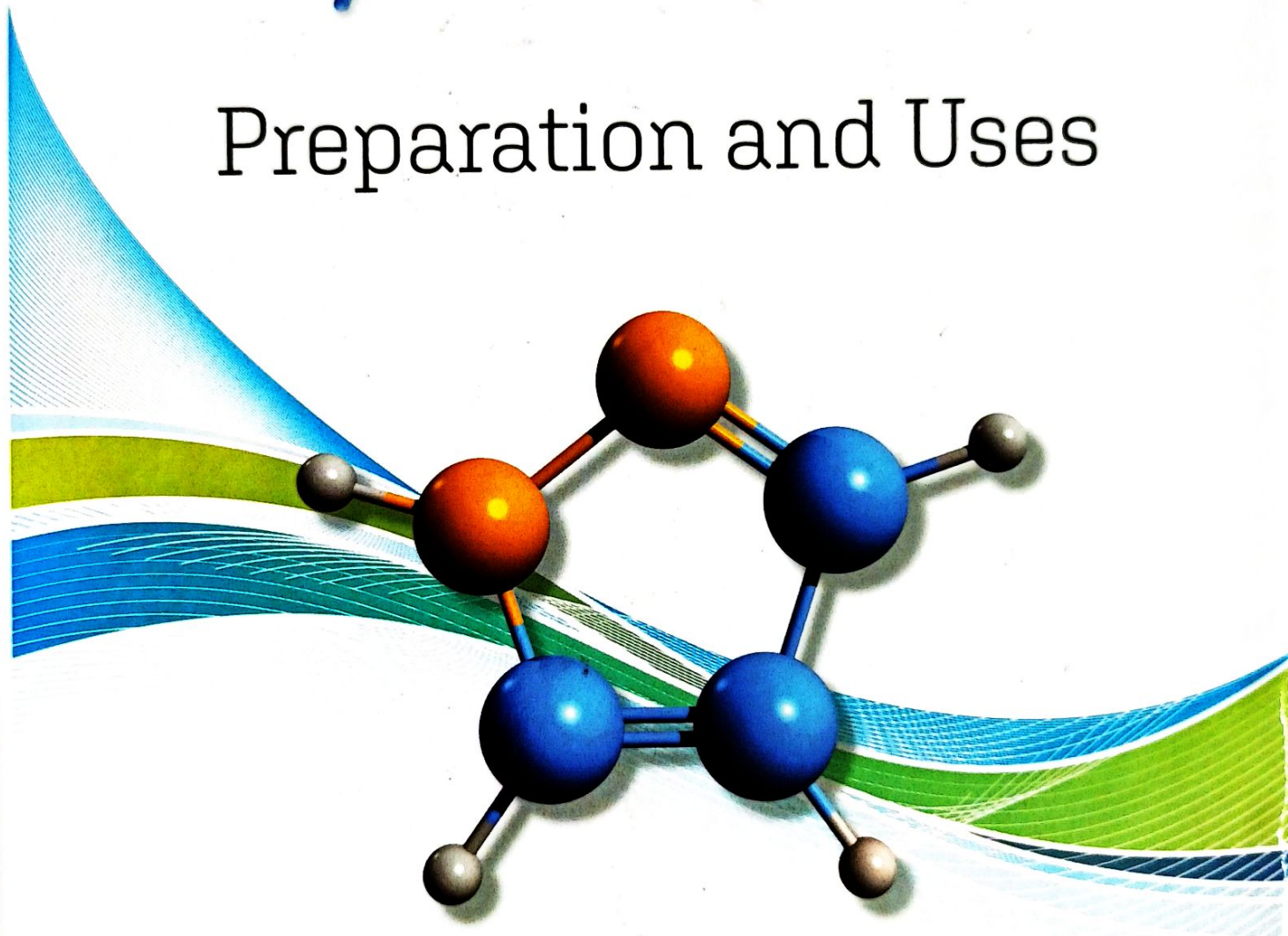


CHEMISTRY RESEARCH AND APPLICATIONS

Pyrazole

Preparation and Uses



Dilipkumar Pal

Editor

NOVA

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CONTENTS

Preface		xi
Chapter 1	Current Status of Pyrazolo Moiety in Drug Discovery (Synthetic vs. Natural) <i>Chandi Charan Kandar and Dilipkumar Pal</i>	1
Chapter 2	Synthesis and Therapeutic Applications of Pyrazole Scaffold <i>Roli Mishra and Satyendra Mishra</i>	27
Chapter 3	Pyrazole Based Ligands: Versatile Building Blocks <i>Preeti Oswal, Aayushi Arora, Gyandshwar Kumar Rao, Sushil Kumar, Arun Kumar and Ajai Kumar Singh</i>	49
Chapter 4	Pyrazole and Its Analogues as Potential Anti-Angiogenesis Agents <i>Dilipkumar Pal and Souvik Mukherjee</i>	91
Chapter 5	Green Chemistry Methods in Pyrazole Synthesis <i>Maja Molnar and Mario Komar</i>	107
Chapter 6	Pyrazoles as Antiviral Agents <i>Jeanne Fichez and Patricia Busca</i>	145
Chapter 7	Recent Research Advances in Aqueous Phase Synthesis of Pyrazoles <i>Venkata Durga Nageswar Yadavalli, Nelson L. C. Domingues, Ramesh Katla and Rakhi Katla</i>	179
Chapter 8	Pyrazole Moiety as a Source of Natural Products <i>Dilipkumar Pal, Souvik Mukherjee, Om Prakash Panda, Sitansu Sekhar Nanda and Dong Kee Yi</i>	195

Chapter 9	Pyrazole and Its Derivatives, Preparation, SAR and Uses as Antioxidative Agent <i>Supriyo Saha and Dilipkumar Pal</i>	211
Chapter 10	Role of Pyrazole Ring in Neurological Drug Discovery <i>Supriyo Saha and Dilipkumar Pal</i>	245
Chapter 11	Pyrano[2,3-c]pyrazole Derivatives: Synthesis and Applications <i>Devendra Dewangan, Trimurti L. Lambat, Sami H. Mahmood and Subhash Banerjee</i>	265
Chapter 12	Pyrazole and Pyrazole Derivatives: A Versatile Platform in Anti-Convulsive Drug Discovery <i>Dilipkumar Pal, Suvadeep Mal and Souvik Mukherjee</i>	301
Chapter 13	Pyrazole Affixed Heterocycles: Synthesis and Their Herbicidal Activity <i>Shridevi Doddamani and Srikantamurthy Ningaiah</i>	323
Chapter 14	Development in Chemistry and Synthesis of Pyrazole Derivatives as Potential Anticancer Agents <i>Ashish D. Patel, Vinod Kumar Gurjar and Dilipkumar Pal</i>	347
Chapter 15	Recent Advances in Chemistry and Synthesis of Pyrazole Derivatives as Potential Promising Antimicrobial Agents <i>Vinod Kumar Gurjar, Dilipkumar Pal and Ashish D. Patel</i>	377
Chapter 16	Scaffold of Pyrazole Derivatives for Enzyme Inhibition <i>Neetu Sachan, Phool Chandra and Dilipkumar Pal</i>	411
Chapter 17	Role of Pyrazolo Ring in Plant System <i>Chandi Charan Kandar</i>	447
Chapter 18	Pyrazole and Its Derivatives: Preparation, SAR and Anthelmintic Activity <i>Arindam Maity</i>	471
Chapter 19	Pyrazole and Its Derivatives, Preparation, SAR and Anti-Inflammatory Activity <i>Kiran Gangarapu, Gouthami Thumma, Niveditha Nakka, Krishna Prasad Devarakonda, Dilipkumar Pal and Arivarasan Vishnu Kirthi</i>	485
Chapter 20	Pyrazole and Its Derivatives as Anti-Diabetic Agents <i>Dilipkumar Pal and Khushboo Raj</i>	505

Chapter 21	Future Prospects of Pyrazole Ring in Drug Discovery	523
	<i>Sajal Kumar Jha and Tanmoy Guria</i>	
About the Editor		533
List of Contributors		535
Index		539

Chapter 16

SCAFFOLD OF PYRAZOLE DERIVATIVES FOR ENZYME INHIBITION

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ABSTRACT

Pyrazole, a five membered heterocyclic ring containing two nitrogen atoms, has a unique place in medicinal chemistry. It is an indispensable core scaffold present in many natural (1-pyrazolyl-alanine) and synthetic biologically important compounds. In 1883, first time Ludwig Knorr coined the term 'Pyrazole' in the field of heterocyclic chemistry. Pyrazole derivatives have displayed a broad spectrum of pharmacological and biological activities such as anti-microbial, anti-fungal, antitumor, anti-tubercular, antiviral, anti-inflammatory, antidepressant, anticonvulsant, antihyperglycemic, cholecystokinin-1 receptor antagonist, estrogen receptor (ER) ligand activity, and enzyme inhibitory activities. This chapter features an important synthesis of pyrazole derivatives as the enzyme inhibitors with an emphasis on recent developments. Enzyme inhibition includes carbonic anhydrase, acetylcholine esterase, Plasmodium falciparum dihydroorotate dehydrogenase, cyclooxygenase, tyrosinase, α -glucosidase, etc.

Keywords: pyrazole derivatives, scaffold, enzyme inhibitors

INTRODUCTION

Pyrazole, a five membered heterocyclic ring containing two nitrogen atoms, has a unique place in medicinal chemistry [1].



Pyrazole

It is an indispensable core scaffold present in many natural (1-pyrazolyl-alanine) and synthetic biologically important compounds. In 1883, first time Ludwig Knorr coined the term 'Pyrazole' in the field of heterocyclic chemistry [2]. Pyrazole derivatives have displayed broad spectrum of pharmacological and biological activities such as anti-microbial, anti-fungal, antitumor, anti-tubercular, antiviral, anti-inflammatory, antidepressant, anticonvulsant, antihyperglycemic, cholecystokinin-1 receptor antagonist, estrogen receptor (ER) ligand activity, and enzymes inhibitory activities [3].

In this chapter authors presented the important synthesis of pyrazole derivatives as the enzyme inhibitors with an emphasis on recent developments. Enzyme inhibition includes carbonic anhydrase, acetylcholine esterase, Plasmodium falciparum dihydroorotate dehydrogenase, cyclooxygenase, tyrosinase, α -glucosidase, phospholipase A-2 and serine hydrolase.

CARBONIC ANHYDRASE INHIBITORS

Two genetically distinguished human carbonic anhydrase (hCA) isoforms designated hCA I, and II isoenzymes are present in RBC cells. Both isoforms exhibit 60% sequence homology, several particular activities and several immunologic specificities [4]. While, CA II isoform is expressed in an extensive diversity of tissues and cells, CA I isoform has a more restricted cellular expression. Also, hCA II isoform can produce NO molecule, owing to the structural similarity between nitrite and bicarbonate [5]. The hCA II isoform is a zinc ion (Zn^{2+}) and catalysis reversible interconversion of carbon dioxide (CO_2) and bicarbonate (HCO_3^-). It is found in platelets, vascular smooth muscle, and erythrocytes. Also, hCA II isoenzyme contributes to vascular adjustment and could be a source of good hCA II-mediated generation of nitric oxide (NO) from nitrite [6]. Since nitrite exhibits similar to sp^2 geometry as HCO_3^- , it is hypothesized that hCA II isoform acts as a nitrous anhydrase factor, wherein nitrite binds hCA II active site and is dehydrated, analogously to HCO_3^- [7, 8]. CA isoforms are zinc-containing metallocatalysts that perform the