

SYNLETT Spotlight 387

Phenylglyoxal

Compiled by Ali Akbari

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Ali Akbari was born in 1981 in Naghadeh, Iran. He received his B.Sc. degree in applied chemistry from the Tabriz University in 2005 and completed his master program in the field of organic chemistry at the Chemistry and Chemical Engineering Research Center of Iran (CCERCI) in 2009. Since then he has been working in the group of Dr. Eftekhari-Sis as a research assistant at the University of Maragheh. His research interests focus on the use of phenylglyoxal in synthetic heterocyclic chemistry.

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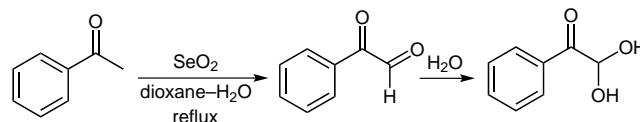
Dedicated to my parents and my research supervisor Dr. Bagher Eftekhari-Sis.



Introduction

Phenylglyoxal is a yellow liquid that polymerized on standing which stored as monohydrate form ($\text{PhCOCHO}\cdot\text{H}_2\text{O}$), a white crystalline solid with a melting point of 77 °C. It can be prepared via different procedures,^{1,2} but the most popular method for synthesis of phenylglyoxal is the oxidation of acetophenone with selenium dioxide³ (Scheme 1). Because phenylglyoxal contains both an aldehyde and ketone functional group it is useful in both organic and biological chemistry. As a versatile reagent, it has been used extensively in synthesizing a broad range of N-heterocyclic compounds with biological and pharmaceutical activities. The aldehyde and ke-

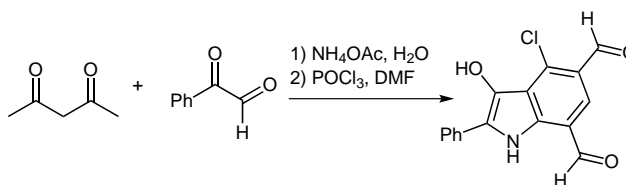
tone functional group of phenylglyoxal can be converted into other useful groups such as hydroxyl, carboxylic acid and ester which are more attractive groups in organic synthetic chemistry. Phenylglyoxal has also many indispensable roles in biological chemistry. As a reagent, it is useful for the chemical modification of arginine residues in proteins. It reacts with the guanidino group of the arginine residue under mild conditions.⁴



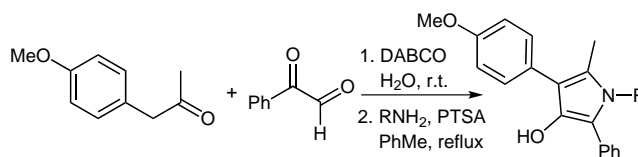
Scheme 1 Preparation of phenylglyoxal monohydrate

Abstracts

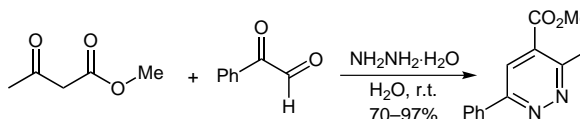
(A) Eftekhari-Sis et al. reported the synthesis of novel 2-aryl-4-chloro-3-hydroxy-1*H*-indole-5,7-dicarbaldehydes via Vilsmeier–Haack reaction starting from phenylglyoxal.⁵



(B) To the best of our knowledge, there are no reports in the literature for the formation of pyrrole-3-ol derivatives via condensation of ketones with phenylglyoxal. In this paper, a simple method for the synthesis of new *N*-alkyl(aryl)-2,4-diaryl-1*H*-pyrrole-3-ol derivatives via aldol reaction of 1-(4-methoxyphenyl)propan-2-one with phenylglyoxal in the presence of a catalytic amount of DABCO, followed by Paal–Knorr cyclization with primary amines is described.⁶



(C) For the first time, Khalafy and Rimaz⁷ have reported the synthesis of pyridazines via condensation of phenylglyoxal with β -keto esters in the presence of an excess amount of hydrazine hydrate in 70–97% yield.



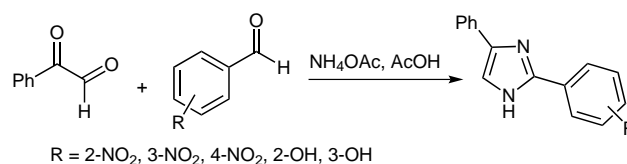
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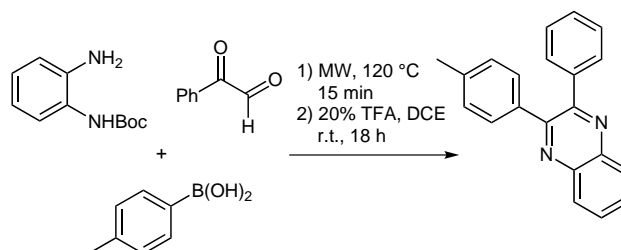
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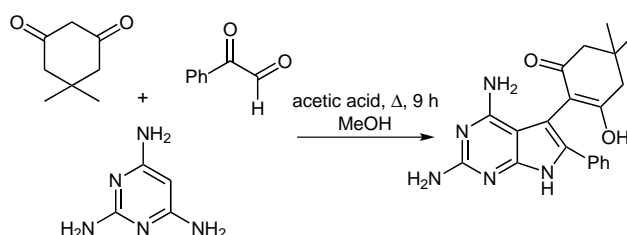
(D) Disubstituted imidazoles were prepared by reacting phenylglyoxal with different aryl aldehydes in the presence of ammonium acetate. The compounds showed good anti-inflammatory activities in carrageenan-induced rat paw edema test with very low ulcerogenic activity. Fair number of compounds were found to have significant antimicrobial activity especially against fungal species.⁸



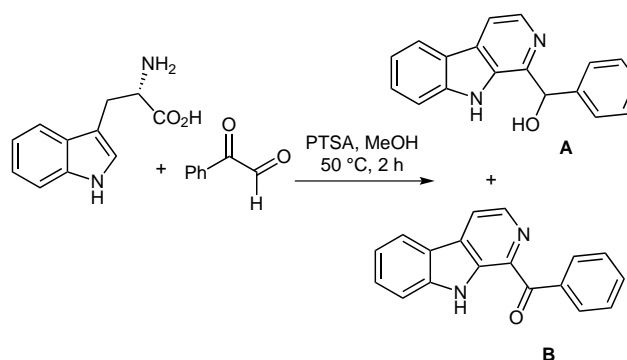
(E) M. Ayaz et al.⁹ used phenylglyoxal in a Petasis reaction in order to synthesize quinoxalines, which exhibit a large variety of biological activities such as antibacterial, antimalarial, antifungal, and anti-thrombotic activity.



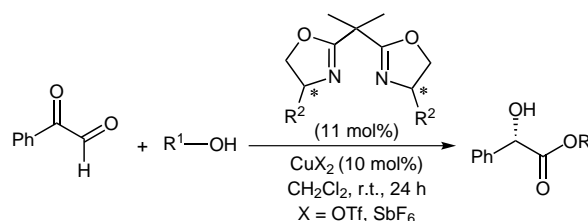
(F) Phenylglyoxal was used in a simple, practical, and a very regioselective three-component one-step procedure with 6-aminopyrimidines and dimedone for the preparation of a novel pyrrolo[2,3-*d*]pyrimidine ring system, a common motif in several natural products and biologically active molecules.¹⁰



(G) A Pictet–Spengler reaction for the synthesis of 1-substituted β-carboline has been developed. Products **A** and **B** were synthesized via a reaction between phenylglyoxal and L-tryptophan in 45% and 35% yield, respectively.¹¹



(H) Ishihara and co-workers have reported a CuX₂-catalyzed enantioselective intramolecular Cannizzaro reaction of phenylglyoxal. They have also found that the use of phenylglyoxal provides a solution to the problem of low reactivity in the asymmetric intramolecular Cannizzaro reaction with alcohols.¹²



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