

SYNTHESIS OF PYRROLE AND SUBSTITUTED PYRROLES (REVIEW)

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ABSTRACT

Pyrrole is widely known as a biologically active scaffold which possesses a diverse nature of activities. The combination of different pharmacophores in a pyrrole ring system has led to the formation of more active compounds. Pyrrole containing analogs are considered as a potential source of biologically active compounds that contains a significant set of advantageous properties and can be found in many natural products.

The present review highlights the synthetic methods of representatives of nitrogen heterocycles such as pyrrole, substituted pyrroles and other related compounds. The aim of this review is to indicate and summarise the different methods for the synthesis of nitrogen containing heterocycles from the group of pyrrole and pyrrole related structures.

Keywords: pyrrole, synthesis, pharmacological activity.

INTRODUCTION

Pyrrole is a five membered heterocyclic compound, corresponding to the C_4H_5NH general formula [1]. It is a colorless volatile liquid, unstable in the presence of air, where it easily darkens. Thus a preliminary distillation before use is necessary [2].

Pyrrole is included in the group of aromatic compounds, and its hydrogenated is difficult. The Diels-Alder reactions or usual olefin reactions are not characteristic for this ring. Due to the fact, that it can easily polymerize, most of the electrophilic reaction, used in benzene chemistry, are not applicable to pyrroles. On the other hand, the substituted pyrrole derivatives have been included in various transformations [3].

REACTION OF PYRROLE WITH ELECTROPHILES

In general pyrroles most commonly react with electrophiles at α -position, due to the highest stability of the obtained intermediate protonation (Scheme 1).

From the group of electrophilic addition, pyrroles are easily nitrated, halogenated and sulfonated, where normally polyhalogenated derivatives are obtained, but monohalogenation may also occur (Scheme 2)[6]. When the pyrrole nitrogen is silylated, a halogenation on 3rd position is also possible, thus this is considered as a useful procedure for functionalization of the less active 3rd position [4].

Origin of pyrrole

In 1834 F.F. Runge has detected pyrrole for the first time as a constituent of coal tar [5]. Later in 1857 it has



Scheme 1. Mechanism of the reaction of pyrrole with electrophiles.

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Richard A. Jones



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amino acids All their reactivities have been compiled and updated The other volumes include Volume 1 Protecting Groups Volume 3 N Carboxyanhydrides N Thiocarboxyanhydrides and Sydnone Volume 4 Azlactones and Oxazolidinones All together this unique 4 volume set thoroughly covers the two types of heterocyclic compounds that are originated from alpha amino acids providing carefully compiled updated information with detailed examples The author has shared many thoughtful insights based on his strong background in physical organic chemistry The volumes will be highly valuable for graduate students and senior students as well as for professors and researchers working in the field of medicinal and pharmaceutical chemistry organic chemistry organic synthesis heterocycles and proteins and peptides *Handbook of Reagents for Organic Synthesis* André B. Charette, 2015-09-28 Heteroarenes are among the most prevalent structural units in natural products pharmaceuticals agrochemicals and other compounds of scientific or commercial interest In the last decade a broad range of novel synthetic methods has been developed to not only facilitate construction of the heteroarene motif but to enable its modification through direct C H functionalization This Handbook describes 117 key reagents for selective heteroarene functionalization reactions including both traditional and transition metal catalyzed C H functionalization Since these reactions typically involve one heteroarene a coupling partner and a catalyst the handbook not only focuses on the catalyst itself but also contains other key reaction species All the information compiled in this volume is also available in electronic format on Wiley Online Library The 117 reagents represented here are but a small fraction of the ca 5 000 reagents available in the electronic Encyclopedia of Reagents for Organic Synthesis e EROS e EROS offers various search interfaces to locate reagents of interest including chemical structure substructure and reactions search modes e EROS is updated regularly with new and updated entries **Modeling of Molecular Properties** Peter Comba, 2011-10-05 Molecular modeling encompasses applied theoretical approaches and computational techniques to model structures and properties of molecular compounds and materials in order to predict and or interpret their properties The modeling covered in this book ranges from methods for small chemical to large biological molecules and materials With its comprehensive coverage of important research fields in molecular and materials science this is a must have for all organic inorganic and biochemists as well as materials scientists interested in applied theoretical and computational chemistry The 28 chapters written by an international group of experienced theoretically oriented chemists are grouped into four parts Theory and Concepts Applications in Homogeneous Catalysis Applications in Pharmaceutical and Biological Chemistry and Applications in Main Group Organic and Organometallic Chemistry The various chapters include concept papers tutorials and research reports *Advances in Nitrogen Heterocycles* C.J. Moody, 1999-01-19 This volume contains a range of topics such as the activation and manipulation of pyrroles the synthesis of annelated pyrroles using acylation reactions and the synthesis of kainoids a family of highly biologically active nitrogen heterocycles *Organic Reactions, Volume 92*, 2017-06-26 The latest volume in this series for organic chemists in industry presents critical discussions of widely used organic reactions or particular phases

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