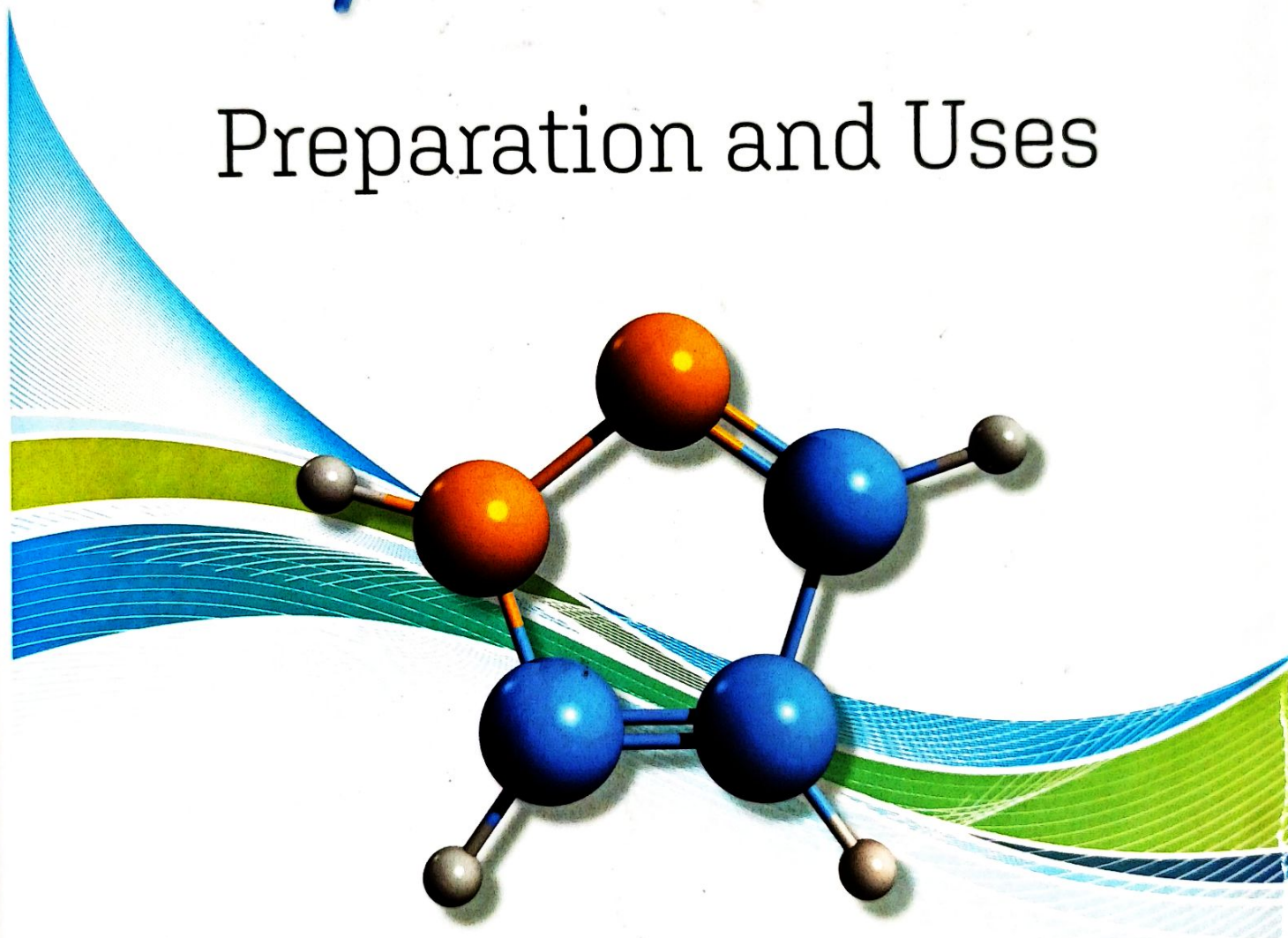


CHEMISTRY RESEARCH AND APPLICATIONS

Pyrazole

Preparation and Uses



Dilipkumar Pal

Editor

NOVA

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Chapter 14

DEVELOPMENT IN CHEMISTRY AND SYNTHESIS OF PYRAZOLE DERIVATIVES AS POTENTIAL ANTICANCER AGENTS

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ABSTRACT

Now a days, for management of various health issue, heterocyclic compounds play a vital role in the development of effective drugs. Pyrazole, the five-membered nitrogen-containing heterocycle is an important scaffold possessing amenable to extensive, promising biological activities. Due to potential applications of pyrazoles, many recent novel routes for synthesizing pyrazoles is developed for the treatment of disease. As a consequence, in this chapter covering advances in the synthesis and application of pyrazoles for treatment of cancer in the past decades. This advancements on pyrazole synthesis will draw a clear picture to the researchers' lobby for the development of active pyrazoles scaffold with improvement in current methodologies.

Keywords: pyrazole, heterocyclic compounds, synthesis, cancer

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1. INTRODUCTION

Heterocyclic compounds are a useful class of organic chemistry which show a broad spectrum of physicochemical and biological characteristics [1, 2] which structural nucleus of occurring in many natural products like alkaloids, vitamins, antibiotics and hormones. Moreover, various heterocycles are extensively distributed and exhibit metabolic mechanism [3–5]. However, nitrogen-containing heterocycles are comprehensively acted as a basic framework in a library of heterocyclic chemistry and express several employments in life science [6]. Pyrazole and its derivatives are five-member nitrogen-containing families of heterocyclic compounds which gaining importance in medicinal and organic chemistry and exhibited a broad spectrum of pharmacological and biological activities like anti-TB [7], anti-HIV [8], anti-protozoal [9], antibacterial [10], antifungal [6], antitumor [11, 12] and anticancer [13, 20-37]. Furthermore, pyrazoles and its scaffold also possess anti-diabetic [14], anti-depressant [15], anti-seizure [16], antipyretic [17] and anti-anxiety [18, 19] activity. In this chapter, some important synthetic protocols for the treatment of cancer have been discussed.

2. RECENT METHODOLOGY FOR SYNTHESIS OF PYRAZOLE DERIVATIVES AS ANTI-CANCER AGENTS

Mohamed A. and his teammates reported a novel series of 2-(3,6-dimethyl-1-phenyl-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy)-N-(4-substituted benzyldene)acetohydrazide (12a–g) for treatment of breast, lung cancer and human colorectal cancer by MTT assays.

The intermediate 3,6-dimethyl-1-phenyl-1,5-dihydropyrazolo[3,4-d]pyrimidin-4-one (9) can be synthesized by base catalysed ester hydrolysis of pyrazole-4-carboxylate (6) to form pyrazole carboxylic acid intermediate (7) which further cyclized to afford with acetic anhydride under reflux condition to afford compound 1H-pyrazolo[3,4-d][1,3]oxazin-4-one (8) which also react with formamide under reflux for 6 hr to form 1,5-dihydropyrazolo[3,4-d]pyrimidin-4-one (9). Moreover, the reaction of intermediate (9) with ethyl chloroacetate afforded ethyl 1H-pyrazolo[3,4-d]pyrimidin-4-yloxy acetate (10) which form acetohydrazide intermediate (11) by reaction with hydrazine hydrate under reflux condition followed by condensation with a substituted aromatic aldehyde in acidic medium afforded targeted molecules (12a–g) which depicted in Scheme 1 [20].