Bioorganic Chemistry 75 (2017) 406–423

Contents lists available at ScienceDirect

Bioorganic Chemistry

journal homepage: www.elsevier.com/locate/bioorg

Reviews

Synthetic and medicinal perspective of thiazolidinones: A review

Sundeep Kaur Manjal [a], Ramandeep Kaur [a], Rohit Bhatia [a], Kapil Kumar [a], Virender Singh [b], Ravi Shankar [c], Rupinder Kaur [a], Ravindra K. Rawal [a,*]

[a] Department of Pharmaceutical Chemistry, Indo-Soviet Friendship College of Pharmacy (ISFCP), Moga Punjab-142001, India
[b] Department of Chemistry, National Institute of Technology (NIT) Jalandhar, 144011 Punjab, India
[c] Bio-Organic Chemistry Division, Indian Institute of Integrative Medicine (CSIR), Jammu 180001, India

ARTICLE INFO

Article history:
Received 6 April 2017
Revised 29 September 2017
Accepted 22 October 2017
Available online 23 October 2017

Keywords:
Thiazolidinones
Thiazolidine-2
4-dione
Antifungal
Anti-HIV
Anticancer
Rhodanines

ABSTRACT

In the modern scenario, thiazolidinone scaffold has emerged as a very potent scaffold as per its clinical significance concerned. It has attracted the keen interest of the researchers due to its great diversity in biological activities. Thiazolidinones are the saturated form of thiazole, called thiazolidine with a carbonyl group. The 1,3-thiazolidin-4-ones possess wide range of pharmacological activities such as anticancer, anti-diabetic, anti-microbial, anti-viral, anti-inflammatory and anti-convulsant. In the past few years, various newer synthetic approaches have been designed to synthesize diverse scaffolds to explore the various types of biological activities. In this review, an attempt has been made by the authors to summarize various synthetic strategies for thiazolidinone derivatives as well as their biological significance.

Contents

* Corresponding author.
E-mail address: rawal.ravindra@gmail.com (R.K. Rawal).

https://doi.org/10.1016/j.bioorg.2017.10.014
0045-2068/

1. Introduction

Heterocyclic compounds are the important part of the chemical and life sciences. Heterocyclic compounds have crucial role in our biological system. Heterocyclic compounds are also present in large diversity of drug candidates like antibiotic, anti-tumor, anti-inflamatory, antiviral, antimicrobial, antifungal and antidiabetic. Thiazolidinone is a very potent heterocyclic ring due to its varied biological activities. This nucleus is continuously being explored to design and synthesize novel compounds. Thiazolidine is the tetrahydro derivative of thiazole and oxo derivative which is known as thiazolidinone. A large number of substitutions are possible on the 2, 3 and 5-positions which lead to change in the properties of compounds. Variations in the substituents attached to the nitrogen atom and the methylene carbon atom are also possible to design new derivatives. The carbonyl group of 4-thiazolidinone is highly unreactive [1]. Thiazolidine 2,4-dione is widely used for designing novel anti-diabetic drugs. This scaffold exhibits a number of activities such as anti-diabetic, anti-cancer, anti-arthritic, anti-inflammatory, anti-microbial and anti-melanoma [2]. Among all of these, anti-diabetic activity has been widely carried out and a significant number of drugs are already available in the market such as rosiglitazone, pioglitazone, lobeglitazone and troglitazone. These drugs act as hypoglycemic agents by acting upon peroxisome proliferator activity receptor γ (PPARγ) [3]. The other targets reported in literature where thiazolidinones bind to exhibit different biological activities such as aldose reductase (ALR2), phosphoinositide 3-kinases (PI3Ks), mitogen activated protein kinase (MEK), pim kinase, protein tyrosine phosphatase 1B (PTP1B), cyclooxygenase-2 (COX-2), UDP-*N*-acetylmuramoylalanine D-glutamate ligase (MurD ligase), histone deacetylase (HDAC) and tyrosinases [4]. In the present review, various synthetic strategies for synthesis of thiazolidinone derivatives have been discussed with an emphasis on diverse pharmacological properties associated with substituted thiazolidinones and structurally related thiazolidines (see Fig. 1).

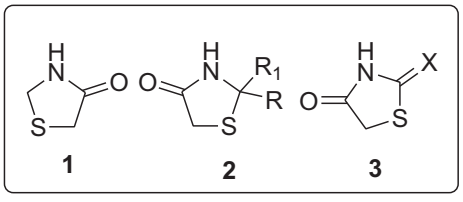


Fig. 1. Different types of substituted thiazolidinones (X = O, S).

2. Synthetic strategies

The synthesis of thiazolidine-2,4-dione derivatives has been carried out by using different methods. Depending upon their substitution, their synthesis is categorized as:

2.1. Synthesis of thiazolidine-2,4-diones (TZD)

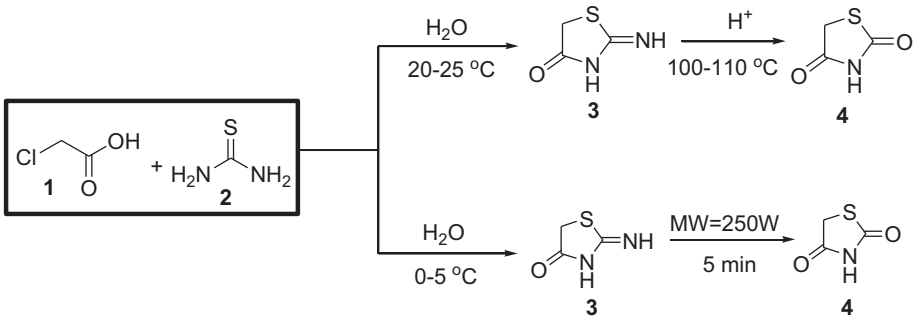
The synthesis of thiazolidine-2,4-dione utilizes α-chloroacetic acid **1** and thiourea **2** as the starting material. This method includes the refluxing of α-chloroacetic acid **1** with thiourea **2** to give thiazolidine-2,4-diones (TZD) **4** as shown in Scheme 1. This reaction can be further facilitated by performing the same reaction initially under cold conditions and then irradiated with microwave to afford TZD **4** (Scheme 1) [2].

2.2. Synthesis of monosubstituted thiazolidinone/thiazolidine-2,4-diones

This synthesis involves the reaction of substituted acetophenone with thiourea and iodine at 60 °C to afford the intermediate **6**, followed by the refluxing of chloroacetyl chloride in dioxane gave the respective 2-chloroacetamido substituted thiazoles **7**, which was cyclized in the presence of ammonium thiocyanate to afford 2-substituted thiazolidinone derivatives **8** (Scheme 2).

The 3-substituted thiazolidine-2,4-dione has been reported to synthesize by treatment of carbonyl sulphide **9** with primary amine **10** in the presence of potassium hydroxide (Scheme 1) to obtain alkyl thiocarbamates **11**, which is then further treated with α-haloalkanoic acid **1** and cyclized to generate corresponding 3-substituted TZD **13** (Scheme 3).

In another approach, 5-substituted dialkyl thiazolidinones have been synthesized using dialkyl substituted bromoacetic acid **14** or bromoacetyl chloride **15** as starting material. The reaction commences with the refluxing of dialkyl substituted bromoacetic acid **14** or bromoacetyl chloride **15** with thiourea in the presence of



Scheme 1. Synthesis of thiazolidine-2,4-dione using thiourea and chloroacetic acid.