

University of Texas Rio Grande Valley

ScholarWorks @ UTRGV

Chemistry Faculty Publications and
Presentations

College of Sciences

2017

CARBON DIOXIDE-MEDIATED PREPARATION OF PYRROLES IN WATER FOLLOWING PAAL KNORR METHOD

Ram Naresh Yadav

Bimal K. Banik

The University of Texas Rio Grande Valley

Follow this and additional works at: https://scholarworks.utrgv.edu/chem_fac

 Part of the [Chemistry Commons](#)

Recommended Citation

Yadav, R. N., & Banik, B. K. (2017). CARBON DIOXIDE-MEDIATED PREPARATION OF PYRROLES IN WATER FOLLOWING PAAL KNORR METHOD. *Heterocyclic Letters*, 7(3), 893–894.

This Article is brought to you for free and open access by the College of Sciences at ScholarWorks @ UTRGV. It has been accepted for inclusion in Chemistry Faculty Publications and Presentations by an authorized administrator of ScholarWorks @ UTRGV. For more information, please contact justin.white@utrgv.edu, william.flores01@utrgv.edu.



CARBON DIOXIDE-MEDIATED PREPARATION OF PYRROLES IN WATER FOLLOWING PAAL KNORR METHOD

Ram Naresh Yadav^a and Bimal K. Banik^{a, b*}

¹Department of Chemistry, University of Texas-Pan American, 1201 W. University Dr., Edinburg, TX 78539 USA; ²Current Address: Community Health Systems of South Texas; 3135 S Sugar Road, Edinburg, TX 78539, USA; bimalbanik10@gmail.com; bimal.banik@chsst.org

Abstract

Carbon dioxide-mediated new reaction of 2,5-hexanedione and primary amino compounds in water-THF produced N-substituted pyrroles in excellent yield. This method for the preparation of pyrroles is novel, simple, and efficient.

Key words

Carbon dioxide, Pyrrole, Paal-Knorr reaction, Aqueous acidic solution

Introduction

Pyrrole groups are fundamental component of numerous biologically active essential molecules: porphyrinsheme, chlorins, vitamin B12, bilirubin, biliverdin, chlorophyll, bacteriochlorins, and porphyrinogens [1]. A few pyrrole-containing metabolites are pyrroloquinoline (PQQ), makaluvamine M, ryanodine, rhazinilam, lamellarin, prodigiosin, myrmicarin, and sceptrin. Atorvastatin, ketorolac, and sunitinib have pyrrole systems in their structures. Many methods for the preparation of pyrroles are described in books [2].

Primary amines react with dicarbonyl compound in the presence of an acid and produces pyrroles [3]. An excess amount of hazardous acids are used in this method. Due to the acidity of the reaction media and sensitivity of pyrroles, our laboratory have developed mild and effective synthesis of pyrroles by iodine, bismuth nitrate, polystyrene sulfonate and NBS-catalyzed reactions [4].

We have identified a new and novel carbon dioxide-mediated procedure for the preparation of N-1,C-2,C-5-subsbtituted pyrroles by reacting aromatic amines and 2,5-hexanedione.

Results and Discussions

Paal-Knorr reaction for the preparation of pyrroles requires acidic catalysts or reagents. In the old days, strong acids were used for the preparation of pyrroles following Paal-Knorr method. However, pyrroles are acid-sensitive molecules. Therefore, to avoid the polymerization of pyrroles, new methods are necessary (**Table 1**). Carbon dioxide is naturally abundant, but the use of this gas in the synthesis of pyrroles has never been explored. We demonstrate here

a new and novel carbon dioxide-mediated synthesis of pyrroles through Paal-Knorr method. Carbon dioxide in water generates carbonic acid and this weak acid is responsible for the success of an acid-catalyzed nucleophilic addition and subsequent dehydration process. Electron withdrawing group in the aromatic system is not helpful for the success of this reaction.

Table 1: Carbon dioxide-mediated synthesis of N-substituted pyrroles

Entry	Starting Compounds	Products	Yield (%)
1	2,5-Hexanedione and Aniline	N-Phenyl 2,5-dimethylpyrrole	95
2	2,5-Hexanedione and 4-Methoxyaniline	N-4-Methoxyphenyl 2,5-dimethylpyrrole	95
3	2,5-Hexanedione and 4-Methylaniline	N-4-Methylphenyl 2,5-dimethylpyrrole	90
4	2,5-Hexanedione and Allylamine	N-Allyl 2,5-dimethylpyrrole	85
5	2,5-Hexanedione and Benzylamine	N-Benzyl 2,5-dimethylpyrrole	90
6	2,5-Hexanedione and 4-Nitrobenzylamine	N-4-Nitrobenzyl 2,5-dimethylpyrrole	50
7	2,5-Hexanedione and 2-Methoxyaniline	N-2-Methoxyphenyl 2,5-dimethylpyrrole	88

Experimental

Sodium bicarbonate (5 gm) was taken in a two-necked flask (100 mL size). Acetic acid (2 mL) was added drop wise to sodium bicarbonate. Carbon dioxide thus generated was then bubbled for 2h through a reaction mixture that contains diketone (1.1 mmol), amine (1 mmol) at ice-cold temperature with THF and water (2 mL, 1: 9) as the solvent. The reaction mixture was then shaken with dichloromethane (10 mL) and organic part was evaporated. The pure product was isolated through a short silica gel column with ethylacetate-hexanes (20:80) as the solvent. All physical and spectroscopy data of the compounds prepared by carbon dioxide-mediated method were identical with the reported data [4].

Conclusion

Synthesis of pyrrole derivatives through carbon dioxide-mediated reaction is new and novel. The method has significant potential to generate other heterocycles with simple to complex structures.

References

1. Juselius J, Sundholm D (2000) The aromatic pathway of porphines, chlorins and bacteriochlorins. *Phys. Chem. Chem. Phys.* 2(10): 2145.
2. (a) Gilchrist, TLJ (1998) *J. Chem. Soc. Perkin Trans 1*, 615. (b) Furstner, A, Weintritt, H and A. Hupperts, A (1995) *J. Org. Chem.* 60, 6637. (c) Periasamy, M, Srinivas, G and Bharati, PJ (1999) *J. Org. Chem.* 64, 4204
3. (a) Banik, BK, Samajdar, S and Banik, I (2004) Simple Synthesis of Substituted Pyrroles, *J. Org. Chem.* 69: 213. (b) Banik, BK, Banik, I, Renteria, M and Dasgupta, S (2005) Bismuth Nitrate-Catalyzed Straightforward Synthesis of Pyrroles, *Tetrahedron Lett.* 46: 2643.
4. Banik, BK, Samajdar, S and Banik, I. Simple Synthesis of Substituted Pyrroles (2004) *J. Org. Chem.* 69, 213.

Received on June 8, 2017.