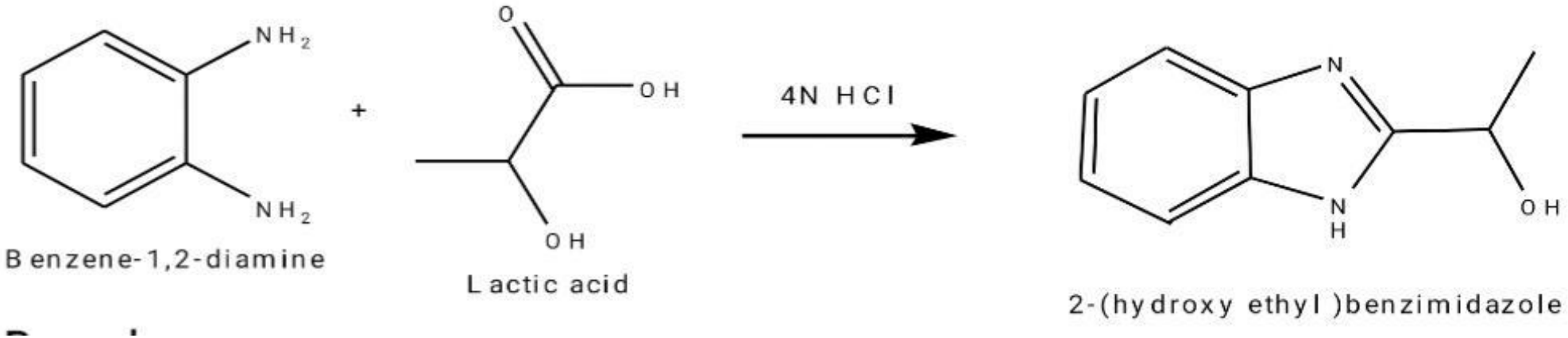


B) Synthesis of pyrazinobenzimidazole derivatives:



Experimental procedure ‘

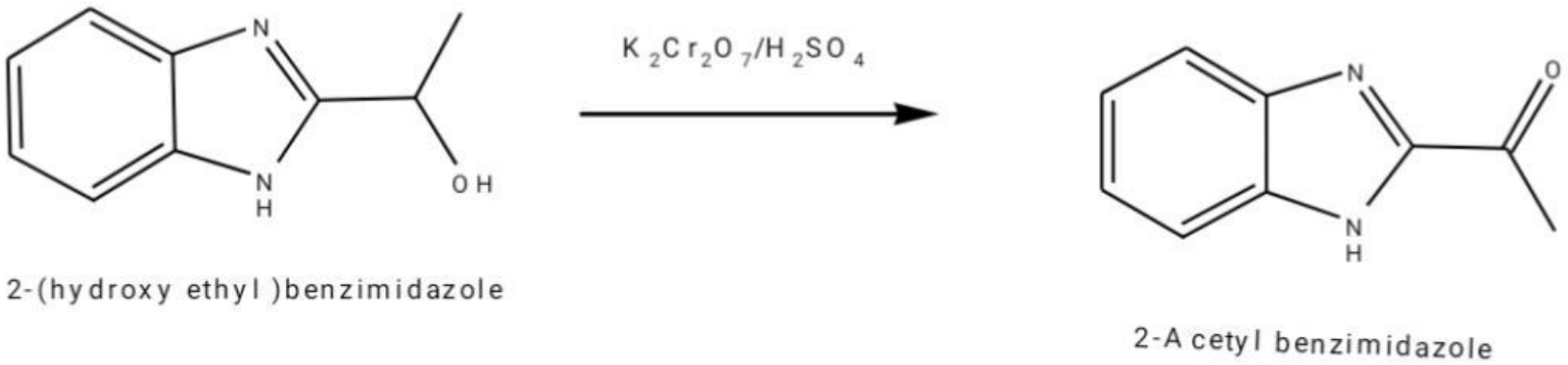
1. A)Preparation of 2-acetyl benzimidazole :
2. *Step 1: Preparation of 2-(hydroxy Ethyl) benzimidazoles:*



Procedure : o-Phenelenediamine (0.01 mol) was mixed with lactic acid (0.01 mol) added to 4N-hydrochloric acid (5 mL) and refluxed for 24 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled and neutralized with NH3 solution. The solid was separated through filter and recrystallized from ethanol.

Step 2) Oxidation of 2-(Hydroxy ethyl) benzimidazoles

Reaction:



2-(hydroxy ethyl)benzimidazole

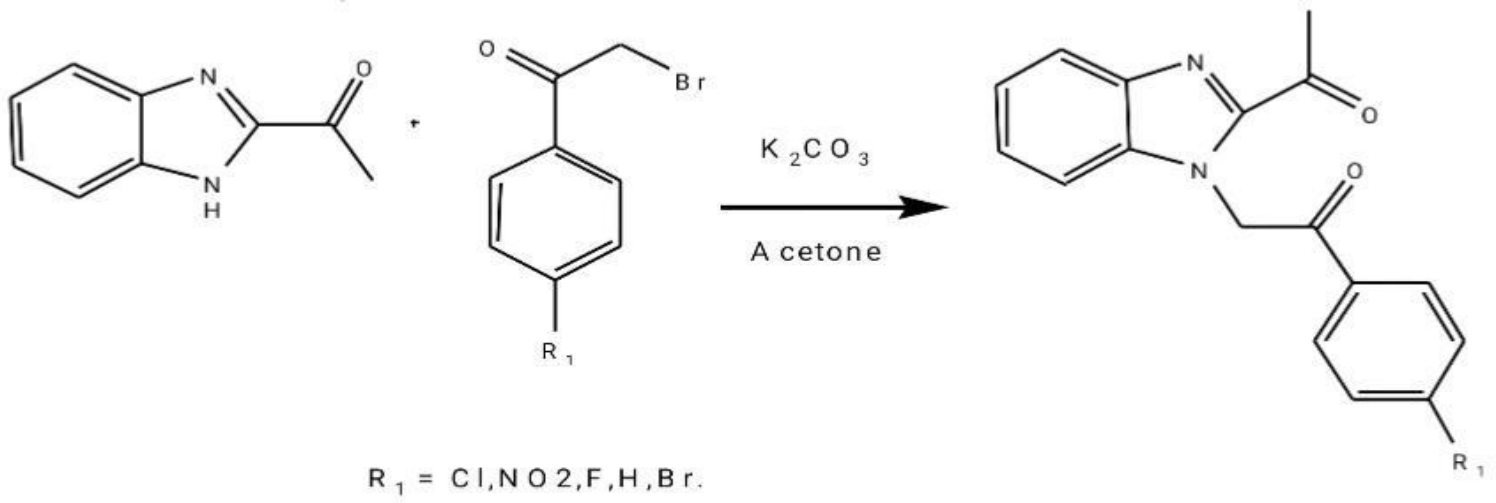
2-Acetyl benzimidazole

Procedure : To a solution of 2-(hydroxy ethyl) benzimidazoles (0.01 mol) in dil. H2SO4 (25%, 40 mL) was dropwise added the solution of K2Cr2O7 (0.15 mol) and H2SO4 (5%, 80 mL) with constant stirring at room temperature over a period of 20 min. Further the reaction mixture was stirred at room temperature for 2 h. resultant orange solid was filtered, washed with water and dried, recrystallized from ethyl acetate.

B) Synthesis Pyrazinobenzimidazole derivatives:

Step 1: 2-(2-Acetyl-benzoimidazol-1-yl)-1-phenyl-ethanone:

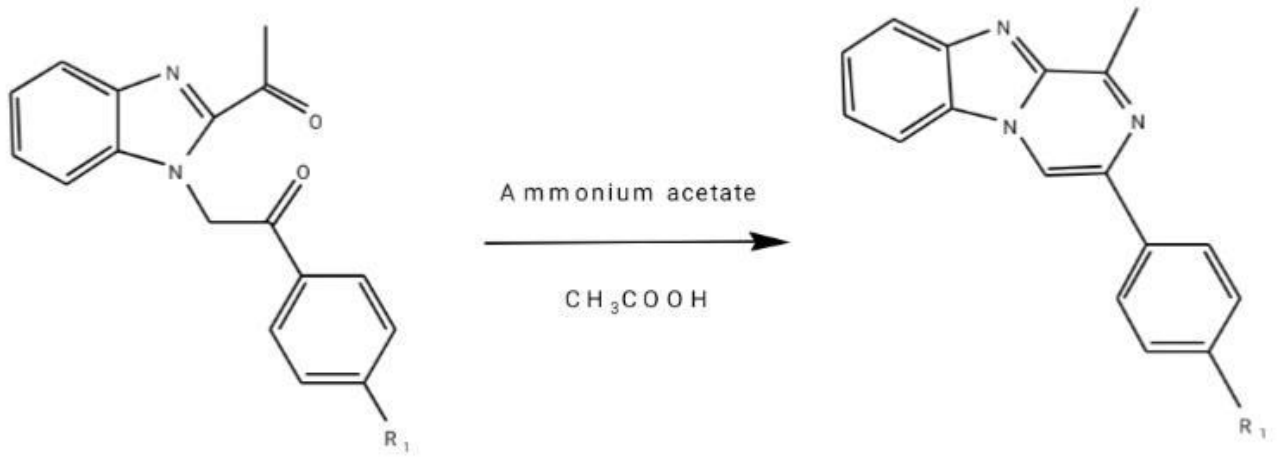
A mixture of 2-acetylbenzimidazole 1 (3 mmol), substituted α bromo acetophenone 2 (3 mmol) and of K2CO3 (3 mmol) in acetone (40 mL) was stirred at RT .The solvent was evaporated and water was added to the residue. The precipitate was filtered and washed with water. Yield 86%; pale orange



R1 = Cl,NO2,F,H,Br.

Step-2: 1-methyl-3-phenyl-benzo(4,5)imidazo[1,2]pyrazine:

A mixture of the 2-(2-acetyl benzimidazole -1-Yl)-1-phenyl-ethanone(2mmol) and an appropriate ammonium acetate (2mmol)was refluxed for 1 hr in acetic acid (50ml).At the end of this time after cooling the mixture,ice water was poured into it and the aq mixture was neutralised with mild base.After removal of water ,the obtained cohesive precipitate was crystallised from ethanol.



4.Analytical Data of synthesized pyrazinobenzimidazole derivative :

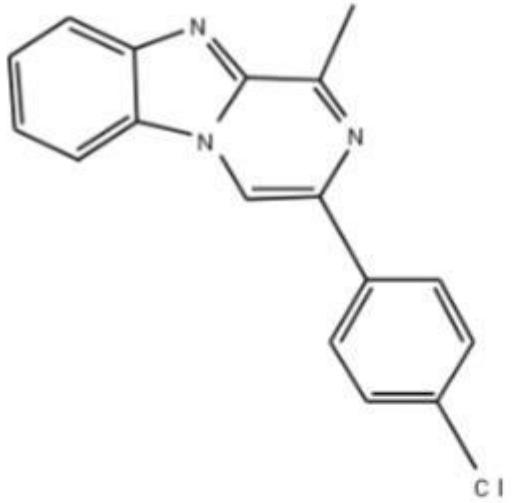
Sr.No.	Name of Compound	M.P.in°C
Comp.-1	1-Methyl-3-phenyl-benzo[4,5]imidazo[1,2-a]pyrazine	110
Comp.-2	3-(4-Chloro-phenyl)-1-methyl-benzo[4,5]imidazo[1,2-a]pyrazine	140
Comp.-3	3-(4-fluoro-phenyl)-1-methyl-benzo[4,5]imidazo[1,2-a]pyrazine	130
Comp.-4	3-(4-Nitro-phenyl)-1-methyl-benzo[4,5]imidazo[1,2-a]pyrazine	148
Comp.-5	3-(4-Bromo-phenyl)-1-methyl-benzo[4,5]imidazo[1,2-a]pyrazine	158

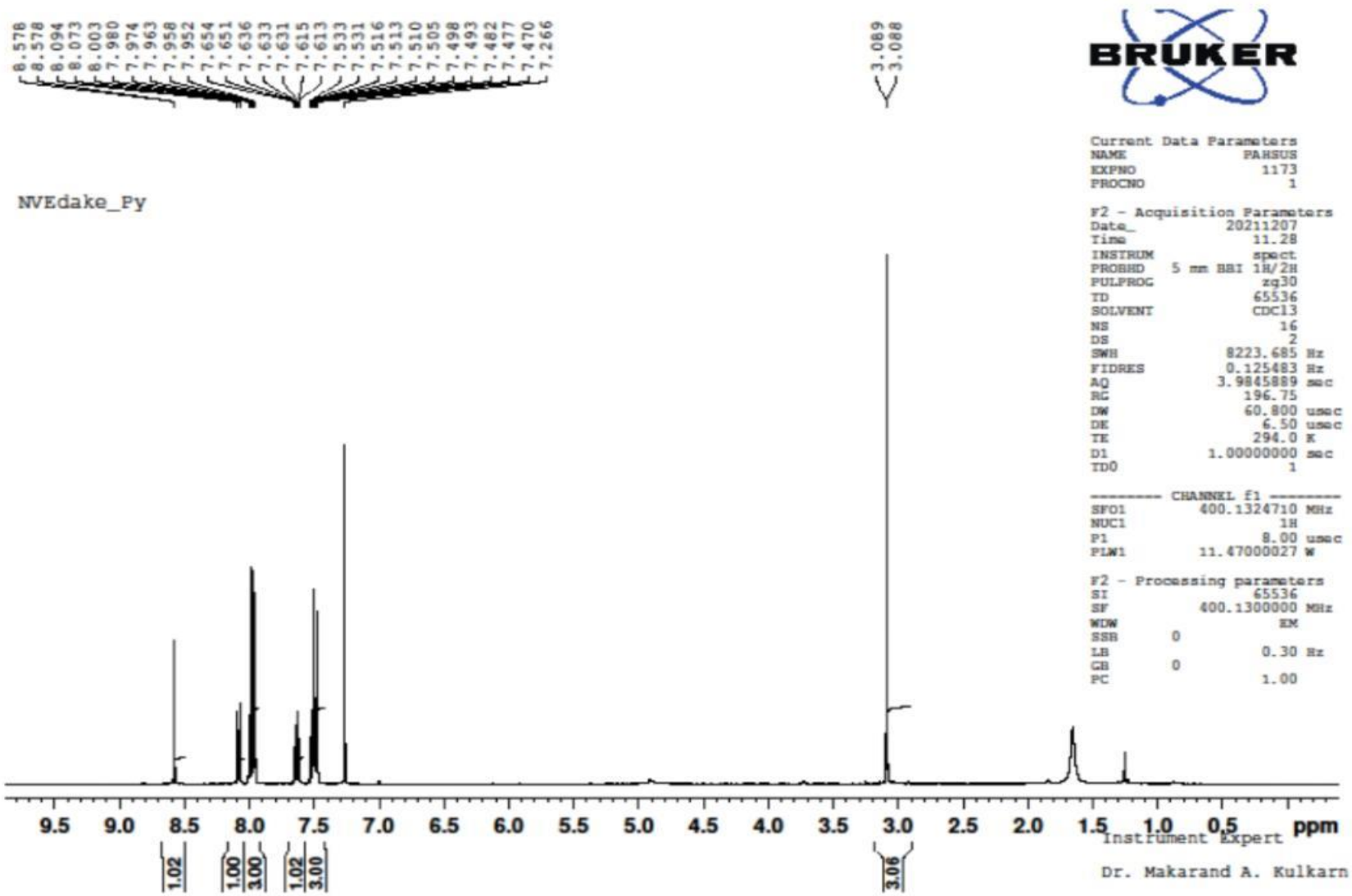
Spectral data:

5.Spectral Data

Spectral data of comp.2

1H-NMR (ppm): 3.0 (s, 3H), 8.5 (s, 1H), 7.5 (d, *J*=8.68 Hz,2H), 7.6 (d, *J*=8.39 Hz, 2H), 7.9(d, *J*=8.16 Hz, 2H), 8.20 (d, *J*=8.11 Hz, 2H).





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PROCNO                     1

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DW                   60.800 usec
DE                    6.50 usec
TE                   294.0 K
D1                1.00000000 sec
TD0                       1

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P1                    8.00 usec
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F2 - Processing parameters
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LB                    0.30 Hz
GB           0
PC                    1.00
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Instrument Expert

Dr. Makarand A. Kulkarn